tahir99

2016/2017

# Top 300 Pharmacy Drug Cards

**The best and easiest way to learn essential information about the top 300 drugs**

Jill Kolesar • Lee Vermeulen

Mc Graw Hill Education

LANGE®

https://kat.cr/user/Blink99/

# Additional Resources

**To access the additional content, included only with the purchase of** Top 300 Pharmacy Drug Cards**:**

To download the Q&A MP3 audio files to your mobile device, go to www.Top300DrugCards.com.

This page intentionally left blank

https://kat.cr/user/Blink99/

# Top 300 Pharmacy Drug Cards—2016/2017

**Jill M. Kolesar, PharmD, BCPS, FCCP**
Professor, University of Wisconsin-Madison School of Pharmacy
Director, Analytical Instrumentation Laboratory for Pharmacokinetics, Pharmacodynamics and Pharmacogenetics (3P)
University of Wisconsin Carbone Comprehensive Cancer Center Madison, Wisconsin

**Lee C. Vermeulen, RPh, MS, FCCP, FFIP**
Clinical Professor, University of Wisconsin-Madison School of Pharmacy
Director, Center for Clinical Knowledge Management, UW Health
Madison, Wisconsin

Mc Graw Hill Education

New York Chicago San Francisco Athens London Madrid Mexico City
Milan New Delhi Singapore Sydney Toronto

## Notice

Medicine is an ever-changing science. As new research and clinical experience broaden our knowledge, changes in treatment and drug therapy are required. The authors and the publisher of this work have checked with sources believed to be reliable in their efforts to provide information that is complete and generally in accord with the standards accepted at the time of publication. However, in view of the possibility of human error or changes in medical sciences, neither the authors nor the publisher nor any other party who has been involved in the preparation or publication of this work warrants that the information contained herein is in every respect accurate or complete, and they disclaim all responsibility for any errors or omissions or for the results obtained from use of the information contained in this work. Readers are encouraged to confirm the information contained herein with other sources. For example and in particular, readers are advised to check the product information sheet included in the package of each drug they plan to administer to be certain that the information contained in this work is accurate and that changes have not been made in the recommended dose or in the contraindications for administration. This recommendation is of particular importance in connection with new or infrequently used drugs.

https://kat.cr/user/Blink99/

Copyright © 2016 by McGraw-Hill Education. All rights reserved. Except as permitted under the United States Copyright Act of 1976, no part of this publication may be reproduced or distributed in any form or by any means, or stored in a database or retrieval system, without the prior written permission of the publisher, with the exception that the program listings may be entered, stored, and executed in a computer system, but they may not be reproduced for publication.

ISBN: 978-0-07-184235-8

MHID: 0-07-184235-7

The material in this eBook also appears in the print version of this title: ISBN: 978-0-07-184233-4,
MHID: 0-07-184233-0.

eBook conversion by codeMantra
Version 1.0

All trademarks are trademarks of their respective owners. Rather than put a trademark symbol after every occurrence of a trademarked name, we use names in an editorial fashion only, and to the benefit of the trademark owner, with no intention of infringement of the trademark. Where such designations appear in this book, they have been printed with initial caps.

McGraw-Hill Education eBooks are available at special quantity discounts to use as premiums and sales promotions or for use in corporate training programs. To contact a representative, please visit the Contact Us page at www.mhprofessional.com.

TERMS OF USE

This is a copyrighted work and McGraw-Hill Education and its licensors reserve all rights in and to the work. Use of this work is subject to these terms. Except as permitted under the Copyright Act of 1976 and the right to store and retrieve one copy of the work, you may not decompile, disassemble, reverse engineer, reproduce, modify, create derivative works based upon, transmit, distribute, disseminate, sell, publish or sublicense the work or any part of it without McGraw-Hill Education's prior consent. You may use the work for your own noncommercial and personal use; any other use of the work is strictly prohibited. Your right to use the work may be terminated if you fail to comply with these terms.

THE WORK IS PROVIDED "AS IS." McGRAW-HILL EDUCATION AND ITS LICENSORS MAKE NO GUARANTEES OR WARRANTIES AS TO THE ACCURACY, ADEQUACY OR COMPLETENESS OF OR RESULTS TO BE OBTAINED FROM USING THE WORK, INCLUDING ANY INFORMATION THAT CAN BE ACCESSED THROUGH THE WORK VIA HYPERLINK OR OTHERWISE, AND EXPRESSLY DISCLAIM ANY WARRANTY, EXPRESS OR IMPLIED, INCLUDING BUT NOT LIMITED TO IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. McGraw-Hill Education and its licensors do not warrant or guarantee that the functions contained in the work will meet your requirements or that its operation will be uninterrupted or error free. Neither McGraw-Hill Education nor its licensors shall be liable to you or anyone else for any inaccuracy, error or omission, regardless of cause, in the work or for any damages resulting therefrom. McGraw-Hill Education has no responsibility for the content of any information accessed through the work. Under no circumstances shall McGraw-Hill Education and/or its licensors be liable for any indirect, incidental, special, punitive, consequential or similar damages that result from the use of or inability to use the work, even if any of them has been advised of the possibility of such damages. This limitation of liability shall apply to any claim or cause whatsoever whether such claim or cause arises in contract, tort or otherwise.

This page intentionally left blank

https://kat.cr/user/Blink99/

# Contents


Contributors xv
Introduction xvii
Acknowledgments xix
Preface Card Summary xxi
Preface A: Anatomy of a Flash Card xxiii
Preface B: Weight and Measure Equivalents xxxiii
Preface C: General Content Related to All Oral Contraceptives xxxv
Preface D: General Content Related to the Treatment of Hypertension xxxix
Preface E: General Content Related to the Treatment of Hypercholesterolemia xlv
Preface F: Guide to Combination Cardiovascular Products xlix
Preface G: Guide to Combination Vaccines liii
Preface H: Guide to Cytochrome P450 (CYP) and UGT1A1 Metabolism lv
Preface I: Guide to Transporters lxi
Preface J: Drugs That Affect Cardiac Rhythm lxiii
Preface K: Drugs Affected by Gastric pH lxv
Preface L: Abbreviations lxvii

**ACYCLOVIR** 1
**ADAPALENE** 2
**ALBENDAZOLE** 3
**ALBUTEROL** 4
**ALENDRONATE** 5
**ALLOPURINOL** 6
**ALPRAZOLAM** 7
**AMITRIPTYLINE** 8
**AMLODIPINE** 9
**AMOXICILLIN** 10
**AMOXICILLIN/CLAVULANATE** 11
**ANASTROZOLE** 12
**ARIPIPRAZOLE** 13
**ATAZANAVIR** 14
**ATENOLOL** 15
**ATOMOXETINE** 16
**ATORVASTATIN** 17
**AZELASTINE** 18
**AZITHROMYCIN** 19
**BACLOFEN** 20
**BENAZEPRIL** 21
**BENZONATATE** 22
**BENZTROPINE** 23
**BIMATOPROST** 24
**BISOPROLOL** 25
**BRIMONIDINE** 26
**BUDESONIDE** 27
**BUDESONIDE/FORMOTEROL** 28
**BUPRENORPHINE/NALOXONE** 29

| | |
|---|---|
| BUPROPION | 30 |
| BUSPIRONE | 31 |
| CANDESARTAN | 32 |
| CARBAMAZEPINE | 33 |
| CARBIDOPA/LEVODOPA | 34 |
| CARISOPRODOL | 35 |
| CARVEDILOL | 36 |
| CEFDINIR | 37 |
| CEFUROXIME | 38 |
| CELECOXIB | 39 |
| CEPHALEXIN | 40 |
| CETIRIZINE | 41 |
| CHLORHEXIDINE | 42 |
| CHLORTHALIDONE | 43 |
| CIPROFLOXACIN ORAL | 44 |
| CIPROFLOXACIN OTIC | 45 |
| CITALOPRAM | 46 |
| CLARITHROMYCIN | 47 |
| CLINDAMYCIN ORAL | 48 |
| CLINDAMYCIN TOPICAL | 49 |
| CLOBAZAM | 50 |
| CLOBETASOL | 51 |
| CLONAZEPAM | 52 |
| CLONIDINE | 53 |
| CLOPIDOGREL | 54 |
| CLOTRIMAZOLE/BETAMETHASONE | 55 |
| CODEINE | 56 |
| COLCHICINE | 57 |
| COLESEVELAM | 58 |
| CONJUGATED ESTROGENS | 59 |
| CYANOCOBALAMIN | 60 |
| CYCLOBENZAPRINE | 61 |
| CYCLOSPORINE OPHTHALMIC | 62 |
| DABIGATRAN | 63 |
| DARBEPOETIN | 64 |
| DARIFENACIN | 65 |
| DESVENLAFAXINE | 66 |
| DEXAMETHASONE ORAL | 67 |
| DEXLANSOPRAZOLE | 68 |
| DEXMETHYLPHENIDATE | 69 |
| DIAZEPAM | 70 |
| DICLOFENAC | 71 |
| DICYCLOMINE | 72 |
| DIGOXIN | 73 |
| DILTIAZEM | 74 |
| DIPHENOXYLATE/ATROPINE | 75 |




https://kat.cr/user/Blink99/

| | |
|---|---|
| DIPHTHERIA TOXOID | 76 |
| DIPYRIDAMOLE | 77 |
| DIVALPROEX | 78 |
| DONEPEZIL | 79 |
| DOXAZOSIN | 80 |
| DOXEPIN | 81 |
| DOXYCYCLINE | 82 |
| DULOXETINE | 83 |
| DUTASTERIDE | 84 |
| EFAVIRENZ | 85 |
| ELETRIPTAN | 86 |
| EMTRICITABINE/TENOFOVIR | 87 |
| ENALAPRIL | 88 |
| ENOXAPARIN | 89 |
| ENTECAVIR | 90 |
| EPINEPHRINE | 91 |
| EPOETIN | 92 |
| ESCITALOPRAM | 93 |
| ESOMEPRAZOLE | 94 |
| ESTRADIOL ORAL | 95 |
| ESTRADIOL TRANSDERMAL PATCH | 96 |
| ESZOPICLONE | 97 |
| ETHINYL ESTRADIOL AND ETONOGESTREL RING | 98 |
| EXENATIDE | 99 |
| EZETIMIBE | 100 |
| FAMOTIDINE | 101 |
| FEBUXOSTAT | 102 |
| FELODIPINE | 103 |
| FENOFIBRATE | 104 |
| FENTANYL TRANSDERMAL | 105 |
| FEXOFENADINE | 106 |
| FIDAXOMICIN | 107 |
| FINASTERIDE | 108 |
| FLUCONAZOLE | 109 |
| FLUOCINONIDE TOPICAL | 110 |
| FLUOXETINE | 111 |
| FLUTICASONE NASAL INHALER | 112 |
| FLUTICASONE ORAL INHALER | 113 |
| FLUTICASONE/SALMETEROL | 114 |
| FOLIC ACID | 115 |
| FOSINOPRIL | 116 |
| FUROSEMIDE | 117 |
| GABAPENTIN | 118 |
| GATIFLOXACIN OPHTHALMIC | 119 |
| GEMFIBROZIL | 120 |
| GLIMEPIRIDE | 121 |
| GLIPIZIDE | 122 |
| HAEMOPHILUS INFLUENZAE, TYPE B, CONJUGATE | 123 |

HEPATITIS A VACCINE, INACTIVATED 124
HEPATITIS B VACCINE, RECOMBINANT 125
HUMAN PAPILLOMAVIRUS VACCINE 126
HYDRALAZINE 127
HYDROCHLOROTHIAZIDE 128
HYDROCODONE 129
HYDROCORTISONE TOPICAL 130
HYDROXYCHLOROQUINE 131
HYDROXYZINE 132
IBANDRONATE 133
IBUPROFEN 134
IMIQUIMOD 135
INDOMETHACIN 136
INFLUENZA VIRUS VACCINE, INACTIVATED 137
INFLUENZA VIRUS VACCINE, LIVE 138
INSULIN 139
INSULIN ASPART 140
INSULIN DETEMIR 141
INSULIN GLARGINE 142
INSULIN LISPRO 143
IPRATROPIUM/ALBUTEROL 144
IRBESARTAN 145
ISOSORBIDE MONONITRATE 146
KETOCONAZOLE TOPICAL 147
LABETALOL 148
LACOSAMIDE 149
LAMOTRIGINE 150
LANSOPRAZOLE 151
LATANOPROST 152
LEVALBUTEROL 153
LEVETIRACETAM 154
LEVOCETIRIZINE 155
LEVOFLOXACIN 156
LEVOTHYROXINE 157
LIDOCAINE TOPICAL PATCH 158
LINAGLIPTIN 159
LIRAGLUTIDE 160
LISDEXAMFETAMINE 161
LISINOPRIL 162
LITHIUM CARBONATE 163
LORAZEPAM 164
LOSARTAN 165
LOTEPREDNOL 166
LOVASTATIN 167
LUBIPROSTONE 168
MARAVIROC 169




https://kat.cr/user/Blink99/

| | |
|---|---|
| MEASLES, MUMPS, RUBELLA VACCINE, LIVE | 170 |
| MECLIZINE | 171 |
| MEDROXYPROGESTERONE | 172 |
| MELOXICAM | 173 |
| MEMANTINE | 174 |
| MENINGOCOCCAL VACCINE | 175 |
| METAXALONE | 176 |
| METFORMIN | 177 |
| METHADONE | 178 |
| METHOCARBAMOL | 179 |
| METHOTREXATE | 180 |
| METHYLPHENIDATE | 181 |
| METHYLPREDNISOLONE | 182 |
| METOCLOPRAMIDE | 183 |
| METOPROLOL | 184 |
| METRONIDAZOLE | 185 |
| MINOCYCLINE | 186 |
| MIRTAZAPINE | 187 |
| MODAFINIL | 188 |
| MOMETASONE NASAL | 189 |
| MONTELUKAST | 190 |
| MORPHINE ER | 191 |
| MOXIFLOXACIN | 192 |
| MOXIFLOXACIN OPHTHALMIC | 193 |
| MUPIROCIN | 194 |
| NAPROXEN | 195 |
| NEBIVOLOL | 196 |
| NIACIN | 197 |
| NIFEDIPINE | 198 |
| NITAZOXANIDE | 199 |
| NITROFURANTOIN | 200 |
| NITROGLYCERIN | 201 |
| NORTRIPTYLINE | 202 |
| NYSTATIN SYSTEMIC | 203 |
| NYSTATIN TOPICAL | 204 |
| OLANZAPINE | 205 |
| OLMESARTAN | 206 |
| OLOPATADINE | 207 |
| OMEGA-3-ACID ETHYL ESTERS | 208 |
| OMEPRAZOLE | 209 |
| ONDANSETRON | 210 |
| ORAL CONTRACEPTIVE—BIPHASIC | 211 |
| ORAL CONTRACEPTIVE—MONOPHASIC | 212 |
| ORAL CONTRACEPTIVE—TRIPHASIC | 213 |
| OSELTAMIVIR | 214 |
| OXCARBAZEPINE | 215 |
| OXYBUTYNIN | 216 |
| OXYCODONE | 217 |

| | |
|---|---|
| PANTOPRAZOLE | 218 |
| PAROXETINE | 219 |
| PENICILLIN | 220 |
| PENTOSAN | 221 |
| PERTUSSIS VACCINE, ACELLULAR | 222 |
| PHENAZOPYRIDINE | 223 |
| PHENOBARBITAL | 224 |
| PHENTERMINE | 225 |
| PHENYTOIN | 226 |
| PIOGLITAZONE | 227 |
| PNEUMOCOCCAL VACCINE | 228 |
| POLIOVIRUS VACCINE, INACTIVATED | 229 |
| POLYETHYLENE GLYCOL | 230 |
| POTASSIUM CHLORIDE | 231 |
| POTASSIUM IODIDE | 231 |
| PRAMIPEXOLE | 233 |
| PRASUGREL | 234 |
| PRAVASTATIN | 235 |
| PREDNISOLONE ORAL | 236 |
| PREDNISONE | 237 |
| PREGABALIN | 238 |
| PRENATAL VITAMIN | 239 |
| PROCHLORPERAZINE | 240 |
| PROGESTERONE | 241 |
| PROMETHAZINE | 242 |
| PROPRANOLOL | 243 |
| QUETIAPINE | 244 |
| QUINAPRIL | 245 |
| RABEPRAZOLE | 246 |
| RALOXIFENE | 247 |
| RALTEGRAVIR | 248 |
| RAMIPRIL | 249 |
| RANITIDINE | 250 |
| RANOLAZINE | 251 |
| REPAGLINIDE | 252 |
| RISEDRONATE | 253 |
| RISPERIDONE | 254 |
| RIVAROXABAN | 255 |
| ROPINIROLE | 256 |
| ROSIGLITAZONE | 257 |
| ROSUVASTATIN | 258 |
| ROTAVIRUS VACCINE, LIVE | 259 |
| SAXAGLIPTIN | 260 |
| SERTRALINE | 261 |
| SILDENAFIL | 262 |
| SIMVASTATIN | 263 |




https://kat.cr/user/Blink99/

| | |
|---|---|
| SITAGLIPTIN | 264 |
| SOLIFENACIN | 265 |
| SPIRONOLACTONE | 266 |
| SUMATRIPTAN | 267 |
| TACROLIMUS | 268 |
| TADALAFIL | 269 |
| TAMSULOSIN | 270 |
| TEMAZEPAM | 271 |
| TERAZOSIN | 272 |
| TERBINAFINE | 273 |
| TESTOSTERONE | 274 |
| TETANUS TOXOID | 275 |
| THYROID | 276 |
| TIOTROPIUM | 277 |
| TIZANIDINE | 278 |
| TOLTERODINE | 279 |
| TOLVAPTAN | 280 |
| TOPIRAMATE | 281 |
| TRAMADOL | 282 |
| TRAVOPROST | 283 |
| TRAZODONE | 284 |
| TRIAMCINOLONE NASAL | 285 |
| TRIAMCINOLONE TOPICAL | 286 |
| TRIAMTERENE/HYDROCHLOROTHIAZIDE | 287 |
| TRIMETHOPRIM (TMP)/SULFAMETHOXAZOLE (SMZ) | 288 |
| VALACYCLOVIR | 289 |
| VALSARTAN | 290 |
| VARDENAFIL | 291 |
| VARENICLINE | 292 |
| VARICELLA VACCINE, LIVE | 293 |
| VENLAFAXINE | 294 |
| VERAPAMIL | 295 |
| VILAZODONE | 296 |
| WARFARIN | 297 |
| ZIPRASIDONE | 298 |
| ZOLPIDEM | 299 |
| ZOSTER VACCINE, LIVE | 300 |

This page intentionally left blank

https://kat.cr/user/Blink99/

# Contributors


**Editors**
Jill M. Kolesar, PharmD, BCPS, FCCP
Professor, University of Wisconsin-Madison School of Pharmacy
Director, Analytical Instrumentation Laboratory for Pharmacokinetics, Pharmacodynamics and Pharmacogenetics (3P)
University of Wisconsin Carbone Comprehensive Cancer Center
Madison, Wisconsin

**Contributing Editor**
Karen J. Kopacek, RPh
Associate Professor (CHS), Associate Dean for Student Affairs
University of Wisconsin-Madison School of Pharmacy
Madison, Wisconsin

**Faculty Advisory Panel**
Trisha N. Branan, PharmD, BCPS
Clinical Assistant Professor
University of Georgia College of Pharmacy
Critical Care Clinical Pharmacist
Athens Regional Medical Center
Athens, Georgia

Fred Doloresco, PharmD, MS
Clinical Assistant Professor
University at Buffalo
Consultant Pharmacist
Erie County Medical Center
Buffalo, New York

Rachel Eyler, PharmD, BCPS
Assistant Clinical Professor
University of Connecticut
Storrs, Connecticut

Alex N. Isaacs, PharmD, BCPS
Clinical Assistant Professor
Purdue University College of Pharmacy
Clinical Pharmacist—Internal Medicine
Eskenazi Health
Indianapolis, Indiana

Lee C. Vermeulen, RPh, MS, FCCP, FFIP
Clinical Professor, University of Wisconsin-Madison School of Pharmacy
Director, Center for Clinical Knowledge Management
UW Health
Madison, Wisconsin

**Author—Vaccine Content**
Mary S. Hayney, PharmD, MPH, FCCP, BCPS
Professor of Pharmacy (CHS)
University of Wisconsin-Madison School of Pharmacy
Madison, Wisconsin

Emily N. Israel, PharmD, BCPS
Clinical Assistant Professor
Purdue University College of Pharmacy
Clinical Pharmacy Specialist
Riley Hospital for Children
Indianapolis, Indiana

Amanda Peters Johnson, PharmD
Clinical Instructor
UNC Eshelman School of Pharmacy
Chapel Hill, North Carolina

Nicholas Messinger, PharmD, BCPS, BCACP
Assistant Professor of Pharmacy Practice and Administrative Sciences
University of Cincinnati James L. Winkle College of Pharmacy
Cincinnati, Ohio

Andrea L. Porter, PharmD
Assistant Professor
University of Wisconsin School of Pharmacy
Clinical Pharmacy Specialist
William S. Middleton Memorial Veterans Hospital
Madison, Wisconsin

Brian A. Potoski, PharmD, BCPS (AQ-ID)
Associate Professor
University of Pittsburgh School of Pharmacy
Associate Director, Antibiotic Management Program
University of Pittsburgh Medical Center, Presbyterian Hospital
Pittsburgh, Pennsylvania

Jennifer Pruskowski, PharmD, BCPS, CGP
Assistant Professor, Department of Pharmacy and Therapeutics
University of Pittsburgh School of Pharmacy
Palliative Care Clinical Pharmacy Specialist
UPMC Palliative Supportive Institute
Pittsburgh, Pennsylvania

Stacey Schneider, PharmD
Associate Professor of Pharmacy Practice
Northeast Ohio Medical University
MTM Services Manager
Giant Eagle Pharmacy
Rootstown, Ohio

Sachin Shah, PharmD, BCOP, FCCP
Texas Tech University HSC—School Of Pharmacy
Advanced Hematology/Oncology Clinical Pharmacist
Dallas VA Medical Center
Dallas, Texas

Nicole Rockich Winston, MS, PharmD
Assistant Professor of Pharmacy Practice
Marshall University School of Pharmacy
Huntington, West Virginia



https://kat.cr/user/Blink99/

# Introduction

The selection of the most commonly prescribed medications was based on a number of reports evaluating medication use based on the number of prescriptions filled in the United States and the cost of those prescriptions.[1-3] Most estimates rely on data from IMS Health, using data from their National Prescription Audit. In addition to these sources, additional information was drawn from a wide range of professional journals to select the most relevant medications to include in this set of cards. Information on medication safety was drawn from multiple sources, but relied on a number of documents maintained by the Institute for Safe Medication Practices (ISMP), which can be found at www.ismp.org. Photographs were taken by the editors at the University of Wisconsin Hospital and Clinics pharmacies, as well as at Target Pharmacy in Madison, Wisconsin. Products with generic versions available in the US market have a representative generic product pictured. Brand name products are generally pictured if a generic version is not yet available in the United States.

It should be noted that these cards include multiple agents in some drug classes, and the information on those cards is very similar. While redundancy is considered a flaw in textbooks and other educational material, repeating information in these crowded classes of drugs is essential for the successful use of flash cards as a learning tool.


1. Brooks M. Top 100 Selling Drugs of 2013. 2014, Jan 30. Medscape. Available at http://www.medscape.com/viewarticle/820011#1. Accessed November 29, 2014.

2. Barthalow M. Top drugs of 2013. *Drug Topics*. Available at http://www.pharmacytimes.com/publications/issue/2014/July2014/Top-Drugs-of-2013. Accessed November 29, 2014.

3. Schumock GT, Li EC, Suda KJ, Matusiak LM, Hunkler RJ, Vermeulen LC, Hoffman JM. National trends in prescription drug expenditures and projections for 2014. *Am J Health Syst Pharm.* 2014;71(6):482-499.

This page intentionally left blank

https://kat.cr/user/Blink99/

# Acknowledgments

The Editors acknowledge the contributions of the pharmacists at the University of Wisconsin Hospital and Clinics, particularly Joe Cesarz, PharmD and Gloria Call, PharmD, as well as Charlie Lee, RPh from Target Pharmacy, for their assistance with the development of these cards. Pharmacy students Aleta Smithbauer, Nicolette Bonamase, and Marissa Cullen from Northeast Ohio Medical University also contributed.

This page intentionally left blank

https://kat.cr/user/Blink99/

# Preface Card Summary

1. Preface A: Anatomy of a Flash Card
2. Preface B: Weight and Measure Equivalents
3. Preface C: General Content Related to All Oral Contraceptives
4. Preface D: General Content Related to the Treatment of Hypertension
5. Preface E: General Content Related to the Treatment of Hypercholesterolemia
6. Preface F: Guide to Combination Cardiovascular Products
7. Preface G: Guide to Combination Vaccines
8. Preface H: Guide to Cytochrome P450 (CYP) and UGT1A1 Metabolism
9. Preface I: Guide to Transporters
10. Preface J: Drugs That Affect Cardiac Rhythm
11. Preface K: Drugs Affected by Gastric pH
12. Preface L: Abbreviations

This page intentionally left blank

https://kat.cr/user/Blink99/

# Preface A: Anatomy of a Flash Card

## Medication Name

Both generic and common brand names are listed.

## Class

Medications are grouped into classes ("families") based on their chemical, pharmacological, or clinical properties. It is often useful to study medications on a class-by-class basis, identifying similarities and differences among members of each class.

## Controlled Substance Schedule

Title 21 of the United States Code (USC) is the Controlled Substances Act of 1970. It regulates medications with potential for abuse. These Federal regulations are overseen by the Drug Enforcement Administration, but many States have enacted more strict regulations based on them. Medications are placed into schedules based on their clinical use and their risk of abuse and dependence. It is important to note that some States change the Federal scheduling of certain medications. Under Federal law, a State cannot place a medication in a lower schedule than where it is placed by the Federal government (eg, States cannot change a drug placed in Federal Schedule II to Schedule III, IV, or V), but States can and do place certain medications in higher schedules (eg, changing a drug placed in Federal Schedule V into Schedule II, III, or IV, or changing a drug which is not a controlled substance under Federal law into a controlled substance within that State).

- *Schedule I:* No medical use, high abuse, and dependence potential.
- *Schedule II:* Legitimate medical use, high abuse, and dependence potential.
- *Schedule III:* Legitimate medical use, abuse, and dependence potential somewhat less than Schedule II.
- *Schedule IV:* Legitimate medical use, abuse, and dependence potential less than Schedule III.
- *Schedule V:* Legitimate medical use, limited abuse, and dependence potential.

## Dosage Forms

The most common dosage forms and strengths are listed. Other dosage forms may exist, and may be referenced in the Clinical Pearls section.

## Common FDA Label Indication, Dosing, and Titration

The US Food and Drug Administration (FDA) approves medications for market, and also approves specific indications for use and the doses for those uses. Some medications are approved for only one indication, while others are approved for many indications. In most cases, all FDA-approved ("labeled") indications are listed with their approved doses.

## Off-Label Uses

While every medication must be approved by the FDA for at least one indication before it is marketed, FDA approval is not always sought for subsequent indications. Prescribers are legally entitled to prescribe medications for any indication they feel is appropriate and clinically justified. In most cases, prescribers limit their use of medications to indications for which evidence supports safety and efficacy, as demonstrated in published clinical trials. While these may not be FDA-approved indications, "off-label" use is common and often completely appropriate. Common off-label uses are included, along with dosing recommendations.

## MOA (Mechanism of Action)

The MOA is a succinct summary of the pharmacological properties of each medication.

## Drug Characteristics

Each card includes a table summarizing key drug parameters, as outlined below.

*Dose Adjustments Hepatic*

A Child-Pugh Score can be used to assess hepatic dysfunction. The score employs five clinical measures of liver disease. Each is scored 1-3, with 3 indicating the most severe derangement of that measure. Based on the number of points for each measure, liver disease can be classified into Child-Pugh class A, B, or C.



https://kat.cr/user/Blink99/

| Measure | 1 Point | 2 Points | 3 Points |
|---|---|---|---|
| Total bilirubin, mg/dL | <2 | 2-3 | >3 |
| Serum albumin, g/L | >35 | 28-35 | <28 |
| INR | <1.7 | 1.71-2.20 | >2.20 |
| Ascites | None | Mild | Severe |
| Hepatic encephalopathy | None | Grade I-II | Grade III-IV |

| Points | Class | One-Year Survival | Two-Year Survival | Liver Dysfunction |
|---|---|---|---|---|
| 5-6 | A | 100% | 85% | Mild |
| 7-9 | B | 81% | 57% | Moderate |
| 10-15 | C | 45% | 35% | Severe |

*Dose Adjustments Renal*

Dose adjustments for some (but not all) of medications that are renally eliminated are necessary in patients with renal dysfunction and hepatically eliminated medications in patients with hepatic dysfunction. Dose adjustments are made by either lowering the dose or dosing less frequently (eg, reducing from tid to daily dosing). The degree of renal dysfunction usually determines the degree of the dose adjustment. Definitions of renal and hepatic dysfunction are often inconsistent, but the recommended dose adjustments included in these flash cards are drawn from product package inserts and other sources. Clinicians should always exercise caution when treating patients with liver and/or kidney disease, and monitor carefully for signs of toxicity, even if dose adjustments are made.

In general, CrCl is used to assess renal function and is calculated with the following equations:

**Cockcroft and Gault Equation:**
CrCl (males) = [(140 – age) × IBW]/(Scr × 72)
CrCl (females) = [(140 – age) × IBW]/(Scr × 72) × (0.85)

**Estimate Ideal Body Weight in (kg):**
Males: IBW = 50 kg + 2.3 kg for each inch over 5 ft
Females: IBW = 45.5 kg + 2.3 kg for each inch over 5 ft

**Normal Renal Function:** CrCl = 50 mL/min or greater
**Moderate Renal Impairment:** CrCl = 30-50 mL/min
**Severe Renal Impairment:** CrCl =10-29 mL/min
**Renal Failure:** CrCl = 9 mL/min or less

*Dialyzable*

Medications may be removed by peritoneal or hemodialysis, requiring dose adjustments and/or redosing after dialysis to replace drug lost. Many references provide details regarding the dialyzability of drugs, and these cards provide basic adjustment recommendations.

*Pregnancy Category*

The FDA rates and categorizes medications based on the level of risk of fetal harm that medications pose when taken by pregnant women. While these categories are discrete, it is important to recognize that they are sometimes set on the basis of theoretical risks. Clinical decisions must be made individually, weighing the potential risk to both the pregnant woman and the fetus. The pregnancy category of each medication is provided.

- *Category A:* Adequate and well-controlled studies have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no evidence of risk in later trimesters).
- *Category B:* Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women.



https://kat.cr/user/Blink99/

- *Category C:* Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
- *Category D:* There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.
- *Category X:* Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.

For several years, the FDA has considered changes to the pregnancy and lactation risk rating systems, and while the old systems remains in place at the time these cards are being edited, they may change before the next edition is published. Information about the change can be found at the FDA web site, and excellent information about this situation can be found in these two papers: Ramoz LL, Patel-Shori, NM. Recent changes in pregnancy and lactation labeling: Retirement of risk categories. *Pharmacotherapy* 2014;34(4):389-395, and Singh A, Hughes GJ, Mazzola, N. New changes in pregnancy and lactation labeling. *US Pharm.* 2014;39(10):40-43.

*Lactation*

As with pregnancy categories, relatively little evidence is available to guide clinical decision making regarding the use of medications in women who are breast-feeding. In most cases, the risks to the child must be weighed against the benefits to the breast-feeding mother. In general, this assessment is based on the risk that an individual medication will be expressed in breast milk, and the risk that such an expression would cause to the infant who subsequently ingests it. As noted above, the FDA is considering changes to the pregnancy and lactation systems used to describe risk. The articles cited can be reviewed for information about this pending change.

*Contraindications*

Some medications should never be used in certain circumstances or under certain conditions. These situations are known as contraindications and are usually related to common and very dangerous adverse effects that must be avoided by selecting alternative therapeutic options.

*Absorption*

Pharmacokinetic parameters related to oral bioavailability (F) and the impact of food on absorption are provided.

*Distribution*

Pharmacokinetic data on extent and nature of distribution, including volume of distribution (Vd) and the extent of protein binding, are provided.

*Metabolism*

Pharmacokinetic data on metabolic pathways, including cytochrome P450 pathway of elimination and whether a drug is an enzyme inducer or inhibitor, are provided.

*Elimination*

Pharmacokinetic data on extent of renal (or other) elimination, as well as elimination half-life, are provided.

*Pharmacogenetics*

Pharmacogenetic information is included if the drug has pharmacogenetic information in the drug label. Generally, information is provided when a patient's genetic composition can affect drug exposure and clinical response variability, risk for adverse events, genotype-specific dosing, or mechanism of drug action. A complete list of drugs with pharmacogenetic information can be found at the following web site: http://www.fda.gov/Drugs/ScienceResearch/ResearchAreas/Pharmacogenetics/ucm083378.htm.

*Black Box Warnings*

The FDA requires manufacturers to list certain significant safety-related concerns in boxed warnings in their approved product package inserts. These "black box warnings" contain critical information for the safe use of those medications. Key black box warning content is included on each card. Additional information on black box warnings can be found at the following web site: https://blackboxrx.com/app/index.

## Medication Safety Issues

Each card includes a table summarizing key medication safety concerns, as outlined as follows.



https://kat.cr/user/Blink99/

*Suffixes*

Many products are available in multiple formulations, for example, in delayed-release dosage forms. These dosage forms are often distinguished through the use of suffixes appended to the name of a different formulation of that same product. It is essential to exercise caution to avoid errors caused by confusing one product with another by omitting or not recognizing the additional suffix. Products that are available in multiple formulations, distinguished by a suffix (or occasionally, a prefix), are noted in this field.

*"Tall Man" Letters*

Many medications are spelled similarly, leading to substitution errors during prescribing, dispensing, or administration. The use of "Tall Man" lettering—distinguishing one medication from a different, similarly named medication, by capitalizing specific portions of the medication name (either brand or generic name)—has been shown to help prevent substitution errors. Those products for which Tall Man lettering is recommended are noted in this field.

*Do Not Crush*

Many solid oral dosage formulations are developed to release their active ingredient slowly over time. Crushing those dosage forms (eg, to enable administration through a nasogastric tube, or to make easier to swallow by patients with swallowing disorders) may be particularly dangerous. The formulations of certain products that should not be crushed are noted in this field. Sublingual dosage forms are meant to be dissolved under the tongue and swallowing these dosage forms without allowing them to dissolve lowers the efficacy of the drug. Some taste really bad, and patients prefer to swallow them without allowing them to dissolve.

*High Alert*

The Institute for Safe Medication Practices (ISMP) maintains a list of medications that are often involved in medication errors, or that are associated with a heightened risk of causing significant patient harm when used in error. Specific care must be exercised when prescribing, dispensing, or administering these products. More information on this field can be found at the ISMP web site at www.ismp.org.

*Confused Names*

Many medications are confused with other medications based on similarities in the spelling or pronunciation of their names, resulting in substitution errors. Those products that may be confused with different "look-alike or sound-alike" products are noted in this field.

*Beers Criteria*

The initial Beers Criteria identified medications for which risks outweigh benefits and those that should be avoided or used with caution in adults aged 65 and older. The list was first published in 1991 by Mark Beers, MD (Beers MH, Ouslander JG, Rollingher I, et al. Explicit criteria for determining inappropriate medication use in nursing home residents. *Arch Int Med.* 1991;151:1825–1832). The list has been revised several times subsequently, most recently by the American Geriatrics Society in 2012 (American Geriatrics Society 2012 Beers Criteria Update Expert Panel. American Geriatrics Society updated Beers criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2012;60:616–631). In this version of these drug cards, only warnings included in the first Table 1 of the Beers Criteria, "Agents Potentially Inappropriate Medication Use in Older Adults," have been noted. Two other tables, listing drugs to be used with caution due to drug-disease or drug-syndrome interactions and drugs to be used with caution in older adults, are also included in the Beers guideline, but have not been noted in these cards.

## Drug Interactions

Concurrent use of multiple medications (poly-pharmacy) introduces significant risks as certain drugs interact with others to create adverse effects. Many interactions are caused when one agent affects the metabolism of another, thereby either increasing the risk of toxicity (when metabolism is decreased) or decreasing efficacy (when metabolism is increased). Examples of drugs that are inhibitors or inducers of the cytochrome P450 system, or are substrates (drugs metabolized by that system), and other metabolic issues, are included in Prefaces H, I, J, and K. Other mechanisms can also result in negative outcomes. The most common interactions are listed in these cards. Note that in many cases, drugs interact in a similar way with entire classes of other drugs, and in those situations, the class of interacting agent is listed. Lists of the agents that are members of those classes are listed in other prefaces in this card set. Since some interactions are unavoidable, strategies for managing some interactions are provided.

## Adverse Reactions

Every drug is associated with potential risks. Adverse effects are evaluated based on the frequency with which they occur and the degree of severity of the reaction, if it does occur. Most medications have a few common adverse effects that may or may not be severe enough to limit the use of the medication, and a few that occur rarely, but are very serious. Common adverse



https://kat.cr/user/Blink99/

effects (that occur in >10% of patients who take the medication) and less common (that occur in 1-10% of patients) are summarized in these cards. Rare (occurring in <1% of patients) but serious adverse effects are also listed.

### Monitoring Parameters—Efficacy and Toxicity

Patients receiving medications should be monitored to ensure that the treatment is achieving its desired outcome without causing adverse effects. Specific efficacy and toxicity monitoring parameters are listed for each medication.

### Key Patient Counseling Points

In order for medications to be used effectively and safely, patients must understand their therapies. Key information that patients should be provided with is summarized for each medication.

### Clinical Pearls

Clinical information regarding the use of each medication, including place in therapy, is provided in this section. Special alerts from the FDA, which are usually related to adverse reactions that are being evaluated and have not been included in the product package insert, are included here as well.

This page intentionally left blank

https://kat.cr/user/Blink99/

# Preface B: Weight and Measure Equivalents

## Apothecary Weight Equivalents

| | |
|---|---|
| 1 scruple (℈) | = 20 grains (gr) |
| 60 grains (gr) | = 1 dram (ʒ) |
| 8 drams (ʒ) | = 1 ounce (ʒ) |
| 1 ounce (ʒ) | = 480 grains |
| 12 ounces (ʒ) | = 1 pound (lb) |

## Apothecary Volume Equivalents

| | |
|---|---|
| 60 minims (m) | = 1 fluidram (fl ʒ) |
| 8 fluidrams (fl ʒ) | = 1 fluid ounce (fl ʒ) |
| 1 fluid ounce (fl ʒ) | = 480 minims |
| 16 fluid ounces (fl ʒ) | = 1 pint (pt) |

## Avoirdupois Equivalents

| | |
|---|---|
| 1 ounce (oz) | = 437.5 grains |
| 16 ounces (oz) | = 1 pound (lb) |

## Weight/Volume Equivalents

| | |
|---|---|
| 1 mg/dL | = 10 µg/mL |
| 1 mg/dL | = 1 mg% |
| 1 ppm | = 1 mg/L |

## Conversion Equivalents

| | |
|---|---|
| 1 gram (g) | = 15.43 grains |
| 1 grain (gr) | = 64.8 milligrams |
| 1 ounce (℥) | = 31.1 grams |
| 1 ounce (oz) | = 28.35 grams |
| 1 pound (lb) | = 453.6 grams |
| 1 kilogram (kg) | = 2.2 pounds |
| 1 milliliter (mL) | = 16.23 minims |
| 1 minim (m) | = 0.06 milliliter |
| 1 fluid ounce (fl oz) | = 29.57 mL |
| 1 pint (pt) | = 473.2 mL |
| 0.1 mg | = 1/600 gr |
| 0.12 mg | = 1/500 gr |
| 0.15 mg | = 1/400 gr |
| 0.2 mg | = 1/300 gr |
| 0.3 mg | = 1/200 gr |
| 0.4 mg | = 1/150 gr |
| 0.5 mg | = 1/120 gr |
| 0.6 mg | = 1/100 gr |
| 0.8 mg | = 1/80 gr |
| 1 mg | = 1/65 gr |



https://kat.cr/user/Blink99/

# Preface C: General Content Related to All Oral Contraceptives

**MOA.** As contraceptives, estrogens suppress follicle-stimulating hormone (FSH) and luteinizing hormone (LH) to inhibit ovulation, cause edematous endometrial changes that are hostile to implantation of the fertilized ovum, accelerate ovum transport, and produce degeneration of the corpus luteum (luteolysis). Progestins inhibit ovulation by suppression of LH, inhibit sperm capacitation, slow ovum transport, produce a thinning endometrium that hampers implantation, and cause cervical mucus changes that are hostile to sperm migration.

## Pharmacokinetics of Progestins

| Agent | Absorption | Distribution | Metabolism | Elimination |
|---|---|---|---|---|
| Norgestrel | Unknown | Unknown | Unknown | Unknown |
| Norethindrone | F = 64%; food has no effect on absorption | Vd = 4 L/kg; highly protein bound | Hepatic not via CYP450 | Renal elimination with a half-life of 8 h |
| Drospirenone | F = 76-85%; food has no effect on absorption | Vd = 4.2 L/kg; highly protein bound | Hepatic not via CYP450 | Renal elimination is 38-47% with a half-life of 36-42 h |
| Desogestrel | F = Almost 100%; food has no effect on absorption | Unknown | Hepatic via CYP2C9 to active metabolite, etonogestrel | Renal elimination of etonogestrel 45% with a half-life of 37 h |
| Levonorgestrel | F = 100%; food has no effect on absorption | Vd = 1.8 L/kg; highly protein bound | Hepatic not via CYP450 | Renal elimination is 45% with a half-life of 17-27 h |

## Drug Interactions: Oral Contraceptives

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP1A2 substrates | Contraceptives inhibit CYP1A2-mediated metabolism, resulting in increased substrate concentrations and toxicity | Avoid or monitor and reduce substrate dose as needed |
| CYP2C8 substrates | Contraceptives inhibit CYP2C8-mediated metabolism, resulting in increased substrate concentrations and toxicity | Avoid or monitor and reduce substrate dose as needed |
| CYP3A4/5 inducers | Increased contraceptive metabolism reduces contraceptive effectiveness | Use an alternative form of birth control |
| CYP3A4/5 inhibitors | Decreased contraceptive metabolism increases risk of contraceptive toxicity | Monitor for toxicity and discontinue contraceptive if necessary |
| CYP3A4/5 substrates | Competitive inhibition of CYP3A4/5 metabolism of other CYP3A4/5 substrates | Monitor for adverse effects and reduce substrate dose as necessary |
| Antibiotics | Alters intestinal flora which, in turn, reduces the enterohepatic circulation of estrogen metabolites resulting in decreased efficacy of contraceptive | Use an alternative form of birth control |
| Corticosteroids | Corticosteroid metabolism inhibited by the contraceptive resulting in toxicity | Monitor for corticosteroid toxicity and reduce dose if necessary |
| Warfarin | Contraceptive may increase or decrease warfarin effectiveness; mechanism unknown | Carefully monitor INR |



https://kat.cr/user/Blink99/

## Adverse Reactions: Oral Contraceptives

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Weight change, breast tenderness, breast swelling | Bloating, nausea, stomach cramps, vomiting, depression | Arterial thromboembolism, myocardial infarction, thrombophlebitis, cerebral hemorrhage, cerebral thrombosis, pulmonary embolism, hypertension |

**Key Patient Counseling Points.** Hormonal contraceptives do not protect against HIV infection or other sexually transmitted diseases. Take this drug at approximately the same time each day. If spotting occurs and no doses have been missed, continue to take tablets even if spotting continues. Report immediately if new severe or persistent headache; blurred or loss of vision; shortness of breath; severe leg, chest, or abdominal pain; or any abnormal vaginal bleeding occur. If you miss 1 dose, take it as soon as you remember it and take the next tablet at the correct time even if you take 2 tablets on the same day or at the same time. If you miss 2 doses in week 1 or 2, take 2 tablets on the day you remember and 2 tablets the next day. If you miss 2 doses in week 3 or miss 3 or more active tablets, then (if you start on day 1) start a new pack the same day or (if you start on Sunday) take 1 tablet daily until Sunday and then start a new pack that day. Use an alternative form of contraception for the next 7 d after you miss 2 or more doses in weeks 1, 2, or 3.

**Clinical Pearls.** Patients with thrombogenic mutations (eg, factor V Leiden) should not receive oral contraceptives. The CDC provides recommendations for choice of oral contraceptives on their web site at www.cdc.gov. Age, cigarette smoking, concurrent diseases, weight, drug interactions, and reproductive status are all considered when selecting a contraceptive regimen.

This page intentionally left blank

https://kat.cr/user/Blink99/

## Blood Pressure Lowering Therapies

Complete JNC-8 guidelines available at http://jama.jamanetwork.com/article.aspx?articleid=1791497.

## Hypertension Guideline Management Algorithm

| Adults Aged ≥18 y With HTN (JNC-8) | Systolic BP Goal (mm Hg) | Diastolic BP Goal (mm Hg) | Initial Treatment Recommendation: Nonblack Patients | Initial Treatment Recommendation: Black Patients |
|---|---|---|---|---|
| Age ≥60 y without DM or CKD | <150 | <90 | LSM + thiazide-type diuretic or ACE-I or ARB or CCB, alone or in combination | LSM + thiazide-type diuretic or CCB, alone or in combination |
| Age <60 y without DM or CKD | <140 | <90 | LSM + thiazide-type diuretic or ACE-I or ARB or CCB, alone or in combination | LSM + thiazide-type diuretic or CCB, alone or in combination |
| All ages with DM and no CKD | <140 | <90 | LSM + thiazide-type diuretic or ACE-I or ARB or CCB, alone or in combination | LSM + thiazide-type diuretic or CCB, alone or in combination |
| All ages with CKD with or without DM | <140 | <90 | LSM + ACE-I or ARB, alone or in combination with other drug class | LSM + ACE-I or ARB, alone or in combination with other drug class |

ACE-I = ACE inhibitor
ARB = Angiotensin receptor blocker
BP = Blood pressure
CCB = Calcium channel blocker
CKD = Chronic kidney disease
DM = Diabetes mellitus
LSM = Lifestyle modifications, including weight reduction, limit alcohol, aerobic activity, limit sodium intake, tobacco cessation, DASH diet

## Strategies to Dose Antihypertensive Therapy

| |
|---|
| A—Start with 1 drug; titrate to maximum recommended dose to achieve goal BP. Add 2nd drug from list (thiazide-type diuretic, CCB, ACE-I, or ARB)* if goal BP not achieved after titration; titrate 2nd drug to maximum recommended dose to achieve goal BP. If goal BP not reached with 1 drugs, add 3rd agent from list and titrate to maximum recommended dose to achieve BP goal. *AVOID combination of ACE-I and ARB*. |
| B—Start with 1 drug; if goal BP not reached, add 2nd drug from list before achieving maximum recommended dose with 1st drug. Titrate both drugs to maximum recommended doses to achieve BP goal. If goal BP not reached with 2 drugs, add 3rd drug from list and titrate to maximum recommended dose to achieve BP goal. *AVOID combination of ACE-I and ARB*. |
| C—Initiate therapy with 2 drugs when SBP >160 mm Hg and/or DBP is >100 mm Hg (or if SBP >20 mm Hg and/or DBP >10 mm Hg above goal), either as 2 separate drugs or single combination tablet/capsule. If goal BP not achieved with 2 drugs, add 3rd drug from list and titrate 3rd drug to maximum recommended dose. *AVOID combination of ACE-I and ARB*. |

*List reflects those classes of antihypertensive drugs that have demonstrated improved outcomes in randomized controlled trials; drugs from other antihypertensive categories may also be considered.



https://kat.cr/user/Blink99/

## Evidence-Based Dosing for Antihypertensive Medications

| Medication | Initial Daily Dose (mg) | Number of Doses per Day | Target Dose (mg) |
|---|---|---|---|
| **ACE inhibitors** | | | |
| Captopril | 50 | 2 | 150-200 |
| Enalapril | 5 | 1-2 | 20 |
| Lisinopril | 10 | 1 | 40 |
| **Angiotensin receptor blockers** | | | |
| Candesartan | 4 | 1 | 12-32 |
| Irbesartan | 75 | 1 | 300 |
| Losartan | 50 | 1-2 | 100 |
| Valsartan | 40-80 | 1 | 160-320 |
| **Beta-blockers** | | | |
| Atenolol | 25-50 | 1 | 100 |
| Metoprolol | 50 | 1-2 | 100-200 |
| **Calcium channel blockers** | | | |
| Amlodipine | 2.5 | 1 | 10 |
| Diltiazem extended release | 120-180 | 1 | 360 |
| **Thiazide-type diuretics** | | | |
| Chlorthalidone | 12.5 | 1 | 12.5-25 |
| Hydrochlorothiazide | 12.5-25 | 1-2 | 25-50 |
| Indapamide | 1.25 | 1 | 1.25-2.5 |

## Antihypertensive Drug Classif cations

| Class | Commonly Used Drugs |
|---|---|
| ACE inhibitors | Benazepril<br>Captopril<br>Enalapril<br>Fosinopril<br>Lisinopril<br>Moexipril<br>Perindopril<br>Quinapril<br>Ramipril<br>Trandolapril |
| Aldosterone antagonists | Eplerenone<br>Spironolactone |
| $\alpha_1$-Blockers | Doxazosin<br>Prazosin<br>Terazosin |
| Angiotensin receptor blockers | Candesartan<br>Eprosartan<br>Irbesartan<br>Losartan<br>Olmesartan<br>Telmisartan<br>Valsartan |



https://kat.cr/user/Blink99/

| | |
|---|---|
| Beta-blockers: nonselective | Betaxolol<br>Nadolol<br>Propranolol<br>Propranolol long acting<br>Timolol |
| Beta-blockers: cardiac selective | Atenolol<br>Bisoprolol<br>Metoprolol succinate<br>Metoprolol tartrate<br>Nebivolol |
| Beta-blockers: intrinsic sympathomimetic activity | Acebutolol<br>Penbutolol<br>Pindolol |
| Combined alpha- and beta-blockers | Carvedilol<br>Labetalol |
| Calcium channel blockers: dihydropyridines | Amlodipine<br>Felodipine<br>Isradipine<br>Nicardipine sustained release<br>Nifedipine sustained release<br>Nisoldipine |
| Calcium channel blockers: non-dihydropyridines | Diltiazem extended release<br>Verapamil<br>Verapamil long acting |

| | |
|---|---|
| Centrally acting agents | Clonidine<br>Clonidine patch<br>Guanfacine<br>Methyldopa<br>Reserpine |
| Direct renin inhibitor | Aliskiren |
| Direct vasodilators | Hydralazine<br>Minoxidil |
| Diuretics: thiazides | Chlorothiazide<br>Chlorthalidone<br>Hydrochlorothiazide<br>Indapamide<br>Metolazone |
| Diuretics: loops | Bumetanide<br>Furosemide<br>Torsemide |
| Diuretics: potassium sparing | Amiloride<br>Triamterene |



https://kat.cr/user/Blink99/

## Cholesterol Management

2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults available at http://circ.ahajournals.org/content/early/2013/11/11/01.cir.0000437738.63853.7a.

Cardiovascular Risk Calculator available at http://my.americanheart.org/professional/StatementsGuidelines/Prevention-Guidelines_UCM_457698_SubHomePage.jsp.

## Cholesterol Treatment Recommendations to Reduce Atherosclerotic Cardiovascular Disease (ASCVD) Risk in Adults

| Patient Population | | Recommended Treatment (Heart-healthy lifestyle habits are recommended for all patients) |
|---|---|---|
| Diagnosed with clinical ASCVD* (secondary prevention) | Age 21-75 y and no statin safety concerns | High-intensity statin |
| | Age >75 y or statin safety concerns (conditions or drug-drug interactions affecting statin safety or history of statin intolerance) | Medium-intensity statin |
| LDL-C ≥190 mg/dL (primary prevention) | Age ≥21 y | High-intensity statin; if goal LDL-C lowering not achieved, may add nonstatin therapy to achieve >50% reduction in LDL-C |
| Diabetes and LDL-C 70-189 mg/dL (primary prevention) | Age 40-75 y | Moderate-intensity statin<br>If 10-y ASCVD risk ≥7.5%: high-intensity statin |
| No diabetes and LDL-C 70-189 mg/dL (primary prevention) | Age 40-75 y | 10-y ASCVD risk ≥7.5%: moderate- to high-intensity statin<br>10-y risk 5 to <7.5%: moderate-intensity statin |

*Clinical ASCVD includes: acute coronary syndromes, history of myocardial infarction, stable or unstable angina, coronary or other arterial revascularization, stroke, transient ischemic attack (TIA), or peripheral arterial disease.

## Recommended Statin Intensity to Reduce ASCVD Risk

| Low-Intensity Statin Therapy | Moderate-Intensity Statin Therapy | High-Intensity Statin Therapy |
|---|---|---|
| Daily dose lowers LDL-C on average by <30% | Daily dose lowers LDL-C on average by approximately 30% to <50% | Daily dose lowers LDL-C on average by approximately ≥50% |
| Simvastatin 10 mg<br>Pravastatin 10-20 mg<br>Lovastatin 20 mg<br>Fluvastatin 20-40 mg<br>Pitavastatin 1 mg | Atorvastatin 10-20 mg<br>Rosuvastatin 5-10 mg<br>Simvastatin 20-40 mg<br>Pravastatin 40-80 mg<br>Lovastatin 40 mg<br>Fluvastatin XL 80 mg<br>Fluvastatin 40 mg bid<br>Pitavastatin 2-4 mg | Atorvastatin 40-80 mg<br>Rosuvastatin 20-40 mg |



https://kat.cr/user/Blink99/

## Cholesterol-Lowering Drugs

| Class | Drugs | Average Effects on Lipoproteins | Adverse Effects |
|---|---|---|---|
| Bile acid sequestrants | Cholestyramine<br>Colesevelam<br>Colestipol | HDL-C ↑ 3-5%<br>TG No change to ↑ 9%<br>LDL-C ↓ 15-30% | Abdominal discomfort and cramping, constipation, flatulence, nausea/vomiting, vitamin deficiency |
| Cholesterol absorption inhibitor | Ezetimibe | HDL-C ↑ 1%<br>TG ↓ 8%<br>LDL-C ↓ 18% | Arthralgia, diarrhea, myalgia |
| Fibric acid | Fenofibric acid<br>Fenofibrate<br>Gemfibrozil | HDL-C ↑ 10-20%<br>TG ↓ 20-50%<br>LDL-C ↓ 5-20% | Abdominal pain, arthralgia, constipation, diarrhea, headache, increased liver enzymes, indigestion, myalgia, myopathy, nausea, rhabdomyolysis |
| HMG-CoA reductase inhibitors (statins) | Atorvastatin<br>Fluvastatin<br>Fluvastatin XL<br>Lovastatin<br>Pitavastatin<br>Pravastatin<br>Rosuvastatin<br>Simvastatin | HDL-C ↑ 5-15%<br>TG ↓ 7-30%<br>LDL-C ↓ 18-55% | Arthralgia, diarrhea, headache, increased liver enzymes, indigestion, insomnia, myalgia, myopathy, nausea, rhabdomyolysis |
| Nicotinic acid | Niaspan | HDL-C ↑ 15-35%<br>TG ↓ 20-50%<br>LDL-C ↓ 5-25% | Flushing, pruritus, rash, nausea/vomiting, increased glucose levels, increased liver enzymes, myalgia, myopathy |
| Omega-3–acid ethyl ester | Vascepa (EPA) | TG ↓ 21-27% | Joint pain, sore throat |
| Omega-3–acid ethyl esters | Lovaza (EPA/DHA) | HDL-C ↑ 9%<br>TG ↓ 45%<br>LDL-C ↓ 45% | Altered taste, burping, indigestion, pruritus, rash |

## HMG-CoA Reductase Inhibitors Comparison

| Statin Drug | Dose (mg/d) | %Change on Lipoproteins | | |
|---|---|---|---|---|
| | | LDL-C | TG | HDL-C |
| Atorvastatin | 10-80 | ↓ 39-60 | ↓ 19-37 | ↑ 5-9 |
| Fluvastatin | 20-80 | ↓ 22-36 | ↓ 12-25 | ↑ 3-11 |
| Lovastatin | 10-80 | ↓ 24-40 | ↓ 10-19 | ↑ 7-10 |
| Pitavastatin | 1-4 | ↓ 31-45 | ↓ 13-22 | ↑ 1-8 |
| Pravastatin | 10-80 | ↓ 22-37 | ↓ 11-24 | ↑ 2-12 |
| Rosuvastatin | 5-40 | ↓ 45-63 | ↓ 10-35 | ↑ 8-14 |
| Simvastatin | 5-80* | ↓ 26-47 | ↓ 12-33 | ↑ 8-16 |

*80-mg dose restricted to patients who have been taking it for more than 12 mo without evidence of myopathy



https://kat.cr/user/Blink99/

## Hypertension

| Combination Type | Fixed Dose Combination (mg) | Trade Name |
|---|---|---|
| ACE inhibitor and CCB | Amlodipine-benazepril (2.5/10, 5/10, 5/20, 10/20)<br>Enalapril-felodipine (5/5)<br>Trandolapril-verapamil (2/180, 1/240, 2/240, 4/240) | Lotrel<br>Lexxel<br>Tarka |
| ACE inhibitor and diuretic | Benazepril- HCTZ (5/6.25, 10/12.5, 20/12.5, 20/25)<br>Captopril-HCTZ (25/15, 25/25, 50/15, 50/25)<br>Enalapril-HCTZ (5/12.5, 10/25)<br>Fosinopril-HCTZ (10/12.5, 20/12.5)<br>Lisinopril-HCTZ (10/12.5, 20/12.5, 20/25)<br>Moexipril-HCTZ (7.5/12.5, 15/25)<br>Quinapril-HCTZ (10/12.5, 20/12.5, 20/25) | Lotensin HCT<br>Capozide<br>Vaseretic<br>Monopril/HCT<br>Prinzide, Zestoretic<br>Uniretic<br>Accuretic |
| ARB and CCB | Amlodipine-olmesartan (5/20, 5/40, 10/20, 10/40)<br>Amlodipine-telmisartan (5/40, 5/80, 10/40, 10/80)<br>Amlodipine-valsartan (5/160, 5/320, 10/160, 10/320) | Azor<br>Twynsta<br>Exforge |
| ARB and CCB and diuretic | Amlodipine-HCTZ-olmesartan (5/12.5/20, 5/12.5/40, 5/25/40, 10/12.5/40, 10/25/40)<br>Amlodipine-HCTZ-valsartan (5/12.5/160, 5/25/160, 10/12.5/160, 10/25/160, 10/25/320) | Tribenzor<br>Exforge HCT |

| | | |
|---|---|---|
| ARB and diuretic | Azilsartan-chlorthalidone (40/12.5, 40/25)<br>Candesartan-HCTZ (16/12.5, 32/12.5)<br>Eprosartan-HCTZ (600/12.5, 600/25)<br>Irbesartan-HCTZ (150/12.5, 300/12.5)<br>Losartan-HCTZ (50/12.5, 100/25)<br>Olmesartan medoxomil-HCTZ (20/12.5, 40/12.5, 40/25)<br>Telmisartan-HCTZ (40/12.5, 80/12.5)<br>Valsartan-HCTZ (80/12.5, 160/12.5, 160/25) | Edarbyclor<br>Atacand HCT<br>Teveten-HCT<br>Avalide<br>Hyzaar<br>Benicar-HCT<br>Micardis-HCT<br>Diovan-HCT |
| BB and diuretic | Atenolol-chlorthalidone (50/25, 100/25)<br>Bisoprolol-HCTZ (2.5/6.25, 5/6.25, 10/6.25)<br>Metoprolol succinate-HCTZ (25/12.5, 50/12.5, 100/12.5)<br>Metoprolol tartrate-HCTZ (50/25, 100/25)<br>Nadolol-bendroflumethiazide (40/5, 80/5)<br>Propranolol LA-HCTZ (40/25, 80/25) | Tenoretic<br>Ziac<br>Dutoprol<br>Lopressor HCT<br>Corzide<br>Inderide LA |
| Centrally acting drug and diuretic | Chlorthalidone-clonidine (15/0.1, 15/0.2, 15/0.3)<br>Methyldopa-HCTZ (250/15, 250/25, 500/30, 500/50)<br>Reserpine-chlorthalidone (0.125/25, 0.25/50)<br>Reserpine-chlorothiazide (0.125/250, 0.25/500)<br>Reserpine-HCTZ (0.125/25, 0.25/50) | Clorpres<br>Aldoril<br>Regroton<br>Diupres<br>Hydropres |



https://kat.cr/user/Blink99/

| | | |
|---|---|---|
| Direct renin inhibitor and CCB | Aliskiren-amlodipine (150/5, 150/10, 300/5, 300/10) | Tekamlo |
| Direct renin inhibitor and diuretic | Aliskiren-HCTZ (150/12.5, 150/25, 300/12.5, 300/25) | Tekturna HCT |
| Direct renin inhibitor and CCB and diuretic | Aliskiren-amlodipine-HCTZ (150/5/12.5, 300/5/12.5, 300/5/25, 300/10/12.5, 300/10/25) | Amturnide |
| Diuretic combination | Amiloride-HCTZ (5/50)<br>Spironolactone-HCTZ (25/25, 50/50)<br>Triamterene-HCTZ (37.5/25, 75/50) | Moduretic<br>Aldactazide<br>Dyazide, Maxzide |

## Lipid Lowering

| Combination Type | Fixed Dose Combination (mg) | Trade Name |
|---|---|---|
| Statin and cholesterol absorption inhibitor | Ezetimibe-atorvastatin (10/10, 10/20, 10/40, 10/80)<br>Ezetimibe-simvastatin (10/10, 10/20, 10/40, 10/80) | Liptruzet<br>Vytorin |
| Statin and nicotinic acid | Lovastatin-niacin (20/500, 20/750, 20/1000, 40/1000)<br>Niacin-simvastatin (500/20, 500/40, 750/20, 1000/20, 1000/40) | Advicor<br>Simcor |

## Hypertension/Lipid Lowering

| Combination Type | Fixed Dose Combination (mg) | Trade Name |
|---|---|---|
| CCB and statin | Amlodipine-atorvastatin (2.5/10, 2.5/20, 2.5/40, 5/10, 5/20, 5/40, 5/80, 10/10, 10/20, 10/40, 10/80) | Caduet |

## Glucose Lowering/Lipid Lowering

| Combination Type | Fixed Dose Combination (mg) | Trade Name |
|---|---|---|
| Statin and dipetidyl peptidase-4 (DDP-4) enzyme inhibitor | Simvastatin-sitagliptin (10/50, 10/100, 20/50, 20/100, 40/50, 40/100) | Juvisync |

This page intentionally left blank

https://kat.cr/user/Blink99/

# Preface G: Guide to Combination Vaccines

| Vaccine | Trade Name | Type | Route | Comments |
|---|---|---|---|---|
| DTaP | Daptacel<br>Infanrix<br>Tripedia | Inactivated bacterial, toxoid | IM | Diphtheria, tetanus, acellular pertussis |
| DTaP-HepB-IPV | Pediarix | Inactivated bacterial, toxoid, viral | IM | Licensed for doses at 2, 4, and 6 mo of age; can be used through age 6 y |
| DTaP-IPV | Kinrix | Inactivated bacterial, toxoid, viral | IM | Licensed for 5th dose in series at 4-6 y |
| DTaP-IPV-Hib | Pentacel | Inactivated bacterial, toxoid, viral | IM | Licensed for 4 doses at 2, 4, 6, and 15-18 mo |
| *Haemophilus influenzae* type b-hepatitis B | Comvax | Inactivated bacterial, viral | IM | Not used for birth dose of hepatitis B |
| Hib-MenCY | MenHibrix | Inactivated bacterial | IM | Licensed for 4 doses at 2, 4, 6, and 12-15 mo of age |
| Hepatitis A-hepatitis B | Twinrix | Inactivated viral | IM | ≥18 y; 3-dose series |
| Measles-mumps-rubella | MMR-II | Live attenuated viral | SC | Minimum age 12 mo |
| Measles-mumps-rubella-varicella | ProQuad | Live attenuated viral | SC | Licensed for ages 1-12 y |
| Tdap | Boostrix<br><br>Adacel | Inactivated bacterial, toxoid | IM | Tetanus and diphtheria toxoids and pertussis vaccine; ≥10 y of age<br>Tetanus and diphtheria toxoids and pertussis vaccine; 11-64 y of age |

IM = intramuscular
SC = subcutaneous

This page intentionally left blank

https://kat.cr/user/Blink99/

# Preface H: Guide to Cytochrome P450 (CYP) and UGT1A1 Metabolism

## Definitions

*Inhibitors*

- *Strong inhibitor* is one that causes a ≥5-fold increase in the plasma AUC values or >80% decrease in clearance.
- *Moderate inhibitor* is one that causes a ≥2-fold but <5-fold increase in the plasma AUC values or 50-79% decrease in clearance.
- *Weak inhibitor* is one that causes a >1.25-fold but <2-fold increase in the plasma AUC values or 20-49% decrease in clearance.

*Inducers*

- *Strong inducer* is one that causes a ≥80% decrease in the plasma AUC.
- *Moderate inducer* is one that causes a 50-79% decrease in plasma AUC.
- *Weak inducer* is one that causes a 20-49% decrease in plasma AUC.

*Substrates*

- *Sensitive substrates* are when ≥25% of metabolism occurs via a given enzyme.
- *Non-sensitive substrates* are when <25% of metabolism occurs via a given enzyme.

*Clinical Implications*

*Assessment and clinical management of drug-drug interaction:*

1. Are both drugs systemically absorbed? If no, no drug interaction.
2. Do both drugs impact the same enzyme system? If not, no drug interaction.
3. The majority of clinically significant drug interactions involve and enzyme inducer or inhibitor and a sensitive substrate (which is metabolized by the enzyme). For example, itraconazole is a strong inhibitor of CYP3A4/5. Amiodarone is a sensitive substrate. Giving them together may result in higher amiodarone levels and toxicity. Clinical management would be to select an alternative antifungal, of dose reduce amiodarone. Strong inducers increase metabolism and decrease efficacy of substrates. Clinical management would be to select an alternative agent or increase the dose of the substrate.

4. Some drugs are prodrugs and require an enzyme to be activated. For example, itraconazole is a strong inhibitor of CYP3A4/5. Cyclophosphamide is a sensitive substrate that is converted to its active metabolite, acrolein, by CYP3A4/5. Giving them together may result in lower acrolein levels and loss of efficacy. Clinical management would be to select an alternative antifungal. Strong inducers, like carbamazepine, increase metabolism and have higher acrolein levels. Clinical management would be to select an alternative agent or decrease the dose of the cyclophosphamide.

**Note: Only strong and moderate inhibitors and inducers are included in the drug interaction and drug fact sections. Weak inhibitors and inducers are unlikely to be clinically significant.**

### CYP1A2

**Inhibitors (Strong).** Caffeine, ciprofloxacin, enoxacin, fluvoxamine, ketoconazole, lidocaine, methoxselan, mexilitine, norfloxacin, ofloxacin, primaquine, thiabendazole

**Inhibitors (Moderate).** Amlodipine, cimetidine, diclofenac, fluoxetine, fospropofol, gemfibrozil, miconazole, nifedipine, propofol, zileuton

**Inducers.** Aminoglutethimide, carbamazepine, phenobarbital, primadone, rifampin

**Substrates (Sensitive).** Acenocoumarol, aminophylline, betaxolol, caffeine, clomipramine, clozapine, cyclobenzaprine, dacarbazine, doxepin, duloxetine, estrogens, flutamide, fluvoxamine, mexiletine, mirtazapine, pimozide, propranolol, riluzole, ropinorole, tacrine, theophylline, thiothixene, trifluoperazine

### CYP2A6

**Inhibitors (Strong).** Letrozole, methoxselan, miconazole, tranlcypromine

**Inhibitors (Moderate).** Amiodarone, desipramine, isoniazid, ketoconazole

**Inducers.** Amobarbital, pentobarbital, phenobarbital, rifampin, secobarbital

**Substrates (Sensitive).** Dexmedetomidine

### CYP2B6

**Inhibitors (Strong).** None

**Inhibitors (Moderate).** Doxorubicin, paroxetine, sorafenib



https://kat.cr/user/Blink99/

**Inducers.** Carbamazepine, phenobarbital, phenytoin, rifampin

**Substrates (Sensitive).** Bupropion, cyclophosphamide (activated to acrolein by CYP2B6), efavirenz, irinotecan, ketamine, promethazine, propofol, selegiline

## CYP2C8

**Inhibitors (Strong).** Atorvastatin, gemfibrozil, ritonavir

**Inhibitors (Moderate).** Celecoxib, felodipine, fenofibrate, irbesartan, losartan, pioglitazone, quine, rabeprazole, rosiglitazone, tamoxifen, trimethoprim

**Inducers.** Carbamazepine, phenobarbital, phenytoin, primodone, rifampin, secobarbital

**Substrates (Sensitive).** Amitriptyline, mestranol (activated by CYP2C8 to ethinyl estradiol), paclitaxel, pioglitazone, rifabutin, rosuvastatin, tretinoin

## CYP2C9

**Inhibitors (Strong).** Delaviridine, flurbiprofen, fluconazole, ibuprofen, indomethacin, isoniazid, mefenamic acid, miconazole, nicardipine, sulfadiazine, sulfisoxazole, tolbutamide

**Inhibitors (Moderate).** Amiodarone, efavirenz, fenofibrate, fluvastatin, gemfibrozil, irbesartan, ketoconazole, losartan, omeprazole, pantoprazole, pyrimethamine, quinine, sorafenib, sulfamethoxazole, trimethoprim, warfarin, zafirlukast

**Inducers.** Carbamazepine, phenobarbital, phenytoin, primodone, rifampin, rifapentine, secobarbital

**Substrates (Sensitive).** Alprazolam, bosentan, carvedilol, celecoxib, dapsone, fluoxetine, glimeride, glipizide, ketamine, losartan, mestranol (activated by CYP2C9 to ethinyl estradiol), montelukast, paclitaxel, phenytoin, propofol, sulfadiazine, sulfamethoxazole, sulfisoxazole, sulfinpyrazone, tamoxifen, tolbutamide, torsemide, trimethoprim, voriconazole, warfarin, zafirlukast, zopiclone

## CYP2C19

**Inhibitors (Strong).** Delaviridine, fluconazole, fluoxetine, fluvoxamine, gemfibrozil, ketoconazole, miconazole, modafinil, omeprazole, piroxicam, ticlopidine

**Inhibitors (Moderate).** Bortezomib, cimetidine, efavirenz, esomeprazole, fospropofol, lansoprazole, loratadine, nicardipine, propofol, rabeprazole, sertraline

**Inducers.** Aminoglutethimide, carbamazepine, phenytoin, rifampin

**Substrates (Sensitive).** Carisoprodol, citalopram, clobazam, clomipramine, diazepam, escitalopram, esomeprazole, imipramine, lansoprazole, methsuximide, moclobemide, nelfinavir, nilutamide, omeprazole, pantoprazole, pentamidine, phenobarbital, phenytoin, progesterone, rabeprazole, ranitidine, sertraline, trimipramine, voriconazole

## CYP2D6

**Inhibitors (Strong).** Chlorpromazine, cinacalet, cocaine, delaviridine, dexmedetomidine, dextromethorphan, fluoxetine, miconazole, paroxetine, pergolide, quinidine, ritonavir, ropinirole, terbinafine, quinine

**Inhibitors (Moderate).** Amiodarone, chloroquine, cimetidine, clomipramine, clozapine, darifenacin, desipramine, diphenhydramine, duloxetine, haloperidol, imipramine, isoniazid, lidocaine, methadone, methimazole, nicardipine, pioglitazone, pyrimethamine, quinine, ranolazine, sertraline, thioridazine, ticlopidine, trazadone

**Inducers.** None

**Substrates (Sensitive).**

- *Antibiotics:* Chloroquine, doxycycline
- *Cardiovascular:* Atorvastatin, betaxolol, captopril, carvedilol, flecainide, lidocaine, metoprolol, mexiletine, pindolol, propafenone, propranolol, timolol
- *CNS:* Amitriptyline, amphetamine, amoxapine, aripiprazole, chlorpromazine, clomipramine, desipramine, dextroamphetamine, dextromethorphan, dihydroergotamine, duloxetine, fluoxetine, flurazepam, fluvoxamine, haloperidol, imipramine, methylphenidate, mirtazapine, moclobemide, nefazodone, nortriptyline, paroxetine, perphenazine, promethazine, risperidone, sertraline, thioridazine, tramadol, trimipramine, venlafaxine
- *Pain:* Codeine (prodrug, activated by CYP2D6 to morphine), oxycodone
- *Oncology:* Doxorubicin, lomustine, tamoxifen
- *Misc:* Hydrocortisone, lansoprazole, tamulosin



https://kat.cr/user/Blink99/

### CYP2E1

**Inhibitors (Strong).** Disulfiram

**Inhibitors (Moderate).** Isoniazid, miconazole

**Inducers.** None

**Substrates (Sensitive).** Chlorzoxazone, dacarbazine, halothane, isoflurane, isoniazid, sevoflurane, theophylline, trimethadione

### CYP3A4/5

**Inhibitors (Strong).** Atazanavir, amprenavir/fosamprenavir, clarithromycin, conivaptan, delaviridine, enoxacin, imatinib, indinavir, isoniazid, itraconazole, ketoconazole, miconazole, nefazodone, nelfinavir, nicardipine, propofol, ritonavir, telithromycin

**Inhibitors (Moderate).** Amiodarone, aprepitant, cimetidine, clotrimazole, desipramine, dexamethasone, diltiazem, doxycycline, erythromycin, fluconazole, isoniazid, lidocaine, metronidazole, miconazole, norfloxacin, sertraline, tetracycline, verapamil, voriconazole

**Inducers.** Aminoglutethimide, carbamazepine/oxcarbazepine, nevirapine, phenobarbital, phenytoin, pentobarbital/primadone, rifabutin, rifampin

### Substrates (Sensitive)

- *Acid blockers:* Cisapride, lansoprazole, omeprazole, rabeprazole
- *Antibiotics:* Chloroquine, clarithromycin, doxycycline, erythromycin, mefloquine, telithromycin, tetracycline, trimethoprim, spiramycin
- *Antifungals:* Itraconazole, ketoconazole, miconazole
- *Antihistamines:* Azelastine, cerivistatin, chlorpheniramine
- *Cardiovascular:* Amiodarone, bosenten, budesonide, cilostazol, diltiazem, disopyramide, enalapril, felodipine, isosorbide, isradipine, lidocaine, losartan, lovastatin, moricizine, nicardipine, nifedipine, nimodipine, nisoldipine, quinidine, simvastatin, ticlodipine
- *CNS:* Alprazolam, amoxapine, benztropine, buprenorphine, buspirone, carisoprodol, clorazepate, chlordiazepoxide, clobazam, clonazepam, cocaine, dantrolene, diazepam, dihydroergotamine, doxepin, eletriptan, escitalopram, ethosuximide, felbamate, flurazepam, haloperidol, mirtazapine, modafinil, pergolide, phencyclidine, pimozide, quetiapine, ranolazine, trazodone, tiagabine, triazolam

- *HIV:* Amprenavir, atazanavir, delavirdine, efavirenz, indinavir, nefazodone, nelfinavir, nevirapine, primaquine, rifabutin, ritonavir, saquinavir, tipranavir
- *Hormones/Steroids:* Estrogens, exemestane, flutamide, fluticasone, letrozole, medroxyprogesterone, mestranol, progesterone, toremifene
- *Immunosuppressants:* Cyclosporine, dapsone, sirolimus, tacrolimus
- *Oncology:* Bortezomib, busulfan, cyclophosphamide (activated to acrolein by CYP3A4/5), docetaxel, doxorubicin, etoposide, ifosfamide (activated to acrolein by CYP3A4/5), imatinib, irinotecan, paclitaxel, sorafenib, sunitinib, teniposide
- *Pain/Sedation:* Alfentanil, fentanyl, ketamine, methadone, midazolam, sufentanil
- *Pulmonary:* Albuterol, montelukast, salmeterol, theophylline
- *Misc:* Aprepitant, brinzolamide, bromocriptine, colchicine, conivaptan, nateglinide, repaglinide, sibutramine, sildenafil, tamsulosin

## UGT1A1

*Inhibitors*

Atazanavir, gemfibrozil, indinavir

## Inducers

Carbamazepine

## Substrates

Indacaterol, irinotecan, nilotinib, pazopanib, statins



https://kat.cr/user/Blink99/

## Definitions

*Inhibitors*

*Inhibitors* increase the AUC of substrate drugs by ≥1.25-fold.

*Inducers*

*Inducers* decrease the AUC of substrate drugs by ≥1.20-fold.

*Substrates*

- *Sensitive substrates* are when ≥25% of metabolism occurs via a given enzyme.
- *Nonsensitive substrates* are when <25% of metabolism occurs via a given enzyme.

*Clinical Implications*

Understanding the interaction of drugs with Pgp can assist with managing drug interactions. For example, adding carbamazepine (a Pgp inducer) to digoxin (a Pgp substrate) can lead to marked decreases in serum digoxin concentrations. Clinical management would include monitoring digoxin levels and making dose adjustments.

*P-glycoprotein/ABCB1*

P-glycoprotein (Pgp) is a membrane-bound, active transport protein located in a number cells and tissues, including intestinal epithelial cells, various lymphocytes, biliary tract, brain, and proximal tubular cells of the kidney. ABCB1 is the name of the gene, while Pgp is the protein.

Its major function is as an efflux transporter of drugs and chemicals. Effects of inducers and inhibitors vary by their location. For example, Pgp transports substrate drugs out of the brain. Inducers may decrease concentrations in the CSF, because there is increased amount of Pgp available to transport substrates, while inhibitors may increase CSF concentrations.

**Inhibitors.** Abiraterone, amiodarone, atorvastatin, carvedilol, clarithromycin, cobicistat, crizotinib, cyclosporine, darunavir, dipyridamole, dronedarone, erythromycin, grapefruit juice, itraconazole, ivacaftor, ketoconazole, lapatinib, lomitapide, lopinavir, mefloquine, nelfinavir, nicardipine, nilotinib, progesterone, propranolol, quinidine, quinine, ranolazine, reserpine, ritonavir, saquinavir, sunitinib, tacrolimus, tamoxifen, telaprevir, ulipristal, vandetanib, vemurafenib, verapamil.

**Inducers.** Carbamazepine, dexamethasone, doxorubicin, nefazodone, prazosin, rifampin, St. John's wort, tenofovir, tipranavir, trazodone, vinblastine.

**Substrates (Sensitive).** Aliskiren, amiodarone, atorvastatin, bosutinib, carfilzomib, carvedilol, cetirizine, cimetidine, ciprofloxacin, colchicine, crizotinib, cyclosporine, dabigatran, daunorubicin, desloratadine, dexamethasone, digitoxin, digoxin, diltiazem, docetaxel, doxorubicin, erythromycin, estradiol, etoposide, everolimus, fexofenadine, fosamprenavir, hydrocortisone, idarubicin, imatinib, indinavir, irinotecan, ivermectin, lapatinib, linagliptin, loperamide, loratadine, lovastatin, methotrexate, mitomycin, nadolol, nelfinavir, nicardipine, ondansetron, paclitaxel, paclitaxel protein bound, paliperidone, pazopanib, pomalidomide, pravastatin, quinidine, quinine, ranitidine, ranolazine, rifampin, risperidone, ritonavir, rivaroxaban, romidepsin, saquinavir, saxagliptin, silodosin, sirolimus, sitagliptin, tacrolimus, telaprevir, temsirolimus, teniposide, tolvaptan, trabectedin, vemurafenib, verapamil, vinblastine, vincristine, vismodegib.



https://kat.cr/user/Blink99/

# Preface J: Drugs That Affect Cardiac Rhythm

Additional information on drug interactions and specifically agents that affect QT interval can be found on the following web site: https://crediblemeds.org/.

## Drugs that are generally accepted to prolong the QT interval and have an increased risk of torsades de pointes

Alfuzosin, amiodarone, amisulpride, anagrelide, apomorphinete, arformoterol, aripiprazole, arsenictrioxide, asenapine, astemizole, azithromycin, bedaquiline, buserelin, cesium chloride, chloral hydrate, chloroquine, chlorpromazine, ciprofloxacin, cisapride, citalopram, clarithromycin, clozapine, cocaine, crizotinib, dasatinib, disopyramide, dofetilide, dolasetron, domperidone, dronedarone, droperidol, eribulin, erythromycin, flecainide, fluoxetine, formoterol, gatifloxacin, goserelin, granisetron, halofantrine, haloperidol, histrelin, hydroxyzine, hydroxyzine, ibutilide, iloperidone, ivabradine, lapatinib, leuprolide, levofloxacin, lopinavir, loxapine, mefloquine, methadone, metoclopramide, metronidazole, mifepristone, moxifloxacin, nelfinavir, nilotinib, ofloxacin, olanzapine, ondansetron, oxycodone, papaverine, pasireotide, pentamidine, perphenazine, pimozide, pipamperone, posaconazole, probucol, procainamide, propafenone, quetiapine, quinidine, quinine, ranolazine, risperidone, saquinavir, sertindole, sorafenib, sotalol, sparfloxacin, sunitinib, telavancin, telithromycin, terlipressin, thioridazine, thiothixene, toremifene, trazodone, tricyclic and tetracyclic antidepressants, triptorelin, vandetanib, vemurafenib, voriconazole, vorinostat, ziprasidone

## Drugs that prolong the PR interval

Acetylcholinesterase inhibitors (donepezil, rivastigmine, galantamine), adenosine, alendronate, antiarrhythmics (flecainide, propafenone, procainamide), beta-blockers, calcium channel blockers, digoxin, dolasetron, lithium, HIV protease inhibitors, lacosamide, methyldopa, pregabalin, TCAs, vitamin D and derivatives

## Drugs that shorten the PR interval

Atropine, ibutilide

This page intentionally left blank

https://kat.cr/user/Blink99/

## Drugs with pH-dependent absorption

Drugs that alter gastric pH may alter absorption of drugs with pH-dependent absorption. If concurrent use is required, separate administration of drugs with pH-dependent absorption from antacids by 2 hours, H2 antagonists by 12 hours and avoid PPIs.

ACE inhibitors, allopurinol, ascorbic acid, atazanavir, bisacodyl, bisphosphonates, calcitriol, calcium, cefuroxime, chloroquine, citric acid, corticosteroids, dabigatran, dasatinib, deferasirox, deferiprone, delavirdine, eltrombopag, elvitegravir, erlotinib, ethambutol, fexofenadine, gabapentin, iron, isoniazid, itraconazole, ketoconazole, levothyroxine, mesalamine, misoprostol, multivitamins, mycophenolate, nilotinib, phosphorous, ponatinib, quinine, quinolone antibiotics, sodium polystyrene, strontium, tetracyclines, thyroid products, vitamin D and analogues, vismodegib

## Drugs that alter gastric pH

Antacids, $H_2$ antagonists (cimetidine, ranitidine, famotidine, nizatidine), proton pump inhibitors (dexlansoprazole, esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole)

This page intentionally left blank

https://kat.cr/user/Blink99/

# Preface L: Abbreviations

These are the abbreviations used commonly through these flash cards:

| | |
|---|---|
| ACE | Angiotensin-converting enzyme |
| ACE-I | Angiotensin-converting enzyme inhibitor |
| AChE | Acetylcholinesterase |
| ADHD | Attention-deficit hyperactivity disorder |
| ADP | Adenosine diphosphate |
| AEDs | Antiepileptic drugs |
| ALT | Alanine transaminase |
| AMI | Acute myocardial infarction |
| AMP | Adenosine monophosphate |
| AMPA | α-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid |
| aPTT | Activated partial thromboplastin time |
| ARB | Angiotensin II receptor blocker |
| AST | Aspartate transaminase |
| ATP | Adenosine triphosphate |
| AUA | American Urologic Association |
| AUC | Area under the (time-concentration) curve |
| AV | Atrioventricular |
| AVP | Arginine vasopressin |
| *B. fragilis* | *Bacteroides fragilis* |
| bid | Twice daily (*bis in die*) |
| BMD | Bone mineral density |
| BP | Blood pressure |
| BPH | Benign prostatic hyperplasia |
| BUN | Blood urea nitrogen |
| *C. difficile* | *Clostridium difficile* |
| *C. parvum* | *Cryptosporidium parvum* |
| *C. trachomatis* | *Chlamydia trachomatis* |
| CABG | Coronary artery bypass grafting |
| CAD | Coronary artery disease |
| CBC | Complete blood count |
| CCR5 | C-C motif receptor 5 |
| CK | Creatine kinase |
| CKD | Chronic kidney disease |
| Cmax | Concentration, maximum (on time-concentration curve) |
| CNS | Central nervous system |
| COX-1 | Cyclooxygenase-1 |
| COX-2 | Cyclooxygenase-2 |
| COPD | Chronic obstructive pulmonary disease |
| CR | Controlled release |
| CrCl | Creatinine clearance |
| CSF | Cerebrospinal fluid |
| CV | Cerebrovascular |
| CYP | Cytochrome P |
| d | Day |
| DEXA | Dual-energy x-ray absorptiometry |
| DHA | Docosahexaenoic acid |
| DHFR | Dihydrofolate reductase |
| DILE | Drug-induced lupus erythematosus |

| | |
|---|---|
| dL | Deciliter |
| DM | Diabetes mellitus |
| DNA | Deoxyribonucleic acid |
| DPP-4 | Dipeptidyl peptidase-4 |
| DVT | Deep vein thrombosis |
| DTaP | Diphtheria and tetanus toxoids |
| *E. coli* | *Escherichia coli* |
| *E. histolytica* | *Entamoeba histolytica* |
| ECG | Electrocardiogram |
| EEG | Electroencephalogram |
| eGFR | Estimated glomerular filtration rate |
| ELISA | Enzyme-linked immunosorbent assay |
| EPA | Eicosapentaenoic acid |
| ER | Extended release |
| ESR | Erythrocyte sedimentation rate |
| ESRD | End-stage renal disease |
| F | Bioavailability |
| FAA | Federal Aviation Administration |
| FBG | Fasting blood glucose |
| FDA | Food and Drug Administration |
| FPG | Fasting plasma glucose |
| FSH | Follicle-stimulating hormone |
| *G. lamblia* | *Giardia lamblia* |
| GABA | γ-Aminobutyric acid |
| GERD | Gastroesophageal reflux disease |
| GI | Gastrointestinal |
| GMP | Guanosine monophosphate |
| G6PD | Glucose-6-phosphate dehydrogenase |
| h | Hour |
| *H. influenzae* | *Haemophilus influenzae* |
| *H. pylori* | *Helicobacter pylori* |
| Hgb | Hemoglobin |
| $HbA_{lc}$ | Glycosylated hemoglobin (hemoglobin $A_{lc}$) |
| HBV | Hepatitis B virus |
| Hct | Hematocrit |
| HCT | Hydrocortisone |
| HCTZ | Hydrochlorothiazide |
| HDL | High-density lipoprotein |
| HgB | Hemoglobin |
| HIV | Human immunodeficiency virus |
| HMG-CoA | Hydroxymethylglutaryl-CoA |
| HPA | Hypothalamic axis |
| HPV | Human papillomavirus |
| HR | Heart rate |
| hs | At bedtime (*hora somni*) |
| HSV | Herpes simplex virus |
| $5\text{-}HT_1$ | 5-hydroxytryptamine 1 |
| HTN | Hypertension |
| HZV | Herpes zoster virus |
| IM | Intramuscular; infectious mononucleosis |
| INR | International normalized ratio |
| IOP | Intraocular pressure |
| ISMN | Isosorbide mononitrate |



https://kat.cr/user/Blink99/

| | |
|---|---|
| IUD | Intrauterine device |
| IV | Intravenous; Roman numeral four; symbol for class 4 controlled substances |
| LABA | Long-acting beta-agonist |
| LDL | Low-density lipoprotein |
| LH | Luteinizing hormone |
| LFT | Liver function test |
| *M. avium* | *Mycobacterium avium* |
| *M. (B.) catarrhalis* | *Moraxella (Branhamella) catarrhalis* |
| MAOI | Monoamine oxidase inhibitor |
| MCV | Mean corpuscular volume |
| MDD | Major depressive disorder |
| MDI | Metered-dose inhaler |
| mEq | Milliequivalent |
| mg | Milligram |
| MHD | Monohydroxy metabolite |
| MI | Myocardial infarction; mitral insufficiency |
| min | Minute |
| MMR | Measles-mumps-rubella |
| mo | Month |
| MRI | Magnetic resonance imaging |
| MRSA | Methicillin-resistant *S. aureus* |
| *N. meningitides* | *Neisseria meningitides* |
| NG | Nasogastric |
| NMDA | *N*-methyl-d-aspartate |
| NO | Nitric oxide |
| NSAID | Nonsteroidal anti-inflammatory drug |
| NSR | Normal sinus rhythm |
| NYHA | New York Heart Association |
| OCD | Obsessive-compulsive disorder |
| OTC | Over-the-counter |
| *P. aeruginosa* | *Pseudomonas aeruginosa* |
| *P. carinii* | *Pneumocystis carinii* |
| *P. falciparum* | *Plasmodium falciparum* |
| *P. malariae* | *Plasmodium malariae* |
| *P. vivax* | *Plasmodium vivax* |
| PBPs | Penicillin-binding proteins |
| PCP | *Pneumocystis carinii* pneumonia |
| PDE5 | Phosphodiesterase type 5 |
| PDEI | Phosphodiesterase inhibitor |
| PE | Pulmonary embolism |
| PEG | Polyethylene glycol |
| PFOR | Pyruvate ferredoxin oxidoreductase |
| PFT | Pulmonary function test |
| PMDD | Premenstrual dysphoric disorder |
| po | By mouth (*per os*) |
| PPAR-α | Peroxisome proliferator–activated receptor-α |
| PPAR-γ | Peroxisome proliferator–activated receptor-γ |
| PPI | Proton pump inhibitor |
| pr | Per rectum |
| PrEP | Preexposure prophylaxis |
| prn | When necessary, as needed (*pro re nata*) |
| PSA | Prostate-specific antigen |

| | |
|---|---|
| PTSD | Posttraumatic stress disorder |
| PUD | Peptic ulcer diseases |
| qid | Four times daily (*quater in die*) |
| qod | Every other day |
| qwk | Every week |
| REMS | Risk evaluation and mitigation strategy |
| RNA | Ribonucleic acid |
| s | Second |
| *S. aureus* | *Staphylococcus aureus* |
| *S. pneumoniae* | *Streptococcus pneumoniae* |
| SA | Sino-atrial |
| SABA | Short-acting beta-agonists |
| SAD | Seasonal affective disorder |
| SCr | Serum creatinine |
| SERM | Selective estrogen receptor modulator |
| SMZ/TMP | Sulfamethoxazole/trimethoprim |
| SNRI | Serotonin-norepinephrine reuptake inhibitor |
| sq | Subcutaneous |
| SSKI | Saturated solution of potassium iodide |
| SSRI | Selective serotonin reuptake inhibitor |
| *T. mentagrophytes* | *Trichophyton mentagrophytes* |
| *T. rubrum* | *Trichophyton rubrum* |
| *T. vaginalis* | *Trichomonas vaginalis* |
| TCA | Tricyclic antidepressant |
| Tdap | Tetanus and diphtheria toxoid |
| TG | Triglyceride |
| TIBC | Total iron-binding capacity |
| tid | Three times daily (*ter in die*) |
| Tmax | Time to maximum concentration (on time-concentration curve) |
| TSH | Thyroid-stimulating hormone |
| TTP | Thrombotic thrombocytopenic purpura |
| UGT | Uridine diphosphate glucuronosyltransferase |
| UTI | Urinary tract infection |
| Vd | Volume of distribution |
| VLDL | Very low-density lipoprotein |
| VZS | Varicella-zoster virus |
| WBC | White blood cell (count) |
| wk | Week |
| XR | Extended release |
| y | Year |



https://kat.cr/user/Blink99/

# ACYCLOVIR: Zovirax, Various

A

**Class:** Viral DNA Polymerase Inhibitor

**Dosage Forms.** **Capsule:** 200 mg; **Suspension:** 200 mg/5 mL; **Tablet:** 400 mg, 800 mg

Teva generic 200 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Genital herpes simplex: Adults, initial episode, 400 mg po tid or 200 mg po 5 times a day × 7-10 d; Children ≥12 y of age, 1000-1200 mg/d po in 3-5 divided doses for 7-10 d
2. Genital herpes simplex, suppressive therapy: 400 mg po bid for up to 12 mo
3. Herpes zoster, shingles: 800 mg po 5 times a day × 7-10 d
4. Varicella: Adults and Children ≥2 y of age and ≥40 kg, 800 mg po qid × 5 d; Children ≥2 y of age and <40 kg, 20 mg/kg po qid × 5 d

**Off-Label Uses.**

1. Genital herpes simplex in HIV-positive patients, initial or recurrent: 400 mg po tid × 5-10 d
2. Genital herpes simplex in HIV-positive patients, chronic suppression: 400-800 mg po bid-tid

**MOA.** Acyclovir is an acyclic nucleoside analogue of deoxyguanosine that is selectively phosphorylated by the virus-encoded thymidine kinase to its monophosphate form. Cellular enzymes then convert the monophosphate to the active antiviral acyclovir triphosphate, which competitively inhibits viral DNA synthesis by inactivation of viral DNA polymerase and incorporation into and termination of viral DNA replication. Acyclovir has potent activity against herpes simplex virus (HSV) I and II and herpes zoster virus (varicella-zoster virus [VZV]).

**Drug Characteristics: Acyclovir**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 10-20%, food has no effect on absorption |
| **Dose Adjustment Renal** | CrCl 10-25 mL/min, increase interval to q8h; CrCl <10 mL/min, increase interval to q12h | **Distribution** | Vd = 0.8 L/kg; 9-33% protein bound Placenta, CSF, kidney, brain, lung, heart |
| **Dialyzable** | Hemodialysis removes 60% of dose. No adjustment for peritoneal (<10% removed) | **Metabolism** | Not metabolized |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 62-90% with a half-life of 2.5-3.3 h |
| **Lactation** | Compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to acyclovir or valacyclovir | **Black Box Warnings** | None |

### Medication Safety Issues: Acyclovir

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | No |

### Drug Interactions: Acyclovir

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Phenytoin, fosphenytoin, valproic acid | Decreased absorption and lower plasma concentration of phenytoin | Monitor phenytoin levels and adjust, if necessary |
| Varicella virus vaccine | Decreased vaccine effectiveness via antagonism | Avoid concurrent use |

### Adverse Reactions: Acyclovir

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Malaise | Nausea, vomiting, headache, diarrhea | Severe hypersensitivity, renal failure, TTP |

**Efficacy Monitoring Parameters.** Resolution of clinical signs of infection (lesions) within 2-3 d.

**Toxicity Monitoring Parameters.** Seek medical attention if decreased urination, unusual bruising or bleeding, blistering skin rash, shortness of breath, confusion, lethargy, or seizures.

**Key Patient Counseling Points.** Complete full course of therapy. Ensure adequate hydration. For HSV, initiate treatment as soon as possible at first sign of lesion. For VZV, treatment should begin within 24 h of appearance of rash. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner. If using for prophylaxis, this medication should reduce the number of breakouts.

**Clinical Pearls.** Not indicated for children <2 y of age. Use caution with concurrent nephrotoxins. Topical and parenteral products also available.



https://kat.cr/user/Blink99/

# ADAPALENE: Differin, Various

**Class:** Retinoid, Antiacne

**Dosage Forms. Cream:** 0.1%; **Gel/Jelly:** 0.1%, 0.3%; **Lotion:** 0.1%

**Common FDA Label Indication, Dosing, and Titration.**

1. Acne vulgaris: Adults and Children >12 y of age, apply thin film topically to affected area(s) daily hs

Galderma 0.3% gel pictured

**Off-Label Uses.** None

**MOA.** Adapalene exhibits retinoic acid-like activity, reducing important features of the pathology of acne vulgaris by normalizing the differentiation of follicular epithelial cells and keratinization to prevent microcomedone formation. Adapalene enhances keratinocyte differentiation without inducing epidermal hyperplasia and severe irritation, which is associated with retinoic acid. Adapalene decreases formation of comedones, and inflammatory and noninflammatory acne lesions.

**Drug Characteristics: Adapalene**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Not absorbed |
| **Dose Adjustment Renal** | Not required | **Distribution** | Not applicable |
| **Dialyzable** | Unknown | **Metabolism** | Not applicable |
| **Pregnancy Category** | C | **Elimination** | Not applicable |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

**Medication Safety Issues: Adapalene**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | No |

**Drug Interactions: Adapalene**

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Oral contraceptives | Decreased serum concentration of progestin | Consider 2 forms of contraception, particularly if patient is taking progesterone-only preparation |

**Adverse Reactions: Adapalene**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Dry skin, scaly skin, erythema, burning/stinging | Skin irritation, skin discomfort, pruritus | Angioedema |

**Efficacy Monitoring Parameters.** Improvement in acne.

**Toxicity Monitoring Parameters.** Severe dry skin or severe skin irritation.

**Key Patient Counseling Points.** Avoid contact with eyes, lips, angles of nose, and mucous membranes; do not apply on cuts, abrasions, eczematous, or sunburned skin. Wash, then dry hands and affected area prior to application. Use of moisturizers may be necessary for relief of dry skin or irritation. Avoid products that can dry or irritate skin further. If cutaneous reactions (such as erythema, scaling, and stinging/burning) are severe, the frequency should be reduced or adapalene discontinued. Other topical preparations (sulfur, resorcinol, or salicylic acid) should not be used prior to using topical adapalene. Adapalene causes sun sensitivity. Avoid sun exposure and tanning beds. Protective clothing and application of sunscreen are recommended when sun exposure cannot be avoided. Cold temperatures or wind may also increase skin irritation during drug therapy. Symptomatic improvement may not be seen for a few months.

**Clinical Pearls.** Safety and efficacy have not been established in children <12 y of age.



https://kat.cr/user/Blink99/

# ALBENDAZOLE: Albenza



**Class:** Anthelmintic

**Dosage Forms. Tablet:** 200 mg

GlaxoSmithKline 200 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Parenchymal neurocysticercosis caused by *Taenia solium*: Adults ≥60 kg, 400 mg po bid with meals × 8-30 d; Children <60 kg, 15 mg/kg/d (*max* 800 mg/d) in 2 divided doses × 8-30 d
2. Cystic hydatid disease of the liver, lung, and peritoneum caused by *Echinococcus granulosus*: Adults ≥60 kg, 400 mg po bid with meals × 8-30 d; Children <60 kg, 15 mg/kg/d (*max* 800 mg/d) in 2 divided doses × 8-30 d

**Off-Label Uses.**

1. *Ancylostoma caninum, Ascaris lumbricoides* (roundworm), *Ancylostoma duodenale* (hookworm), and *Necator americanus* (hookworm): 400 mg po as a single dose
2. *Enterobius vermicularis* (pinworm): 400 mg po as a single dose, repeat in 2 wk
3. *Giardia duodenalis* (giardiasis): 400 mg po once daily × 5 d

**MOA.** Selective degeneration of cytoplasmic microtubules in intestinal and tegmental cells of intestinal helminths and larvae. This leads to impaired glucose uptake in parasites and ATP production decreases leading to energy depletion and death.

**Drug Characteristics: Albendazole**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Caution with hepatic dysfunction | **Absorption** | F <5%, food enhances absorption up to 5 times |
| **Dose Adjustment Renal** | Not required | **Distribution** | Cyst, CSF |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic to 1 active metabolite; minor substrate of CYP3A4/5, 1A2 |
| **Pregnancy Category** | C | **Elimination** | <1% renal with half-life of 8-15 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to albendazole | **Black Box Warnings** | None |

**Medication Safety Issues: Albendazole**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Aplenzin, Relenza | No |

### Drug Interactions: Albendazole

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Grapefruit juice | Increased oral availability of albendazole | Often administered together to enhance absorption |

### Adverse Reactions: Albendazole

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Headaches, elevated LFTs | Nausea, vomiting, abdominal pain, dizziness, diarrhea, alopecia | Severe hypersensitivity, renal failure, hepatic failure, aplastic anemia, agranulocytosis, Stevens-Johnson syndrome |

**Efficacy Monitoring Parameters.** Monitor fecal specimens for ova and parasites for 3 wk after treatment; if positive, retreat. Ophthalmic examination in those with neurocysticercosis.

**Toxicity Monitoring Parameters.** LFTs and CBC at beginning of each 28-d cycle and every 2 wk. Negative pregnancy test prior to starting therapy.

**Key Patient Counseling Points.** Complete full course of therapy; administer with high-fat meals or grapefruit juice. Avoid pregnancy for at least 1 mo post-treatment. In children or those with difficulty swallowing tablets, tablets can be crushed or chewed and swallowed with water.

**Clinical Pearls.** Single-dose therapy makes this agent a treatment of choice for nematode infections. Neurocysticercosis: Use concurrent corticosteroids to minimize inflammatory reactions and anticonvulsant therapy to prevent seizures. Echinococcosis: More effective than mebendazole, so may be treatment of choice.



https://kat.cr/user/Blink99/

# ALBUTEROL: ProAir HFA, Proventil HFA, Ventolin HFA, Various



**Class:** Selective $\beta_2$-Adrenergic Agonist

**Dosage Forms.** **Metered-Dose Inhaler (MDI):** 90 (base) mcg/actuation; **Tablet:** 2 mg, 4 mg; **Extended-Release Tablet:** 4 mg, 8 mg; **Syrup:** 2 mg/5 mL; **Inhalation Solution:** 0.021%, 0.042%, 0.083%

**Common FDA Label Indication, Dosing, and Titration.**

1. Asthma (acute exacerbation): Adults, MDI, 4-8 inhalations every 20 min up to 4 h, then every 1-4 h prn; Children, 4-8 inhalations every 20 min for 3 doses, then every 1-4 h prn (use mask for children <4 y of age)
2. Asthma (bronchospasm): Adults and Children, MDI, 2 inhalations every 4-6 h prn; Adults and Children ≥12 y of age, oral, 2-4 mg immediate-release tablet po tid or qid or 4-8 mg extended-release tablet po q12h (*max* of 32 mg/d); Children 6-11 y of age, 2 mg immediate-release tablet po tid or qid or 4 mg extended-release tablet po q12h; Children 2-6 y of age, 0.1 mg/kg oral syrup po tid
3. Exercise-induced asthma, prevention: Adults, 2 inhalations 15-30 min prior to exercise; Children ≥4 y of age, 2 inhalations 15-30 min prior to exercise

ProAir HFA by Teva pictured

**Off-Label Uses.**

COPD: 2 inhalations every 4-6 h prn

**MOA.** Albuterol is a selective $\beta_2$-adrenergic agonist that acts on $\beta_2$-adrenergic receptors of intracellular adenyl cyclase to increase cyclic AMP levels resulting in bronchial smooth muscle relaxation.

**Drug Characteristics: Albuterol**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 50-85% (oral tablet), 100% (extended-release tablet), food decreases rate (but not extent) of absorption of extended-release tablet |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 156 L; 10% protein bound |
| **Dialyzable** | Unknown | **Metabolism** | 20% via sulfotransferases |
| **Pregnancy Category** | C | **Elimination** | 80% renal elimination, half-life (inhalation) 3.8 h, (oral) 3.7-5 h |
| **Lactation** | Compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

### Medication Safety Issues: Albuterol

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Do not crush extended-release tablets | No | Albutein, atenolol, Prilosec, Prinivil, Vantin | No |

### Drug Interactions: Albuterol

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Other short-acting sympathomimetics | May potentiate albuterol effect and increase risk of cardiovascular adverse effects | Avoid concurrent use |
| Beta-blockers (nonselective) | May decrease effectiveness of albuterol and produce bronchospasms | Avoid nonselective beta-blockers; monitor PFT if cardioselective beta-blockers used |
| Diuretics (non-potassium sparing) | May potentiate hypokalemia | Monitor potassium levels |
| Digoxin | May decrease digoxin levels | Monitor digoxin levels |
| MAOI and tricyclic antidepressants | May potentiate albuterol effect on cardiovascular system | Consider alternative therapy |

### Adverse Reactions: Albuterol

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Nausea, pharyngitis, rhinitis, throat irritation, upper respiratory tract infections | Angina, tachycardia, hypokalemia, tremor, nervousness, insomnia, cough, headache, viral lower respiratory infection | Paradoxical bronchospasms, pulmonary edema, atrial fibrillation |

**Efficacy Monitoring Parameters.** Resolution of asthma symptoms and PFTs.

**Toxicity Monitoring Parameters.** Use alternative therapy or seek emergency treatment if paradoxical bronchospasm occurs.

**Key Patient Counseling Points.** Instruct patient on inhaler technique, including priming and shaking well before using. Wash the mouthpiece and air dry thoroughly at least once a week (may cease to deliver medication if mouthpiece becomes blocked). Part of the extended-release tablet may pass into stool. Contact prescriber if more albuterol is needed to control symptoms than usual as this may indicate asthma deterioration. Report need to increase frequency of use for symptomatic relief to physician. Do not use more frequently than recommended.

**Clinical Pearls.** The National Heart, Lung, and Blood Institute asthma guidelines recommend short-acting beta-agonists (SABA) as the drug of choice for treating acute asthma symptoms and exacerbations. Do not use SABA as a component of chronic therapy without an anti-inflammatory agent. Solution for nebulization also available. MDI can be used with spacer if need be for proper administration. Some MDIs have a dose counter to help patient keep track of doses.



https://kat.cr/user/Blink99/

# ALENDRONATE: Fosamax, Binosto, Various



**Class:** Bisphosphonate

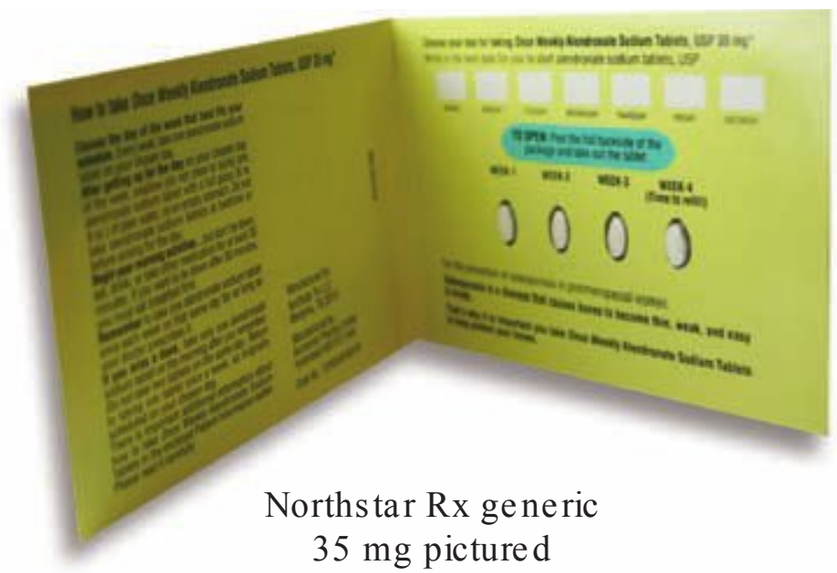
**Dosage Forms. Tablet:** 5 mg, 10 mg, 35 mg, 40 mg, 70 mg; **Solution:** 70 mg/75 mL; **Effervescent Tablet:** 70 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Postmenopausal osteoporosis: 70 mg po once weekly or 10 mg po daily
2. Postmenopausal osteoporosis, prophylaxis: 5 mg po daily or 35 mg po once weekly
3. Paget disease: 40 mg po daily for 6 mo
4. Osteoporosis, male: 10 mg once daily or 70 mg once weekly
5. Glucocorticoid-induced osteoporosis in those with daily dosage ≥7.5 mg of prednisone (or equivalent): 5 mg once daily; a dose of 10 mg once daily should be used in postmenopausal females who are not receiving estrogen

**Off-Label Uses.**

1. Postoperative knee arthroplasty: 10 mg once daily beginning after knee arthroplasty for up to 1 y



Northstar Rx generic
35 mg pictured

**MOA.** Alendronate binds to bone hydroxyapatite, and at the cellular level, inhibits osteoclast activity, thereby inhibiting bone resorption and modulating bone metabolism.

**Drug Characteristics: Alendronate**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F <1%, food impairs absorption, take 30-60 min prior to meal |
| **Dose Adjustment Renal** | CrCl <35 mL/min: avoid use | **Distribution** | Vd = 2576 L; 78% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Not metabolized |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 50% with a half-life in bone of more than 10 y |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Esophageal abnormalities, hypersensitivity, hypocalcemia, inability to sit or stand upright for at least 30 min; increased risk for adverse esophageal effects | **Black Box Warnings** | None |

### Medication Safety Issues: Alendronate

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| Fosamax Plus D | No | No | No | Risedronate, Flomax, Zithromax, fosinopril | No |

### Drug Interactions: Alendronate

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Aluminum, calcium, magnesium, or iron-containing products | Decreased bisphosphonate absorption | Separate administration by at least 30 min after alendronate, ideally 1-2 h |

### Adverse Reactions: Alendronate

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Fever, flu-like syndrome, gastric ulcer | Myalgia, bone pain, esophageal ulcer, abdominal pain, constipation, diarrhea, flatulence, indigestion, headache | Osteonecrosis of the jaw, esophageal cancer, immune hypersensitivity, arrhythmia, fractures |

**Efficacy Monitoring Parameters.** Increased BMD (T-score), decreased incidence of bone fractures.

**Toxicity Monitoring Parameters.** Baseline serum creatinine, calcium, phosphorous, severe skin rash, difficulty swallowing, swelling, tooth problems, severe pain.

**Key Patient Counseling Points.** Swallow the noneffervescent tablet whole with a large glass (240 mL) of plain water only. Dissolve 1 effervescent tablet in 120 mL of room temperature plain water only (not mineral water or flavored water); once effervescence stops, wait ≥5 min and stir the solution for ~10 s and then drink. Wait at least 30 min after you swallow the tablet before you eat or drink anything or take any other medicines. This will help your body absorb the medicine. Do not lie down for at least 30 min after taking this medicine, and do not lie down until after you have eaten some food.

**Clinical Pearls.** Concurrent chemotherapy and poor oral hygiene increase the risk of osteonecrosis of the jaw. Atypical fractures of the thigh have been reported in patients taking bisphosphonates for osteoporosis; discontinue therapy in patients who develop evidence of a femoral shaft fracture. Adequate calcium and vitamin intake required for efficacy. Men >70 y of age and women >50 y of age should consume 1200 mg of elemental calcium from all sources (dietary + supplements) and all adults >50 y of age should consume 800-1000 units of vitamin D daily with a target serum level of >30 ng/mL.



https://kat.cr/user/Blink99/

# ALLOPURINOL: Zyloprim, Various



**Class:** Xanthine Oxidase Inhibitor; Antigout

**Dosage Forms. Tablet:** 100 mg, 300 mg

Northstar Rx generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Gout, mild: 100-300 mg po daily; *max* dose 800 mg/d
2. Gout, moderate to severe: 400-600 mg po daily in 2-3 divided doses, *max* dose 800 mg/d
3. Hyperuricemia, tumor lysis syndrome: Children <6 y, 50 mg po tid or 150 mg po daily for 2-3 d; Children 6-10 y, 100 mg po tid or 300 mg po daily for 2-3 d; Adults, 600-800 mg/d po daily in 2-3 divided doses for 2-3 d; starting 12 h-3 d prior to chemotherapy

**Off-Label Uses.**

1. Malaria: 12 mg/kg/d po in 3 divided doses × 5 d, with quinine

**MOA.** Allopurinol decreases the production of uric acid by inhibiting the action of xanthine oxidase, the enzyme that converts hypoxanthine to xanthine and xanthine to uric acid.

**Drug Characteristics: Allopurinol**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 80-90%, no effect of food on absorption |
| **Dose Adjustment Renal** | CrCl 10-20 mL/min, 200 mg po daily; CrCl 3-9 mL/min, 100 mg po daily, CrCl <3 mL/min, 100 mg at extended intervals (>24 h) | **Distribution** | Vd = 1.6-2.43 L/kg; <1% protein bound |
| **Dialyzable** | Yes, supplementation may be needed after dialysis | **Metabolism** | Metabolized in the liver (78%) and red blood cells |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 80% with a half-life of 2 h, active metabolite (oxypurinol) has half-life of 15-25 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to allopurinol, concurrent use of didanosine | **Black Box Warnings** | None |

### Medication Safety Issues: Allopurinol

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Zovirax, Apresoline | No |

### Drug Interactions: Allopurinol

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Didanosine | Increased didanosine bioavailability | Avoid concurrent use |
| Azathioprine | Xanthine oxidase needed to eliminate azathioprine metabolite, mercaptopurine; when xanthine oxidase is inhibited by allopurinol, increases azathioprine effect and toxicity | Reduce azathioprine dose by 1/3 or avoid concurrent use |
| Cyclophosphamide | Unknown; increased cyclophosphamide toxicity (bone marrow suppression) | Avoid concurrent use |

### Adverse Reactions: Allopurinol

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Rash, maculopapular eruption, acute attacks of gout with initiation | Stevens-Johnson syndrome, toxic epidermal necrolysis, agranulocytosis, aplastic anemia, thrombocytopenia, granulomatous hepatitis, hepatotoxicity, immune hypersensitivity reaction, renal failure |

**Efficacy Monitoring Parameters.** Resolution of clinical signs of gout (pain, stiffness), serum uric acid concentrations measured after 48 h of therapy.

**Toxicity Monitoring Parameters.** LFTs, renal function, CBC.

**Key Patient Counseling Points.** Take after meals to lessen gastric irritation. Maintain adequate hydration during therapy to prevent kidney stones. Patient should avoid alcohol or caffeine while taking allopurinol. Seek medical attention if signs and symptoms of myelosuppression, agranulocytosis (severe neutropenia), or Stevens-Johnson syndrome (flu-like symptoms, spreading red rash, or skin/mucous membrane blistering) occur.

**Clinical Pearls.** Allopurinol for injection is also available, and has been designated an orphan product for use in the treatment of elevated serum or urinary uric acid levels secondary to lymphomas, leukemias, or solid tumors in patients intolerant of oral therapy. Full effect of allopurinol in chronic gout may take 2-6 wk, slow dose titration recommended.



https://kat.cr/user/Blink99/

# ALPRAZOLAM: Xanax, Various



**Class:** Benzodiazepine, Short or Intermediate. C-IV

**Dosage Forms. Tablet:** 0.25 mg, 0.5 mg, 1 mg, 2 mg; **Tablet, Disintegrating:** 0.25 mg, 0.5 mg, 1 mg, 2 mg; **Tablet, Extended Release:** 0.5 mg, 1 mg, 2 mg, 3 mg; **Solution:** 1 mg/mL

Sandoz generic
1 mg pictured

Sandoz generic
2 mg pictured

Dava generic
0.5 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Anxiety: immediate-release or orally disintegrating tablet, 0.25-0.5 mg po tid; *max* daily dose, 4 mg in divided doses
2. Panic disorder, with or without agoraphobia: immediate-release or orally disintegrating tablets, 0.5 mg po tid, extended-release 3-6 mg po daily; dose may be increased every 3-4 d by <1 mg/d

**Off-Label Uses.**

1. Alcohol withdrawal syndrome: 0.5-1 mg po bid × 7-10 d

**MOA.** Enhances the postsynaptic effect of the inhibitory neurotransmitter, γ-aminobutyric acid (GABA).

**Drug Characteristics: Alprazolam**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Reduce initial dose to 0.25 mg in advanced liver disease | **Absorption** | F = 80%, no effect of food on absorption of immediate release, food increases absorption of ER by 25% |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 0.9-1.2 L/kg, 80% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, 20-30%; major substrate of CYP3A4/5 |
| **Pregnancy Category** | D | **Elimination** | Renal 80% with a half-life of 10-12 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to benzodiazepines, narrow-angle glaucoma, concurrent ketoconazole, or itraconazole | **Black Box Warnings** | None |

**Medication Safety Issues: Alprazolam**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | ALPRAZolam | ALPRAZolam ER | No | Zantac, LORazepam, Xopenex | Avoid benzodiazepines (any type) for treatment of insomnia, agitation, or delirium |

## Drug Interactions: Alprazolam

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Alfentanil, opioids, and other respiratory depressants | Additive respiratory depression | Avoid if possible and consider dose reductions of both agents |
| CYP3A4/5 inducers | Increased alprazolam metabolism reduces alprazolam effectiveness | Monitor and consider dose increases of alprazolam |
| CYP3A4/5 inhibitors | Decreased alprazolam metabolism increases risk of alprazolam toxicity | Monitor and consider dose decreases of alprazolam |
| Digoxin | Reduced renal clearance of digoxin and increased digoxin toxicity | Monitor digoxin levels and consider dose reductions |
| Ethinyl estradiol and other estrogen-based birth control products | Inhibition of alprazolam metabolism and additional toxicity | Use with caution |

## Adverse Reactions: Alprazolam

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Ataxia, lethargy, retrograde amnesia, somnolence, weight gain, change in appetite, constipation, fatigue, cognitive dysfunction, decreased libido | Tachycardia, palpitations, nausea and vomiting, blurred vision, confusion | Seizures, mania, depression, liver failure, Stevens-Johnson syndrome |

**Efficacy Monitoring Parameters.** Reduction in anxiety symptoms.

**Toxicity Monitoring Parameters.** Seek medical attention if severe drowsiness, slow or rapid heartbeat or skipped beats, thoughts of suicide.

**Key Patient Counseling Points.** May cause drowsiness; avoid driving or other tasks requiring motor coordination. Do not crush or break extended-release product. Oral disintegrating tablet may be divided, but are unstable after breaking. If only 1/2 tablet taken, discard the other half. Allow oral disintegrating tablet to dissolve on your tongue. Avoid alcohol. Do not self-increase or abruptly discontinue use.

**Clinical Pearls.** Not for use in children. Consider reduced dose of benzodiazepines in hepatic impairment. Avoid use in elderly, appear more sensitive to the effects. Use CNS depressants concurrently with caution, may have additive effects. Avoid abrupt discontinuation after chronic use, may cause seizures. In general, should only be used for short periods of time, reevaluate need frequently.



https://kat.cr/user/Blink99/

# AMITRIPTYLINE: Elavil, Various

Sandoz generic pictured

**Class:** Tricyclic Antidepressant

**Dosage Forms. Tablet:** 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Depression: Adults, 75 mg po divided into 1-3 daily doses, titrate to *max* 300 mg/d; Children ≥12 y of age, 10 mg po tid or 20 mg po daily hs

**Off-Label Uses.**

1. Migraine prophylaxis: 10-25 mg po daily hs; titrate to *max* 150 mg/d
2. Chronic pain: 25-100 mg po daily hs; titrate to *max* 150 mg/d
3. Polyneuropathy, postherpetic neuralgia, treatment and prophylaxis: 10-25 mg po daily hs; may titrate to *max* 200 mg/d
4. Post-traumatic stress disorder (PTSD): 50 mg po daily; titrate to *max* 300 mg/d

**MOA.** Amitriptyline is a tricyclic antidepressant that blocks presynaptic reuptake of serotonin and norepinephrine with subsequent down-regulation of adrenergic receptors.

**Drug Characteristics: Amitriptyline**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Start with low initial doses and increase as needed and tolerated | **Absorption** | F = 100%; no effect of food on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd is highly variable |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic; minor substrate of CYP1A2, 2B6, 2C9, 2C19, and 3A4/5; major substrate of CYP2D6 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is minimal with a half-life of 9-27 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity; concurrent MAOI or MAOI use in last 14 d; use during acute recovery period after MI | **Black Box Warnings** | Suicidality; not approved for children <12 y of age |

## Medication Safety Issues: Amitriptyline

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Enalapril, imipramine, nortriptyline | Avoid. Highly anticholinergic, sedating, and cause orthostatic hypotension |

## Drug Interactions: Amitriptyline

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Anticholinergics | Additive adverse effects | Avoid concurrent use or monitor carefully |
| Antiarrhythmics, and drugs that cause QT prolongation | Increased risk of cardiotoxicity (QT prolongation, torsades de pointes, cardiac arrest) | Avoid concurrent use |
| CYP2D6 inducers | Increased amitriptyline metabolism reduces amitriptyline effectiveness | Monitor and consider dose increases of amitriptyline |
| CYP2D6 inhibitors | Decreased amitriptyline metabolism increases risk of amitriptyline toxicity | Monitor and consider dose decreases of amitriptyline |
| Linezolid, MAOIs, methylene blue, SSRIs | Increased risk of serotonin syndrome | Concomitant use with MAOIs contraindicated, others with caution |

## Adverse Reactions: Amitriptyline

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Sedation | Blurred vision, confusion, constipation, dizziness, sexual dysfunction, somnolence, urinary retention, weight gain, xerostomia | Cardiac dysrhythmia, hepatotoxicity, seizures, suicidal thoughts |

**Efficacy Monitoring Parameters.** Improvement in target symptoms of depression. Reduction or improvement in pain or decreased frequency of migraines.

**Toxicity Monitoring Parameters.** Worsening of depression, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases. Monitor ECGs and LFTs.

**Key Patient Counseling Points.** Avoid activities requiring mental alertness, alcohol, and other CNS depressants. Symptomatic improvement may not be seen for a few weeks. Avoid sudden discontinuation of drug. Do not use alcohol.

**Clinical Pearls.** Safety and effectiveness in children <12 y of age have not been established. Antidepressants increased the risk of suicidal thinking and behavior in children, adolescents, and young adults in short-term studies with major depressive disorder (MDD) and other psychiatric disorders. This drug can cause anticholinergic side effects.



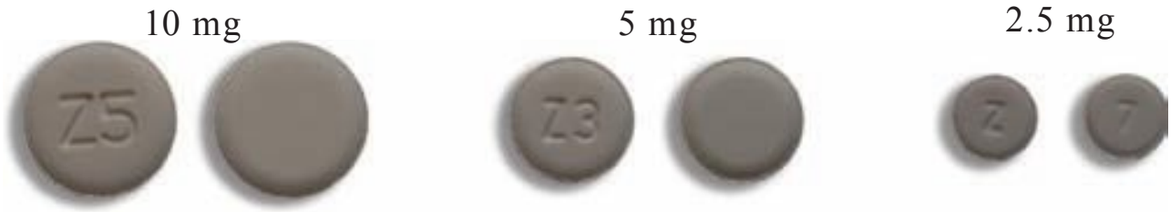
https://kat.cr/user/Blink99/

# AMLODIPINE: Norvasc, Various

A

**Class:** Calcium Channel Blocker

**Dosage Forms. Tablet:** 2.5 mg, 5 mg, 10 mg



Zygenerics generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Hypertension: Children 6-17 y of age , 2.5-5 mg po daily; Adults, 5-10 mg po daily
2. Stable angina: 5-10 mg po daily
3. Variant angina: 5-10 mg po daily

**Off-Label Uses.**

1. Diabetic nephropathy: 5-15 mg po daily
2. Left ventricular hypertrophy: 5-10 mg po daily
3. Raynaud phenomenon: 10 mg po daily

**MOA.** Amlodipine is a long-acting dihydropyridine calcium-channel-blocking drug with potent arterial and coronary vasodilating properties.

**Drug Characteristics: Amlodipine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Reduce initial dose to 2.5 mg po daily in hepatic impairment | **Absorption** | F = 64-90%; no effect of food on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 21 L/kg; 93% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, 90%; major substrate of CYP3A4/5 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 10% with a half-life of 30-50 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to amlodipine | **Black Box Warnings** | None |

**Medication Safety Issues: Amlodipine**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | AmLODIPine | No | No | aMILoride Navane, Norvir, Vascor | No |

## Drug Interactions: Amlodipine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Beta-blockers | Increased risk of hypotension, bradycardia | Avoid concurrent use or monitor BP and HR |
| Clopidogrel | Decreased antiplatelet activity of clopidogrel by amlodipine | Avoid concurrent use |
| CYP3A4/5 inducers | Increased amlodipine metabolism reduces amlodipine effectiveness | Monitor and consider dose increases of amlodipine |
| CYP3A4/5 inhibitors | Decreased amlodipine metabolism increases risk of amlodipine toxicity | Monitor and consider dose decreases of amlodipine |
| NSAIDs | Decreased antihypertensive effect of amlodipine | Avoid concurrent use or monitor BP |

## Adverse Reactions: Amlodipine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Peripheral edema, pulmonary edema | Abdominal pain, arthralgia, constipation, dizziness, fatigue, f ushing, headache, hypotension, hyperkalemia, impotence, myalgia, nausea, palpitations, pruritus, rash, tachycardia, urticaria | Hepatotoxicity, thrombocytopenia, AMI, angina |

**Efficacy Monitoring Parameters.** Decreased BP, reduction in chest pain, decreased number of weekly angina attacks, reduction in use of prophylactic nitroglycerin to relieve chest pain, improvement in signs/symptoms of heart failure.

**Toxicity Monitoring Parameters.** Signs/symptoms of peripheral edema, increased HR, LFTs.

**Key Patient Counseling Points.** Instruct patient to report signs/symptoms of hypotension or exacerbation of angina with initial dosing and dose changes. Avoid alcohol while taking drug. Report signs/symptoms of peripheral edema, fatigue, hypotension, or hepatic dysfunction. Do not discontinue drug suddenly as this may cause rebound hypertension. This medicine may cause dizziness. Avoid activities that could be dangerous if not alert. Dizziness may be worse if too much water is lost from the body due to excessive sweating, diarrhea, or vomiting.

**Clinical Pearls.** Safety and efficacy not established in pediatric patients <6 y of age. Elderly, small, or frail patients, or when adding to other antihypertensive therapy, decrease initial dose by 2.5 mg po daily.



https://kat.cr/user/Blink99/

# AMOXICILLIN: Amoxil, Various



**Class:** β-Lactam Antibiotic

**Dosage Forms. Capsule:** 250 mg, 500 mg; **Chewable Tablet:** 125 mg, 200 mg, 250 mg, 400 mg; **Drop:** 50 mg/mL; **Suspension:** 125 mg/5 mL, 200 mg/5 mL; 250 mg/5 mL, 400 mg/5 mL; **Tablet:** 500 mg, 875 mg; **Tablet, Extended Release:** 775 mg

Sandoz generic 250 mg pictured

Teva generic 250 mg pictured

Aurobindo generic 875 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Acute otitis media: Adults, 500-875 mg po q12h × 10 d; Children, 80-90 mg/kg/d po in 2-3 divided doses
2. Lower respiratory tract infection: Adults, 1 g po tid × 10 d; Children, 45 mg/kg/d divided q12h
3. Pharyngitis, tonsillitis: Adults and Children >12 y, 775 mg po daily × 10 d
4. Streptococcal pharyngitis: Adults, 1 g po daily × 10 d; Children, 50 mg/kg po once daily for 10 d, *max* 1 g daily
5. Ear, nose, and throat infection, infection of skin and/or subcutaneous tissue, infection of genitourinary system: Adults, 500-875 mg po q12h × 10 d; Children, 25-45 mg/kg/d po divided q12h
6. *Helicobacter pylori* gastrointestinal tract infection: 1 g po bid with PPI

**Off-Label Uses.**

1. Bacterial endocarditis, prophylaxis: Adults, 2 g po 1 h before procedure; Children, 50 mg/kg po 1 h prior to procedure, *max* 2 g daily
2. Lyme disease: 500 mg po tid × 21-30 d; Children: 50 mg/kg/d po in 3 divided doses × 21-30 d

**MOA.** Semisynthetic penicillin derivative that inhibits the biosynthesis of bacterial cell wall mucopeptide. Typically active against *Streptococcus*, *Enterococcus, Staphylococcus*, and Enterobacteriaceae.

**Drug Characteristics: Amoxicillin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 85%, no effect of food on absorption |
| **Dose Adjustment Renal** | Moderate, increase interval to 8-12 h; severe, increase interval to q24h | **Distribution** | 17-20% protein bound. Lung, pleural f uid, bile, liver, and inner ear |
| **Dialyzable** | Yes (hemodialysis only) | **Metabolism** | Partially hepatic |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 50-70% with a half-life of 1-2 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

### Medication Safety Issues: Amoxicillin

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Extended-release tablet | No | Amoxapine, Augmentin | No |

### Drug Interactions: Amoxicillin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Methotrexate | Decreased methotrexate clearance | Avoid concurrent use or consider methotrexate dose reduction or monitoring levels |
| Venlafaxine | Increased risk of serotonin syndrome | Avoid concurrent use |
| Warfarin | Increased risk of bleeding | Increase warfarin monitoring |

### Adverse Reactions: Amoxicillin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Diarrhea, nausea | Skin rash, vomiting, headache | Severe hypersensitivity, renal failure, hepatic failure, pancytopenia |

**Efficacy Monitoring Parameters.** Resolution of clinical signs of infection.

**Toxicity Monitoring Parameters.** Severe diarrhea, dark urine, yellowing of skin or eye, unusual bruising or bleeding, blistering skin rash, or shortness of breath.

**Key Patient Counseling Points.** Complete full course of therapy and take exactly as directed. For the suspension, shake well and store in the refrigerator. Note short expiration after reconstitution. Can take with food if causes upset stomach. Avoid mixing suspension with food or beverages and use with measuring device that comes with prescription. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner.

**Clinical Pearls.** There is cross-hypersensitivity between penicillin and cephalosporins; use with caution in cephalosporin allergic. May resume normal activities after 24 h of antibiotics if afebrile. Extended-release tablet not approved for children <12 y of age. Combination with clavulanate preferred for acute bacterial rhinosinusitis. May decrease effectiveness of oral contraceptives.



https://kat.cr/user/Blink99/

# AMOXICILLIN/CLAVULANATE: Augmentin, Various



**Class:** β-Lactam Antibiotic

875 mg/125 mg 500 mg/125 mg

Teva generic pictured

**Dosage Forms. Tablet:** 250 mg amoxicillin/125 mg clavulanate, 500 mg amoxicillin/125 mg clavulanate; 875 mg amoxicillin/125 mg clavulanate; **Tablet, Extended Release:** 1000 mg amoxicillin/62.5 mg clavulanate; **Chewable Tablet:** 200 mg amoxicillin/28.5 mg clavulanate, 400 mg amoxicillin/57 mg clavulanate; **Suspension:** 125 mg amoxicillin/31.25 mg clavulanate/5 mL, 200 mg amoxicillin/28.5 mg clavulanate/5 mL, 250 mg amoxicillin/62.5 mg clavulanate/5 mL; 400 mg amoxicillin/57 mg clavulanate/5 mL, 600 mg amoxicillin/42.9 mg clavulanate/5 mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Acute otitis media: Adults, 500-875 mg po q12h × 10 d; Children, 80-90 mg/kg/d po in 2-3 divided doses
2. Community acquired pneumonia: Adults, 2000 mg po bid × 7-10 d
3. Lower respiratory tract infection: Adults, 1000 mg po tid × 10 d; Children, 45 mg/kg/d po divided q12h
4. Sinusitis, infection of skin or subcutaneous tissue, infectious disease of genitourinary system: Adults, 500-875 mg po q12h × 10 d; Children, 25-45 mg/kg/d po divided q12h

**Other Uses.**

1. Streptococcal pharyngitis: Adults, 875 mg po q12h or 500 mg po q8h; Children, 45 mg/kg/d divided q12h

**MOA.** Amoxicillin is a semisynthetic penicillin derivative. Typically active against *Streptococcus, Enterococcus, Staphylococcus*, and Enterobacteriaceae. Amoxicillin is not effective against β-lactamase–producing bacteria. Clavulanate, a β-lactamase inhibitor, has weak antibacterial activity but is a potent inhibitor of plasmid-mediated β-lactamases and protects amoxicillin from degradation by β-lactamases.

**Drug Characteristics: Amoxicillin/Clavulanate**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Consider dose adjustment in severe impairment | **Absorption** | F = 85%, no effect of food on absorption |
| **Dose Adjustment Renal** | CrCl 10-30 mL/min, increase interval to q12h; CrCl <10 mL/min, increase interval to q24h; avoid 875 mg tablet and extended-release tablet for those on hemodialysis or CrCl <30 mL/min | **Distribution** | 17-20% protein bound. Lung, pleural f uid, bile, liver, and inner ear |
| **Dialyzable** | Yes (peritoneal and hemodialysis) | **Metabolism** | Amoxicillin not metabolized, extensive metabolism of clavulanic acid |
| **Pregnancy Category** | B | **Elimination** | Renal elimination of amoxicillin is 50-70% with a half-life of 1-2 h |
| **Lactation** | Compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to penicillins, extended-release products are contraindicated in patients on dialysis or severe renal dysfunction | **Black Box Warnings** | None |

### Medication Safety Issues: Amoxicillin/Clavulanate

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| Augmentin XR, ES 600 | No | Extended-release tablet | No | Amoxicillin | No |

### Drug Interactions: Amoxicillin/Clavulanate

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Methotrexate | Decreased methotrexate clearance | Avoid concurrent use or consider methotrexate dose reduction or monitoring levels |
| Venlafaxine | Increased risk or serotonin syndrome | Avoid concurrent use |
| Warfarin | Increased risk of bleeding | Increase warfarin monitoring |

### Adverse Reactions: Amoxicillin/Clavulanate

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Nausea, diarrhea | Skin rash, vomiting, mycosis, candidiasis | Severe hypersensitivity, renal failure, hepatic failure, pancytopenia |

**Efficacy Monitoring Parameters.** Resolution of clinical signs of infection.

**Toxicity Monitoring Parameters.** Severe diarrhea, dark urine, yellowing of skin or eye, unusual bruising or bleeding, blistering skin rash, or shortness of breath.

**Key Patient Counseling Points.** Complete full course of therapy. Take dose with food to ensure proper absorption. For the suspension, shake well and store in the refrigerator. Note short expiration after reconstitution of 10 d. Avoid mixing suspension with food or beverages. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner.

**Clinical Pearls.** There is cross-hypersensitivity between penicillin and cephalosporin; use with caution in cephalosporin-allergic patients. Incidence of diarrhea is higher than with amoxicillin alone. May decrease effectiveness of oral contraceptives.



https://kat.cr/user/Blink99/

# ANASTROZOLE: Arimidex, Various



**Class:** Aromatase Inhibitor

**Dosage Forms. Tablet:** 1 mg

Astra Zeneca 1 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Breast cancer, adjuvant, postmenopausal, hormone receptor-positive: 1 mg po daily × 5 y
2. Breast cancer, advanced or metastatic, postmenopausal, following tamoxifen therapy: 1 mg po daily, until tumor progression

**Off-Label Uses.**

1. Breast cancer, neoadjuvant, postmenopausal, hormone receptor-positive: 1 mg po daily for 3-6 mo
2. Breast cancer, prophylaxis, postmenopausal women at high risk: 1 mg po daily × 5 y

**MOA.** Adrenally generated androstenedione is the primary source of estrogen in postmenopausal women and is converted to estrone by aromatase. Anastrozole is a nonsteroidal aromatase inhibitor.

**Drug Characteristics: Anastrozole**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Severe, use with caution | **Absorption** | F = 80%, minimal food effect |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 300-500 L; 40% protein bound |
| **Dialyzable** | Unknown | **Metabolism** | 85% metabolism but not by CYP |
| **Pregnancy Category** | X | **Elimination** | Renal elimination is 10% with a half-life of 50 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity and pregnancy | **Black Box Warnings** | None |

**Medication Safety Issues: Anastrozole**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | Yes | Aromasin, letrozole | No |

**Drug Interactions: Anastrozole**

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Tamoxifen | Reduced anastrozole levels | Avoid concurrent use |

**Adverse Reactions: Anastrozole**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Edema, hypertension, vasodilation, nausea, vomiting, arthralgia, arthritis, osteoporosis, hot f ashes, depression, GI tract disorder | Angina, chest pain, thrombophlebitis, alopecia, pruritus, rash, weight gain, hyperlipidemia, xerostomia, elevated LFTs, thromboembolic events, ischemic cardiovascular disease, diarrhea, elevated serum cholesterol | Myocardial infarction, endometrial cancer, cerebrovascular accident |

**Efficacy Monitoring Parameters.** Decrease in tumor size if used in metastatic or neoadjuvant setting. Absence of tumor recurrence if used in adjuvant setting.

**Toxicity Monitoring Parameters.** BP, cholesterol panel, BMD panel (serum albumin, calcium and alkaline phosphatase, and phosphate and osteocalcin measurements), dual-energy x-ray absorptiometry for monitoring osteoporosis.

**Key Patient Counseling Points.** Seek medical attention if shortness of breath, swelling, chest pain, vaginal bleeding, blistering rash, rapid weight gain, severe nausea and vomiting, yellowing of the eyes or skin. Take with or without food. Because anastrozole lowers level of estrogen, can lead to loss of BMD and increase risk of fractures.

**Clinical Pearls.** As effective as tamoxifen in treating metastatic breast cancer, but decreased incidence of adverse effects (thromboembolic events and endometrial cancer). Not indicated in premenopausal women.



https://kat.cr/user/Blink99/

# ARIPIPRAZOLE: Abilify



**Class:** Antipsychotic

**Dosage Forms. Tablet:** 2 mg, 5 mg, 10 mg, 15 mg, 20 mg, 30 mg; **Tablet (Disintegrating):** 10 mg, 15 mg; **Solution:** 1 mg/mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Bipolar disorder, manic or mixed episodes: Adults, 2 mg po daily, may titrate to 15-30 mg po daily; Children >10 y, 2 mg po daily, may titrate to 10 mg po daily
2. Schizophrenia: Adults, 10-15 mg po daily, may titrate to *max* 30 mg/d; Children >13 y, 2 mg po daily, may titrate to 10 mg po daily
3. Depression, adjunctive with antidepressant: 2-4 mg po daily, may titrate to 15 mg po daily

Bristol-Myers Squibb 15 mg pictured

**Off-Label Uses.** None

**MOA.** Aripiprazole is an atypical antipsychotic agent (quinolinone derivative). It exhibits relatively high affinity for dopamine $D_2$ and $D_3$ receptors and serotonin 5-$HT_{1A}$ and 5-$HT_{2A}$ receptors.

**Drug Characteristics: Aripiprazole**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 87%; no effect of food on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 4.9 L/kg; >99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, 80%; major substrate of CYP2D6 and 3A4/5 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 10-20% with a half-life of 75-94 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | CYP2D6 poor metabolizers should receive 50% lower dose |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | Dementia, suicidality |

**Medication Safety Issues: Aripiprazole**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | ARIPiprazole | No | No | Omeprazole, pantoprazole, RABEprazole | Avoid use for behavioral problems of dementia unless nonpharmacologic options have failed and patient is threat to self or others |

### Drug Interactions: Aripiprazole

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inducers | Increased aripiprazole metabolism reduces aripiprazole effectiveness | Use with caution; monitor efficacy. Consider aripiprazole dose increase of 50% |
| CYP3A4/5, 2D6 inhibitors | Decreased aripiprazole metabolism increases risk of aripiprazole toxicity | Initiate aripiprazole at 50% lower doses; monitor for side effects |

### Adverse Reactions: Aripiprazole

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Akathisia, anxiety, extrapyramidal disease, headache, increased appetite, somnolence, weight gain | Blurred vision, constipation, diarrhea, dizziness, excessive salivation, fatigue, hyperglycemia, insomnia, nausea, orthostatic hypotension, rash, restlessness, somnolence, tremor, vomiting, xerostomia | Neuroleptic malignant syndrome, pancytopenia, QT prolongation, seizures, suicidal thoughts, tardive dyskinesia |

**Efficacy Monitoring Parameters.** Improvement in mental status (schizophrenia, mania, depression symptoms).

**Toxicity Monitoring Parameters.** FPG and CBC prior to treatment and periodically in patients with risk factors for diabetes. Patients at high risk for suicide should be closely supervised during therapy. Monitor ECG at baseline and periodically during therapy.

**Key Patient Counseling Points.** Avoid activities requiring mental alertness or coordination until drug effects are realized. Drug may impair heat regulation. Drug may also lower seizure threshold. Patients with history of seizures or conditions that lower seizure threshold should report increased seizure activity. Report worsening depression, suicidal ideation, or unusual changes in behavior, especially at initiation of therapy or with dose changes. Children, adolescents, and young adults are at higher risk for these effects during the first few months of therapy. Report signs/symptoms of hyperglycemia, extrapyramidal effects, and neuroleptic malignant syndrome. Avoid sudden discontinuation. Avoid alcohol.

**Clinical Pearls.** Solution may be substituted for the tablet dosages on an mg-per-mg basis for up to a 25-mg dose; patients on 30-mg tablets should receive 25 mg of the solution. Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Injectable formulation also available.



https://kat.cr/user/Blink99/

# ATAZANAVIR: Reyataz



**Class:** Antiretroviral Agent, Protease Inhibitor

**Dosage Forms. Capsule:** 150 mg, 200 mg, 300 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Treatment of HIV-1 infections in combination with at least 2 other antiretroviral agents: Adults and Children ≥13 y of age and ≥40 kg, 300-400 mg po daily; Children <13 y of age, weight based and used in combination with ritonavir

**Off-Label Uses.** None

**MOA.** Binds to the site of HIV-1 protease activity and inhibits cleavage of viral Gag-Pol polyprotein precursors into individual functional proteins required for infectious HIV. This results in the formation of immature, noninfectious viral particles.

300 mg 200 mg

Bristol-Myers Squibb pictured

**Drug Characteristics: Atazanavir**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Use with caution if moderate hepatic impairment | **Absorption** | F approaches 100%, food increases absorption by 50% |
| **Dose Adjustment Renal** | Not required | **Distribution** | CSF and semen |
| **Dialyzable** | Yes | **Metabolism** | Hepatic; substrate of CYP3A4/5, strong inhibitor of CYP3A4/5 and UGT1A1 |
| **Pregnancy Category** | B | **Elimination** | 80% hepatic, with half-life of 7 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | Resistance is associated with HIV mutations |
| **Contraindications** | Hypersensitivity or concurrent therapy with alfuzosin, cisapride, ergot derivatives indinavir, irinotecan, lovastatin, midazolam (oral), pimozide, rifampin, sildenafil, simvastatin, or triazolam | **Black Box Warnings** | None |

**Medication Safety Issues: Atazanavir**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Do not open capsule | Yes | No | No |

### Drug Interactions: Atazanavir

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Antacids | Decreased absorption of atazanavir | Separate use by 2 h |
| CYP3A4/5 inhibitors | Decreased metabolism and increased toxicity of atazanavir | Avoid strong inhibitors, monitor and dose reduce atazanavir with concurrent moderate or weak inhibitors |
| CYP3A4/5 inducers | Increased metabolism and decreased efficacy of atazanavir | Avoid |
| CYP3A4/5 substrates | Decreased metabolism and increased toxicity of CYP3A4/5 substrates via inhibition of CYP3A4/5 | Avoid sensitive CYP3A4/5 substrates |
| Drugs that prolong PR or QT | Additive PR or QT prolongation and cardiotoxicity | Avoid or monitor ECGs |
| Oral contraceptives | Reduced efficacy of oral contraceptives, unknown mechanism | Use an alternative form of contraception |
| Proton pump inhibitors, $H_2$ antagonists | Decreased absorption of atazanavir | Avoid |
| UGT1A1 substrates | Decreased metabolism and increased toxicity of UGT1A1 substrates via inhibition of UGT1A1 | Avoid sensitive UGT1A1 substrates |

### Adverse Reactions: Atazanavir

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Rash, hyperlipidemia, elevated LFTs, abdominal pain, elevated bilirubin level, cough, fever | Nausea, vomiting, diarrhea, headaches, hyperglycemia, nausea, AV block, peripheral edema | Hypersensitivity, renal failure, PR and QT prolongation, torsades de pointes, cholelithiasis, left bundle branch block |

**Efficacy Monitoring Parameters.** HIV viral load, CD4 count, drug levels with some concomitant medications.

**Toxicity Monitoring Parameters.** LFTs, bilirubin, ECG monitoring in patients with prolonged PR interval or with concurrent AV nodal blocking drugs, CBCs, lipid panel.

**Key Patient Counseling Points.** Multiple, potentially serious drug interactions; do not take new medications without consulting health-care provider. Take with food. Do not open, chew, or crush capsule. Does not prevent transmission of HIV; practice safe sex. Do not skip doses. Report cardiac symptoms to physician. Do not take antacids within 2 h of this medication.

**Clinical Pearls.** Not recommended for infants <3 mo of age. Atazanavir dose varies with concurrent medications, pregnancy, and prior HIV therapy.



https://kat.cr/user/Blink99/

# ATENOLOL: Tenormin, Various



**Class:** β-Adrenergic Blocker, Cardioselective

**Dosage Forms. Tablet:** 25 mg, 50 mg, 100 mg

Sandoz generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Angina pectoris, chronic: 50 mg po daily; titrate to 100-200 mg po daily
2. Hypertension: Adults, 50 mg po daily, titrate to 100 mg po daily; Children, 0.5-1 mg/kg/d po in 1-2 divided doses, titrate to 2 mg/kg/d po in 1-2 divided doses (*max* 100 mg/d)

**Off-Label Uses.**

1. Cardiac dysrhythmia: Adults, 50-100 mg po daily; Children, 0.3-1.4 mg/kg po daily, titrate to 2 mg/kg po daily
2. Migraine prophylaxis: 50-100 mg po daily

**MOA.** Atenolol is a cardioselective β-adrenergic that decreases AV nodal conduction in supraventricular tachycardias and blockade of catecholamine-induced dysrhythmias.

**Drug Characteristics: Atenolol**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 50%; food decreases AUC by 20% |
| **Dose Adjustment Renal** | CrCl 15-35 mL/min, *max* dose 50 mg po daily; CrCl <15 mL/min, *max* dose 25 mg po daily | **Distribution** | Vd = 50-75 L; <5% protein bound |
| **Dialyzable** | Yes, give 25-50 mg after each dialysis procedure | **Metabolism** | Not metabolized |
| **Pregnancy Category** | D | **Elimination** | Renal elimination of atenolol is 40-50% and 50% in feces as unchanged drug, with a half-life of 6-7 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to atenolol, severe sinus bradycardia, 2nd- or 3rd-degree AV block, overt heart failure or cardiogenic shock | **Black Box Warnings** | Avoid abrupt withdrawal |

## Medication Safety Issues: Atenolol

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Albuterol | No |

## Drug Interactions: Atenolo

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| NSAIDs | Decreased antihypertensive effect of atenolol | Avoid concurrent use or monitor blood pressure |
| Amiodarone, dronedarone | Increased risk of bradycardia, heart block, sinus arrest | Avoid concurrent use in patients with sick sinus syndrome or AV block |
| Antidiabetic drugs | Decreased glycemic control | Monitor blood glucose levels |
| Calcium channel blockers, quinidine | Increased risk of hypotension and/or bradycardia and AV block | Avoid concurrent use |
| Clonidine | Exaggerated clonidine withdrawal response | Avoid abrupt withdrawal of clonidine while on concomitant beta-blocker therapy |
| Digoxin | Increased risk of AV block | Monitor HR, ECG, and serum digoxin concentrations |
| Alpha-blockers, fentanyl | Increased risk of hypotension | Monitor blood pressure |

## Adverse Reactions: Atenolol

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Bradyarrhythmias, cold extremities, dizziness, fatigue, hypotension, depression | Bronchospasm, dyspnea, somnolence, sexual dysfunction | Heart failure, pulmonary embolism |

**Efficacy Monitoring Parameters.** Decreased BP, reduction in chest pain, decreased number of weekly angina attacks, reduction in use of prophylactic nitroglycerin to relieve chest pain, improvement in signs/symptoms of heart failure.

**Toxicity Monitoring Parameters.** Signs/symptoms of heart failure, decreased HR. Monitor serum electrolytes and renal function at baseline and periodically.

**Key Patient Counseling Points.** Take on an empty stomach and avoid alcohol. Avoid abrupt discontinuation; exacerbations of angina may occur. Report signs/symptoms of hypotension, heart failure, or exacerbation of angina with initial dosing and dose changes. May cause dizziness or drowsiness. Diabetic patients to carefully follow blood sugar levels as beta-blockers may mask symptoms of hypoglycemia.

**Clinical Pearls.** Safety and efficacy not established in children. Full effectiveness may not be seen for 1-2 wk. Taper slowly before stopping as sudden discontinuation can cause angina or MI.



https://kat.cr/user/Blink99/

# ATOMOXETINE: Strattera



**Class:** Norepinephrine Reuptake Inhibitor, CNS Stimulant

**Dosage Forms. Capsule:** 10 mg, 18 mg, 25 mg, 40 mg, 60 mg, 80 mg, 100 mg

Lilly pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. ADHD: Children >6 y of age and weighing ≤70 kg, 0.5 mg/kg/d po, may titrate to lower of 1.4 mg/kg/d or 100 mg/d; Children >6 y of age and weighing >70 kg, 40 mg/d po, may titrate to 100 mg/d; Adults, 40 mg po daily, may titrate to 100 mg/d

**Off-Label Uses.** None

**MOA.** Atomoxetine is a selective norepinephrine reuptake inhibitor that produces therapeutic effects in patients with ADHD. The exact mechanism of how selective inhibition of presynaptic norepinephrine exerts effects in ADHD has not been determined.

**Drug Characteristics: Atomoxetine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Child-Pugh Class B: initial and target doses should be reduced to 50% of normal dose; Child-Pugh Class C: initial and target doses should be reduced to 25% of normal dose | **Absorption** | F = 63% (normal metabolizers); 94% (poor metabolizers); food does not affect absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 0.85 L/kg; 98% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic metabolism to 1 active metabolite; major substrate of CYP2D6 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 80% and 17% in feces, with a half-life of 5.2-21.6 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | CYP2D6 poor metabolizers, dose as with drug interaction with CYP2D6 inhibitor |
| **Contraindications** | Hypersensitivity to atomoxetine; concomitant use of MAOIs or use within 2 wk; narrow-angle glaucoma, pheochromocytoma | **Black Box Warnings** | Suicidality in children and adolescents |

## Medication Safety Issues: Atomoxetine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | AtoMOXetine | Do not open capsules | No | AtorvaSTATin | No |

## Drug Interactions: Atomoxetine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP2D6 inhibitors | Decreased atomoxetine metabolism increases risk of atomoxetine toxicity | Children >6 y of age weighing >70 kg, dose 0.5 mg/kg/d po, may titrate up to 1.2 mg/kg/d; Children >6 y of age weighing >70 kg, dose 40 mg po daily, may titrate to 80 mg/d |
| Albuterol | Increased HR | Monitor BP and HR |
| MAOIs | Increased risk of hypertensive crisis (headache, hyperpyrexia, hypertension) | Concomitant use contraindicated |

## Adverse Reactions: Atomoxetine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Abdominal pain, headache, insomnia, loss of appetite, nausea, weight loss, xerostomia | Agitation, anxiety, decreased growth and development, dysmenorrhea, erectile dysfunction, increased blood pressure, rash, somnolence, urinary retention, vomiting, weight loss | Dyskinesia, mania, prolonged QT interval, psychotic disorders, seizure, suicidal thoughts, sudden cardiac death, tachycardia, hepatotoxicity |

**Efficacy Monitoring Parameters.** Improvement of mental and behavioral symptoms of ADHD.

**Toxicity Monitoring Parameters.** BP and HR. Signs of clinical worsening, suicidality, or unusual changes in behavior; particularly at start of and during first few months of therapy or when dose is adjusted. Aggressive behavior or hostility, new onset or worsening; in pediatric patients at start of treatment.

**Key Patient Counseling Points.** Avoid activities requiring mental alertness or coordination until drug effects are realized. Growth rate and weight may need to be monitored more frequently in children. Report new or worsened psychiatric problems, chest pain, palpitations, dyspnea, or signs/symptoms of cardiac dysrhythmias, MI, or cerebrovascular accident. Do not open capsules as atomoxetine is an ocular irritant.

**Clinical Pearls.** Safety and effectiveness not established in children <6 y of age. Increased risk of suicidal ideation in short-term studies in children or adolescents with ADHD. Monitor patients closely for suicidality (suicidal thinking and behavior), clinical worsening, or unusual changes in behavior. Close observation and communication with the prescriber by families and caregivers is recommended.



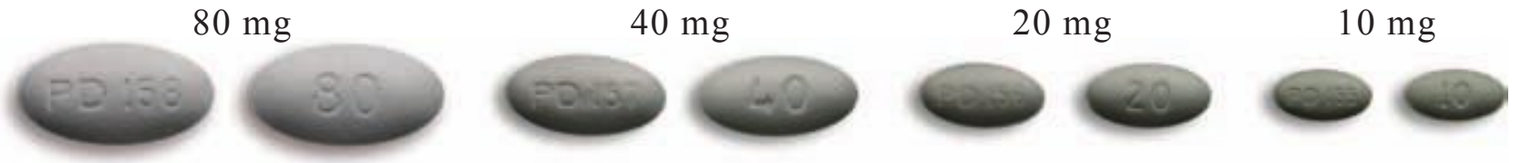
https://kat.cr/user/Blink99/

# ATORVASTATIN: Lipitor, Various



**Class:** HMG-CoA Reductase Inhibitor

**Dosage Forms. Tablet:** 10 mg, 20 mg, 40 mg, and 80 mg




Pfizer pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Hyperlipidemia: 10-20 mg po daily, may increase to 80 mg po daily
2. Primary and secondary prevention of atherosclerotic cardiovascular disease: 20-40 mg po daily, may increase to 80 mg po daily for those patients requiring high-intensity therapy (eg, LDL >190 mg/dL)
3. Secondary prevention of cardiovascular events in patients with or at high risk for CAD: 80 mg daily, may reduce dose to 40 mg po daily if high dose not tolerated
4. Familial hypercholesterolemia (homozygous): Children (boys and postmenarchal girls aged 10-17 y), 10 mg po daily, may titrate to 40 mg po daily; Adults 10-80 mg po daily

**Off-Label Uses.** None

**MOA.** HMG-CoA reductase inhibitors competitively inhibit conversion of HMG-CoA to mevalonate, an early rate-limiting step in cholesterol synthesis. A compensatory increase in LDL receptors, which bind and remove circulating LDL-cholesterol, results. Production of LDL-cholesterol also can decrease because of decreased production of VLDL-cholesterol or increased VLDL; removal by LDL receptors.

**Drug Characteristics: Atorvastatin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Avoid use in patients with active liver disease or unexplained persistent elevated LFTs | **Absorption** | F = 14%; food slows rate of absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 381 L; 98% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic; major substrate of CYP3A4/5 and P-glycoprotein; inhibits P-glycoprotein |
| **Pregnancy Category** | X | **Elimination** | Biliary elimination, renal elimination 1-2%, with a half-life of 7-14 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | LDL receptor alters efficacy |
| **Contraindications** | Hypersensitivity to atorvastatin, pregnancy or lactation | **Black Box Warnings** | None |

## Medication Safety Issues: Atorvastatin

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | AtorvaSTATin | No | No | AtoMOXetine, lovastatin, nystatin, pravastatin, simvastatin | No |

## Drug Interactions: Atorvastatin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Aliskiren | Increased aliskiren concentrations and risk of toxicity | Monitor for hypotension |
| CYP3A4/5 inducers | Increased atorvastatin metabolism reduces atorvastatin effectiveness | Monitor fasting lipid panels |
| CYP3A4/5 inhibitors | Decreased atorvastatin metabolism increases risk of atorvastatin toxicity | Avoid concurrent use or monitor for myopathy and measure CK levels; *max* dose 20 mg/d |
| Clopidogrel | Decreased antiplatelet activity of clopidogrel by atorvastatin | Avoid concurrent use |
| Cyclosporine, HIV protease inhibitors, hepatitis C protease inhibitors | Increased risk of myopathy or rhabdomyolysis | Avoid concurrent use |
| P-glycoprotein substrates | Metabolism of P-glycoprotein substrates inhibited by atorvastatin, resulting in substrate toxicity | Monitor for adverse effects and reduce substrate dose if necessary |

## Adverse Reactions: Atorvastatin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Arthralgia, diarrhea, headache | Increased liver enzymes, indigestion, insomnia, musculoskeletal pain, myalgia, nasopharyngitis, nausea, increased hemoglobin A1c | Rhabdomyolysis, tendon rupture |

**Efficacy Monitoring Parameters.** Total cholesterol, LDL-cholesterol, and triglycerides levels; HDL-cholesterol levels.

**Toxicity Monitoring Parameters.** Signs/symptoms of rhabdomyolysis (myalgias, dark urine, arthralgias, fatigue) or hepatotoxicity; LFTs should be performed at baseline, 12 wk after initiation of therapy, and every 6 mo thereafter; serum creatine kinase should be measured in patients experiencing muscle pain and in those receiving other drugs associated with myopathy.

**Key Patient Counseling Points.** Contact prescriber immediately if pregnancy occurs while taking atorvastatin. Avoid alcohol, grapefruit, and grapefruit juice while taking drug. Atorvastatin does not take the place of lifestyle changes (diet, exercise) to lower cholesterol levels.

**Clinical Pearls.** Lipid level assessment should be done within 6-12 wk following dose initiation or titration, then every 3-12 mo. If 2 consecutive LDL levels are <40 mg/dL, consider decreasing dose. Statins have been reported to increase risk of diabetes, although this data is controversial as statins are only associated with very mild increase in blood glucose and there is no established causal relationship.



https://kat.cr/user/Blink99/

# AZELASTINE: Astelin, Astepro, Various

A

**Class:** Nasal Antihistamine

**Dosage Forms. Nasal Spray:** 0.15%, 137 mcg/actuation

**Common FDA Label Indication, Dosing, and Titration.**

1. Perennial allergic rhinitis: Adults and Children ≥12 y of age, 2 sprays per nostril bid; Children 6-12 y of age, 1 spray per nostril bid
2. Seasonal allergic rhinitis: Adults and Children ≥12 y of age 1-2 sprays per nostril bid; Children 6-12 y of age, 1 spray per nostril bid
3. Vasomotor rhinitis: Adults and Children ≥12 y of age, 2 sprays per nostril bid

**Off-Label Uses.** None

**MOA.** Azelastine is a selective $H_1$-receptor antagonist that blocks release of histamine from cells involved in the allergic response. It also inhibits other mediators of allergic reactions (eg, leukotrienes, etc), and reduces chemotaxis and eosinophil activation.

**Drug Characteristics: Azelastine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 40% when administered nasally |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 14.5 L/kg; 78-95% protein bound |
| **Dialyzable** | Unknown | **Metabolism** | Hepatic, 90% |
| **Pregnancy Category** | C | **Elimination** | Fecal elimination is 75% with a half-life of 22-25 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

Meda pictured

### Medication Safety Issues: Azelastine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Astelin and Astepro | No |

### Drug Interactions: Azelastine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Cimetidine | Inhibition of azelastine metabolism | Avoid concurrent use or monitor for increased azelastine adverse effects |

### Adverse Reactions: Azelastine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Bitter taste in mouth, headache, somnolence | Fatigue, epistaxis, pharyngitis, rhinitis, sneezing | |

**Efficacy Monitoring Parameters.** Decrease in rhinitis symptoms.

**Toxicity Monitoring Parameters.** Seek medical attention if severe allergic reactions occur.

**Key Patient Counseling Points.** Avoid spraying in eyes. Somnolence has been reported with nasal administration; instruct patient to avoid alcohol use and hazardous activities such as driving or operating machinery until level of sedation is known. Review proper instillation technique, including priming the spray with initial use and if have not used for 3 or more days. Blow nose prior to using. Do not spray into wall separating nostrils. To prevent contamination, keep tip of nose spray clean.

**Clinical Pearls.** Also available as ophthalmic product for ocular rhinitis symptoms. Also available in nasal product in combination with fluticasone.



https://kat.cr/user/Blink99/

# AZITHROMYCIN: Zithromax, Various



**Class:** Macrolide Antibiotic

**Dosage Forms. Oral Tablet:** 250 mg, 500 mg, 600 mg; **Microspheres for Suspension:** 2 g/bottle; **Powder for Oral Suspension:** 100 mg/5 mL, 200 mg/5 mL, 1 g packet

Wockhardt generic 250 mg pictured

Teva generic 500 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Acute infective exacerbation of COPD, skin or tissue infection: 500 mg po daily × 3 d or 500 mg po × 1 dose, then 250 mg po daily × 2-5 d
2. Bacterial sinusitis: Adults, 500 mg po daily × 3 d; Children, 10 mg/kg po daily × 3 d, or 2 g po × 1 dose
3. Chancroid, nongonococcal cervicitis, nongonococcus urethritis: 1 g po × 1 dose
4. Community-acquired pneumonia: 500 mg po daily × 3 d or 500 mg po × 1, then 250 mg po daily × 2-5 d; Infants ≥6 mo of age, tablets and immediate-release suspension, 10 mg/kg po on day 1, then 5 mg/kg po daily × 2-5 d *or* extended-release suspension, <34 kg, 60 mg/kg po × 1; >34 kg, 2 g po × 1 dose
5. Gonorrhea, urethritis, or cervicitis: 2 g po × 1 dose
6. Streptococcal pharyngitis: 500 mg po × 1 dose, then 250 mg po daily × 2-5 d; Children, 12 mg/kg po daily × 5 d

**Other Uses.**

1. Traveler's diarrhea: Adults, 1000 mg po × 1 dose, or 500 mg po daily × 3 d; Children, 10 mg/kg po daily × 3 d
2. Bacterial endocarditis, prophylaxis: Adults, 500 mg po 30-60 min prior to procedure; Children, 15 mg/kg po 30-60 min prior to procedure

**MOA.** Azithromycin is a macrolide antibiotic that is slightly less active than erythromycin against gram-positive bacteria but substantially more active against *M.* (*B.*) *catarrhalis, Haemophilus* sp., *Legionella* sp., *Neisseria* sp., *Bordetella* sp., *Mycoplasma* spp., and *C. trachomatis*. Azithromycin binds to the 50S ribosomal subunit, thus interfering with microbial protein synthesis.

**Drug Characteristics: Azithromycin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 38%, no effect of food on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Blister f uid, bronchial secretions, cervix, ear f uid, ovaries, sputum, soft tissue |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 6% with a half-life of 68 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to azithromycin, erythromycin, or any macrolide or ketolide antibiotic | **Black Box Warnings** | None |

## Medication Safety Issues: Azithromycin

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Azathioprine, erythromycin, Fosamax | No |

## Drug Interactions: Azithromycin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Agents that prolong the QT interval and class III antiarrhythmics | Additive cardiotoxicity | Avoid concurrent use |
| Statins | Increased risk of rhabdomyolysis; mechanism unknown | Use caution with concurrent use |
| Digoxin | Increased digoxin toxicity via decreased bacterial metabolism of digoxin in the lower intestine | Use caution with concurrent use |
| Ergot alkaloids | Increased risk of acute ergotism via inhibition of ergot metabolism | Contraindicated |
| Nelfinavir | Increased azithromycin concentrations via decreased clearance | Caution with concurrent use |
| Warfarin | Increased risk of bleeding via inhibition of warfarin metabolism | Monitor INR closely |

## Adverse Reactions: Azithromycin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Diarrhea, nausea, vomiting, abdominal pain | Headache, elevated liver enzymes, flatulence | Stevens-Johnson syndrome, chest pain, severe hypersensitivity, myasthenia gravis, QT prolongation, torsades de pointes, hepatitis |

**Efficacy Monitoring Parameters.** Resolution of signs and symptoms of infection.

**Toxicity Monitoring Parameters.** Seek medical attention if chest pain, blistering skin rash, or extreme fatigue.

**Key Patient Counseling Points.** Complete full course of therapy. Take tablets with or without food, although some patients report increased tolerability when given with food. Avoid mixing suspension with food or beverages, but food can be taken afterward. Take extended-release suspension (Zmax) on empty stomach, at least 1 h before or 2 h after a meal. Zmax must be used in the first 12 h of reconstitution. Avoid concurrent use of aluminum or magnesium-containing antacids (exception: Zmax can be taken without regards to antacids containing magnesium hydroxide and/or aluminum hydroxide). Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner.

**Clinical Pearls.** Use with caution in severe renal, hepatic, or cardiac disease. Pediatric use of extended-release tablets is restricted to community-acquired pneumonia. Max dose in children is 500 mg. There is a small absolute increase in the risk of cardiovascular death during a 5-d course of oral azithromycin. Also available as ophthalmic for bacterial conjunctivitis, and injectable for severe infections.



https://kat.cr/user/Blink99/

# BACLOFEN: Lioresal, Various



**Class:** Centrally Acting Skeletal Muscle Relaxant

**Dosage Forms. Oral Tablet:** 10 mg, 20 mg

Northstar Rx generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Spasticity: 5 mg orally tid; may increase dose in 5-15 mg/d increments; *max* dose in Adults and Children ≥12 y of age, 80 mg/d; *max* dose in children 8-12 y of age, 60 mg/d; *max* dose in children <8 y of age, 40 mg/d

**Off-Label Uses.**

1. Intractable hiccoughs, 5 mg po bid, increasing to 15-45 mg/d in 3 divided doses; or 10-20 mg 2-3 times daily

**MOA.** Baclofen inhibits both monosynaptic and polysynaptic reflexes at the spinal level, possibly by hyperpolarization of afferent terminals, although actions at supraspinal sites may also occur and contribute to its clinical effect. Baclofen is an analogue of γ-aminobutyric acid (GABA), but there is no conclusive evidence that actions on GABA systems are involved in the production of its clinical effects.

**Drug Characteristics: Baclofen**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 100%, no effect of food on absorption |
| **Dose Adjustment Renal** | In patients with renal dysfunction, monitor carefully for toxicity and reduce dose as necessary | **Distribution** | Vd = 59.1 L; 30% protein bound |
| **Dialyzable** | Yes | **Metabolism** | Limited hepatic metabolism |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 60-80% with a half-life of 3-7 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | Avoid abrupt discontinuation of intrathecal product |

**Medication Safety Issues: Baclofen**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | Yes, intrathecal | Bactroban | No |

**Drug Interactions:** **Baclofen.** None known

**Adverse Reactions: Baclofen**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Nausea, asthenia, dizziness, somnolence | Constipation, fatigue, hypotension, shivering, urinary complication | Pneumonia, GI hemorrhage |

**Efficacy Monitoring Parameters.** Reduction in muscle spasm, passive limb movement, pain relief.

**Toxicity Monitoring Parameters.** Seek medical attention if severe dizziness, confusion, sedation, or rebound spasticity occurs.

**Key Patient Counseling Points.** Because of the possibility of sedation, patients should be cautioned regarding the operation of motor vehicles or dangerous machinery while taking baclofen. Patients should be cautioned that the CNS effects of baclofen may be additive to those of alcohol and other CNS depressants.

**Clinical Pearls.** Implantable pumps that administer baclofen intrathecally are also available for patients with spasticity. Constipation occurs in 100% of patients undergoing intrathecal administration, and abrupt discontinuation of intrathecal therapy (intentional or inadvertent) is commonly fatal.



https://kat.cr/user/Blink99/

# BENAZEPRIL: Lotensin, Various



**Class:** ACE-I, Antihypertensive

**Dosage Forms. Oral Tablet:** 5 mg, 10 mg, 20 mg, 40 mg

Teva generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Hypertension: Adults, 10 mg po daily, may titrate to 20-40 mg po daily (*max* 80 mg/d); Children ≥6 y of age, 0.2 mg/kg po daily (*max* 0.6 mg/kg/d or 40 mg/d)

**Off-Label Uses.**

1. Diabetic nephropathy: 10 mg po daily
2. Heart failure: 5-40 mg po daily
3. Kidney disease: 10 mg po daily

**MOA.** Benazepril is a competitive ACE-I. It also reduces serum aldosterone, leading to decreased sodium retention, potentiates the vasodilator kallikrein–kinin system, and can alter prostanoid metabolism, inhibit the sympathetic nervous system, and inhibit the tissue renin–angiotensin system.

**Drug Characteristics: Benazepril**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 37%, no effect of food on absorption |
| **Dose Adjustment Renal** | CrCl <30 mL/min, initial dose is 5 mg po daily, titrate to effect (*max* 40 mg/d) | **Distribution** | Vd = 8.7 L; 97% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic metabolism to 1 active metabolite (benazeprilat) |
| **Pregnancy Category** | D | **Elimination** | Renal elimination is 33%, bile 12% with a half-life of 0.6 h (parent drug) and 22 h (benazeprilat) |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity; history of angioedema; anuria; concomitant use with aliskiren in patients with diabetes mellitus | **Black Box Warnings** | Pregnancy |

**Medication Safety Issues: Benazepril**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Benadryl | No |

### Drug Interactions: Benazepril

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Potassium-sparing diuretics | Increased risk of hypotension, hyperkalemia | Avoid concurrent use or monitor BP and serum potassium levels |
| Angiotensin receptor blockers (ARBs) | Increased risk of hypotension, hyperkalemia, nephrotoxicity | Avoid concurrent use or monitor BP, SCr, and potassium levels |
| Potassium supplements, salt substitutes | Increased risk of hyperkalemia and cardiac arrhythmias | Avoid concurrent use or monitor serum potassium level |
| NSAIDs | Decrease antihypertensive and natriuretic effect of benazepril, increased risk of nephrotoxicity | Avoid concurrent use or monitor BP and SCr level |
| Azathioprine | Increased risk of myelosuppression | Avoid concurrent use, monitor for anemia or leucopenia |
| Diuretics | Increased risk of postural hypotension due to hypovolemia | Monitor BP, rise from seated position slowly |

### Adverse Reactions: Benazepril

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Diarrhea, dizziness, dry cough, fatigue, headache, hyperkalemia, nausea, nephrotoxicity, rash, tachycardia, vomiting | Angioedema, birth defects, liver failure, Stevens-Johnson syndrome |

**Efficacy Monitoring Parameters.** Decreased BP.

**Toxicity Monitoring Parameters.** Signs/symptoms of angioedema (swelling of the face, eyes, lips, tongue, or throat), severe persistent cough, hypotension; monitor baseline and periodic electrolytes, SCr, BUN, urine protein.

**Key Patient Counseling Points.** Avoid pregnancy. Use potassium supplements or salt substitutes only under medical supervision. May cause dizziness that may worsen if dehydrated. Take at the same time daily.

**Clinical Pearls.** Observe patients who are volume depleted for at least 2 h after taking the initial dose of benazepril. A liquid suspension can be made for patients who cannot swallow pills.



https://kat.cr/user/Blink99/

# BENZONATATE: Tessalon Perles, Various



**Class:** Antitussive

**Dosage Forms.** **Oral Capsule, Liquid Filled:** 100 mg, 150 mg, 200 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Cough: Adults and Children >10 y of age, 100-200 mg po tid prn, *max* 600 mg/d

**Off-Label Uses.**

1. Endotracheal intubation hiccups: 100 mg po × 1 dose, may repeat in 4 h

**MOA.** Benzonatate acts peripherally by anesthetizing the stretch receptors located in the respiratory passages, lungs, and pleura by dampening their activity and thereby reducing the cough reflex at its source.

Amneal generic 100 mg pictured

**Drug Characteristics: Benzonatate**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Unknown |
| **Dose Adjustment Renal** | Not required | **Distribution** | Unknown |
| **Dialyzable** | Not dialyzable | **Metabolism** | Unknown |
| **Pregnancy Category** | C | **Elimination** | Unknown |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

**Medication Safety Issues: Benzonatate**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Do not bite, chew, or open; swallow capsule whole | No | No | No |

**Drug Interactions: Benzonatate.** None known

**Adverse Reactions: Benzonatate**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| If capsules are broken or chewed, oral and pharyngeal numbness | Dizziness, headache, sedation, somnolence, bizarre behavior (mental confusion and visual hallucinations) | Severe hypersensitivity reactions |

**Efficacy Monitoring Parameters.** Resolution of clinical signs of cough.

**Toxicity Monitoring Parameters.** Seek medical attention if rash or hives, itching, difficulty breathing or swallowing, confusion, or hallucinations occur.

**Key Patient Counseling Points.** Do not chew capsules or allow capsules to dissolve in mouth as oropharyngeal anesthesia will occur, plus the liquid in the capsule has an incredibly foul taste. Administer with food or milk if GI upset occurs. Accidental ingestion of as few as 1-2 capsules by children <2 y of age has been fatal. The drug appearance (round, clear liquid-filled capsules) may be attractive to children, so particular care should be taken to keep out of reach.

**Clinical Pearls.** Benzonatate was approved by the FDA in 1958. Very little pharmacologic or pharmacokinetic data exist for this product. Do not spill the bottle—will take you hours to track down capsules that are spilled.



https://kat.cr/user/Blink99/

# BENZTROPINE: Cogentin, Various



**Class:** Antiparkinsonian, Anticholinergic

**Dosage Forms. Oral Tablet:** 0.5 mg, 1 mg, 2 mg

Core Pharma generic 1 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Extrapyramidal disease, medication-induced movement disorder: Adults, 1-4 mg po daily or bid; Children ≥3 y of age, 0.02-0.05 mg/kg/dose once or twice daily
2. Parkinsonism: 1-2 mg/d po, may titrate to range 0.5-6 mg/d po

**Off-Label Uses.** None

**MOA.** Benztropine possesses anticholinergic and antihistamine effects. May inhibit reuptake and storage of dopamine.

**Drug Characteristics: Benztropine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 29% |
| **Dose Adjustment Renal** | Not required | **Distribution** | Protein binding unknown |
| **Dialyzable** | Not dialyzable | **Metabolism** | Unknown |
| **Pregnancy Category** | B | **Elimination** | Unknown |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to benztropine, patients <3 y of age | **Black Box Warnings** | None |

**Medication Safety Issues: Benztropine**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Bromocriptine | Avoid |

**Drug Interactions: Benztropine**

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Amantadine | Increased CNS toxicity (confusion, hallucinations) | Monitor for signs of toxicity |
| Phenothiazines | Decreased phenothiazine concentrations, enhanced anticholinergic effects | Monitor for efficacy |
| Haloperidol | Excessive anticholinergic effects | Monitor for signs of toxicity |

**Adverse Reactions: Benztropine**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Blurred vision, confusion, constipation, disorientation, dysuria, mydriasis, nausea, urinary retention, xerostomia | Anhidrosis, drug-induced psychosis, heat stroke, increased body temperature, tachycardia, visual hallucinations |

**Efficacy Monitoring Parameters.** Reduction in extrapyramidal movements, rigidity, tremor, gait disturbances.

**Toxicity Monitoring Parameters.** Monitor for anticholinergic effects including dry mouth and constipation.

**Key Patient Counseling Points.** Drug may impair heat regulation. Advise patient to use caution with activities leading to an increased core temperature, such as strenuous exercise, exposure to extreme heat, or dehydration. Patient should avoid activities requiring mental alertness or coordination until drug effects are realized. Instruct patient to report sudden muscle weakness or stiffness, and signs/symptoms of tardive dyskinesia (tongue thrusting, facial grimacing/tics, random movements of extremities). Patient should not drink alcohol while taking this drug.

**Clinical Pearls.** Benztropine may have more adverse effects than amantadine when used for Parkinson disease. Injectable formulation also available but must be administered at hospital or MD office.



https://kat.cr/user/Blink99/

# BIMATOPROST: Lumigan, Latisse



**Class:** Prostaglandin, Antiglaucoma Agent, Cosmetic Agent for Eyelash Growth

**Dosage Forms. Ophthalmic Solution:** 0.01%, 0.03%

**Common FDA Label Indication, Dosing, and Titration.**

1. Ocular hypertension and open-angle glaucoma: 1 drop in affected eye(s) daily in the evening
2. Hypotrichosis of the eyelashes: 1 drop nightly to clean, upper eyelid margin at base of eyelashes, blot excess, repeat with new sterile applicator to opposite eyelid, do not apply to lower eyelids

**Off-Label Uses.** None

**MOA.** Bimatoprost is a synthetic prostaglandin analogue. Bimatoprost lowers intraocular pressure (IOP) by increasing the outflow of aqueous humor through both the trabecular meshwork and uveoscleral drainage systems. The exact mechanism of action for bimatoprost in stimulating eyelash growth is unknown.

**Drug Characteristics: Bimatoprost**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Systemic absorption following ocular instillation is very low |
| **Dose Adjustment Renal** | Not required | **Distribution** | 88% protein binding after systemic absorption |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic metabolism, extent unknown |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 67% with a half-life of 45 min |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

Allergan 0.03% solution pictured

### Medication Safety Issues: Bimatoprost

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | No |

### Drug Interactions: Bimatoprost

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Latanoprost | Increased IOP | Avoid concurrent use |

### Adverse Reactions: Bimatoprost

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Conjunctival hyperemia, eyelash growth, ocular pruritus | Application pigmentation changes to the eyelid, eyelash and periocular skin, abnormal hair growth, eyelid erythema, dry eye, eye irritation, photophobia | Macular retinal edema, bacterial keratitis |

**Efficacy Monitoring Parameters.** Reduction in IOP. Desired growth of eyelashes and resulting improvement in social life.

**Toxicity Monitoring Parameters.** Seek medical attention if symptoms of ocular irritation are severe.

**Key Patient Counseling Points.** Wash your hands and remove contact lenses before using the medicine. For administration of Lumigan, lie down or tilt head back. With index finger, pull down the lower lid of eye to form a pocket. Hold the dropper close to eye with the other hand. Drop the correct number of drops into the pocket made between lower lid and eyeball. Gently close eyes. Place index finger over the inner corner of eye for 1 min. Do not rinse or wipe the dropper or allow it to touch anything, including eye. Put the cap on the bottle right away. Separate from other eye drops by 5 min. For administration of Latisse, wash face and remove makeup before applying. Do not rinse eye if solution gets into the eye. Do not reuse supplied sterile applicators or use any other brush/applicator other than those supplied. Use a new applicator for second eye. Do not apply to lower lid, or more than once per day. Reinsert contact lens after 15 min.

**Clinical Pearls.** There is a risk of permanent increased iris pigmentation associated with instillation of this product, and with leakage of Latisse into the eye. The effect of Latisse on eyelash length, thickness, and darkness is not permanent and will return to baseline upon discontinuation of bimatoprost.



https://kat.cr/user/Blink99/

# BISOPROLOL: Zebeta, Various



**Class:** Cardioselective β-Adrenergic Blocker

**Dosage Forms. Oral Tablet:** 5 mg, 10 mg

Sandoz generic 5 mg pictured

Sandoz generic 10 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Hypertension: 2.5-5 mg po daily, may titrate to *max* of 20 mg po daily

**Off-Label Uses.**

1. Angina: 5-20 mg po daily
2. Atrial fibrillation: 2.5-10 mg po daily
3. Heart failure: 1.25-10 mg po daily

**MOA.** Bisoprolol is a cardioselective β-adrenergic blocker that decreases AV nodal conduction in supraventricular tachycardia and blockade of catecholamine-induced dysrhythmias. The antihypertensive mechanism is unknown, but contributing factors are, renin blockade, and decreases in myocardial contractility and cardiac output.

**Drug Characteristics: Bisoprolol**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Initiate with 2.5 mg po daily, may titrate to *max* of 10 mg po daily | **Absorption** | F = 80%; food has no effect on absorption |
| **Dose Adjustment Renal** | Initiate with 2.5 mg po daily, may titrate to *max* of 10 mg po daily | **Distribution** | Protein binding 30%; distribution limited to extracellular f uid space and kidneys |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic; major substrate of CYP3A4/5 |
| **Pregnancy Category** | C | **Elimination** | Eliminated 50% unchanged in urine with a half-life of 9-12 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to bisoprolol, severe sinus bradycardia, 2nd- or 3rd-degree AV block, overt heart failure, cardiogenic shock | **Black Box Warnings** | None |

**Medication Safety Issues: Bisoprolol**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | DiaBeta, Zetia | No |

## Drug Interactions: Bisoprolol

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inducers | Increased bisoprolol metabolism reduces bisoprolol effectiveness | Monitor and consider dose increases of bisoprolol |
| CYP3A4/5 inhibitors | Decreased bisoprolol metabolism increases risk of bisoprolol toxicity | Monitor and consider dose decreases of bisoprolol |
| NSAIDs | Decreased antihypertensive effect of bisoprolol | Avoid concurrent use or monitor BP |
| Antidiabetic drugs | Decreased glycemic control | Monitor FBG |
| Calcium channel blockers, amiodarone, dronedarone | Increased risk of hypotension and/or bradycardia and AV block | Avoid concurrent use |
| Clonidine | Exaggerated clonidine withdrawal response | Avoid abrupt withdrawal of clonidine while on concomitant beta-blocker therapy |
| Digoxin | Increased risk of AV block | Monitor heart rate, ECG, and serum digoxin concentrations |
| Alpha-blockers, ACE-Is, fentanyl | Increased risk of hypotension | Monitor BP |

## Adverse Reactions: Bisoprolol

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Bradyarrhythmias, cold extremities, dizziness, fatigue, hypotension | Anorexia, bronchospasm, dyspnea, depression, diarrhea, headache, hyperglycemia, hyperuricemia, hypokalemia, hyponatremia, nausea, orthostatic hypotension, rash, somnolence, sexual dysfunction, vomiting | Heart failure |

**Efficacy Monitoring Parameters.** Decreased BP.

**Toxicity Monitoring Parameters.** Signs/symptoms of heart failure, decreased heart rate, ECG. Baseline and periodic serum, and urine electrolytes; renal function; uric acid and FBG.

**Key Patient Counseling Points.** Instruct patient to report signs/symptoms of dyspnea, hypotension, or heart failure. May cause dizziness; avoid alcohol, CNS depressants, or activities that require alertness. Rise slowly from a sitting/supine position, as drug may cause orthostatic hypotension. Avoid abrupt discontinuation, may cause rebound hypertension. Recommend avoiding NSAIDs while taking this drug.

**Clinical Pearls.** Safety in children has not been established.



https://kat.cr/user/Blink99/

# BRIMONIDINE: Alphagan P, Various



**Class:** Adrenergic Agonist; Antiglaucoma Agent

**Dosage Forms. Ophthalmic Solution:** 0.1%, 0.15%, 0.2%

**Common FDA Label Indication, Dosing, and Titration.**

1. Ocular hypertension: 1 drop in affected eye(s) q8h, strength chosen based on therapeutic effect
2. Open-angle glaucoma: 1 drop in affected eye(s) q8h, strength chosen based on therapeutic effect

**Off-Label Uses.**

1. Capsulotomy of posterior lens capsule: 1 drop of 0.2% solution in operative eye 1 h prior to surgery, then 1 drop in operative eye immediately following procedure

**MOA.** Brimonidine, a relatively selective α-adrenergic agonist, reduces aqueous humor production and increases uveoscleral outflow. It is used to lower IOP in open-angle glaucoma or ocular hypertension.

Allergan 0.15% solution pictured

**Drug Characteristics: Brimonidine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Minor systemic absorption following ocular instillation |
| **Dose Adjustment Renal** | Not required | **Distribution** | Effective penetration of brimonidine into aqueous humor |
| **Dialyzable** | Not dialyzable | **Metabolism** | 24% and occurs by unknown enzymes |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 74% with a half-life of 3 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to brimonidine, concurrent MAOIs, age <2 y | **Black Box Warnings** | None |

**Medication Safety Issues: Brimonidine**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Bromocriptine | No |

### Drug Interactions: Brimonidine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| MAOIs | Increased risk of CNS depression | Avoid concurrent use |

### Adverse Reactions: Brimonidine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Allergic conjunctivitis, conjunctival discoloration | Burning sensation in eye, hypertension, xerostomia, somnolence, hypersensitivity reaction, visual disturbance | Syncope, arrhythmias |

**Efficacy Monitoring Parameters.** Reduction in IOP.

**Toxicity Monitoring Parameters.** Seek medical attention if syncope occurs or if symptoms of ocular irritation are severe.

**Key Patient Counseling Points.** Wash your hands and remove contact lenses before using the medicine. For administration, lie down or tilt head back. With index finger, pull down the lower lid of eye to form a pocket. Hold the dropper close to eye with the other hand. Drop the correct number of drops into the pocket made between lower lid and eyeball. Gently close eyes. Place index finger over the inner corner of your eye for 1 min. Do not rinse or wipe the dropper or allow it to touch anything, including eye. Put the cap on bottle right away. Reinsert contacts after 15 min. Separate administration of other ophthalmic agents by 5 min.

**Clinical Pearls.** This agent has no specific advantage over other similar products for the reduction in IOP in chronic ocular hypertension or in the treatment of glaucoma. Topical product available for treatment of rosacea.



https://kat.cr/user/Blink99/

# BUDESONIDE: Pulmicort Respules, Pulmicort Flexhaler, Various

**Class:** Inhaled Corticosteroid

**Dosage Forms.** **Inhalation Suspension:** 0.25 mg/2 mL, 0.5 mg/2 mL, 1 mg/2 mL; **Metered-Dose Inhaler (MDI):** 90 mcg/actuation, 180 mcg/actuation

**Common FDA Label Indication, Dosing, and Titration.**

1. Asthma: Children 1-8 y of age with no previous inhaled corticosteroid therapy, 0.5 mg inhaled via nebulization in 1 or 2 divided doses; Children 1-8 y of age previously treated with corticosteroids, 0.5 mg inhaled via nebulization daily or bid, may titrate to 1 mg/d; Children >8 y of age and Adults, 180-360 mcg bid via MDI, *max* 720 mcg bid via MDI

**Off-Label Uses.** None

**MOA.** Budesonide is an anti-inflammatory with potent glucocorticoid and weak mineralocorticoid activity. It exhibits a broad range of active inhibition against multiple cell types and mediators involving allergic and nonallergic/irritant-mediated inflammation.

**Drug Characteristics: Budesonide**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 6% |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 3 L/kg; protein binding 85-90% |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic; major substrate of CYP3A4/5 |
| **Pregnancy Category** | B | **Elimination** | Renal elimination 60%, fecal elimination 15-29%, with a half-life of 2-3 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to budesonide; hypersensitivity to milk proteins (Flexhaler); primary treatment of status asthmaticus or other acute episodes of asthma | **Black Box Warnings** | None |

AstraZeneca pictured

B

### Medication Safety Issues: Budesonide

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | No |

### Drug Interactions: Budesonide

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Azole antifungals and macrolides | Increase budesonide concentrations | Avoid long-term concomitant therapy with budesonide |
| CYP3A4/5 inducers | Increased budesonide metabolism reduces budesonide effectiveness | Monitor and consider dose increases of budesonide |
| CYP3A4/5 inhibitors | Decreased budesonide metabolism increases risk of budesonide toxicity | Monitor and consider dose decreases of budesonide |

### Adverse Reactions: Budesonide

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Upper respiratory tract infections | Cough, diarrhea, dysphonia, headache, nausea, oral candidiasis, throat irritation | Cataracts, decreased body growth, decreased bone mineral density |

**Efficacy Monitoring Parameters.** Monitor PFTs. Resolution of asthma symptoms (symptoms, number of exacerbations, nighttime awakenings, need for rescue albuterol).

**Toxicity Monitoring Parameters.** Growth velocity in pediatric patients during prolonged therapy.

**Key Patient Counseling Points.** Advise patient on proper inhalation technique. Gently swirl nebulizer suspension before use. Use entire vial of inhalation suspension immediately after opening to avoid contamination; deliver over 5-15 min using a jet nebulizer with mouthpiece or face mask. After administration, rinse mouth with water and spit, and wash face to minimize risk of developing oral candidiasis. Provided as a strip of 5 small plastic containers with sealed caps; each container holds 1 dose. The strip of containers is sealed inside a foil pouch. Keep any unused containers inside the pouch. Once foil pouch is opened, the containers will only be good for 2 wk.

**Clinical Pearls.** This drug is not indicated for acute asthma attacks. Respules indicated only in children; budesonide in MDI form available for treatment of older children and adults. Also available in rectal and nasal formulations, and in MDI in combination with formoterol. Oral tablets and capsules available for systemic treatment of Crohn disease and ulcerative colitis.



https://kat.cr/user/Blink99/

# BUDESONIDE/FORMOTEROL: Symbicort



**Class:** Inhaled Corticosteroid/Bronchodilator Combination

**Dosage Forms. Metered-Dose Inhaler (MDI):** (Budesonide/Formoterol) 80 mcg/4.5 mcg/inhalation, 160 mcg/4.5 mcg/inhalation

**Common FDA Label Indication, Dosing, and Titration.**

1. Asthma: Children ≥12 y of age and Adults, 80 mcg/4.5 mcg, 2 inhalations bid, may titrate to 160 mcg/4.5 mcg, 2 inhalations bid
2. COPD: 160 mcg/4.5 mcg 2 inhalations bid

**Off-Label Uses.**

1. Asthma: Children 5-11 y of age, 80 mcg/4.5 mcg, 2 inhalations bid

**MOA.** Budesonide is an anti-inflammatory with potent glucocorticoid and weak mineralocorticoid activity. It exhibits a broad range of active inhibition against multiple cell types and mediators involving allergic and nonallergic/irritant-mediated inflammation. Formoterol is a long-acting selective $\beta_2$-adrenergic agonist that produces bronchodilation.

80 mcg/4.5 mcg 160 mcg/4.5 mcg
AstraZeneca pictured

**Drug Characteristics: Budesonide/Formoterol**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 39% for budesonide; unknown for formoterol inhalation |
| **Dose Adjustment Renal** | Not required | **Distribution** | Protein binding 85-90% (budesonide); 31-64% for formoterol |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic; major substrate of CYP3A4/5 (budesonide) |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 60% with a half-life of 2-3 h (budesonide); renal elimination is 1-28% with a half-life of 10 h (formoterol) |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to budesonide or formoterol; primary treatment of status asthmaticus or acute episodes of asthma or COPD | **Black Box Warnings** | Asthma deaths; pediatrics, increased risk of hospitalization |

**Medication Safety Issues: Budesonide/Formoterol**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | No |

## Drug Interactions: Budesonide/Formoterol

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Short-acting sympathomimetics | May potentiate formoterol effect | Avoid concurrent use |
| Beta-blockers | May decrease effectiveness of formoterol and produce bronchospasms | Avoid use of nonselective beta-blocker in patients with COPD. Monitor PFTs if cardioselective beta-blockers clinically indicated |
| MAOI and tricyclic antidepressants | May potentiate formoterol effect on cardiovascular system | Consider alternative therapy |
| Azole antifungals and macrolides | Increased budesonide concentrations | Avoid long-term concomitant therapy with budesonide |
| CYP3A4/5 inducers | Increased budesonide metabolism reduces budesonide effectiveness | Monitor and consider dose increases of budesonide |
| CYP3A4/5 inhibitors | Decreased budesonide metabolism increases risk of budesonide toxicity | Monitor and consider dose decreases of budesonide |

## Adverse Reactions: Budesonide/Formoterol

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Upper respiratory tract infections | Cough, decrease in bone mineral density, dysphonia, headache, tremor, nasopharyngitis, nervousness, oral candidiasis, pain in throat | Asthma-related death, bronchospasm, hypokalemia, arrhythmias |

**Efficacy Monitoring Parameters.** Monitor PFTs. Resolution of asthma symptoms (symptoms, number of exacerbations, nighttime awakenings, need for rescue albuterol).

**Toxicity Monitoring Parameters.** Growth velocity in pediatric patients during prolonged therapy; use alternative therapy or seek emergency treatment if paradoxical bronchospasms occur.

**Key Patient Counseling Points.** Advise patient on proper inhalation technique. If more than 1 inhalation is prescribed, wait 1 min after initial inhalation and shake the inhaler again before the next inhalation. After administration, rinse mouth with water and spit, and wash face to minimize risk of developing oral candidiasis. Wash the mouthpiece and air-dry thoroughly at least once a week.

**Clinical Pearls.** Long-acting beta-agonists (LABAs) increase the risk of asthma-related deaths. Budesonide/formoterol should only be used for patients not adequately controlled on a long-term asthma control medication. This drug is not indicated for acute asthma exacerbations. LABAs may increase the risk of asthma-related hospitalization in pediatric and adolescent patients.



https://kat.cr/user/Blink99/

# BUPRENORPHINE/NALOXONE: Bunavail, Suboxone, Zubsolv, Various



**Class:** Opioid Partial Agonist and Antagonist Combination. C-III

**Dosage Forms. Sublingual Film:** (Buprenorphine/Naloxone) 2 mg/0.5 mg, 8 mg/2 mg; **Sublingual Tablet:** (Buprenorphine/Naloxone) 1.4 mg/0.36 mg, 2 mg/0.5 mg, 5.7 mg/1.4mg, 8 mg/2 mg; **Buccal Film:** (Buprenorphine/Naloxone) 2.1 mg/0.3 mg, 4.2 mg/0.7 mg, 6.3 mg/1 mg

Reckitt Benckiser 8 mg/2 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Opioid dependence: Adults and children >16 y of age, 12-16 mg (buprenorphine component) once daily sublingually, titrate to response; typical dose range from 4 to 24 mg/d

**Off-Label Uses.** None

**MOA.** Buprenorphine is a μ-opioid receptor partial agonist and a κ-opioid receptor antagonist. Naloxone is a μ-opioid receptor antagonist that causes opioid withdrawal when injected parenterally and is included in the formulation to reduce the risk of abuse.

**Drug Characteristics: Buprenorphine/Naloxone**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Use with caution | **Absorption** | F = 15% (buprenorphine); F = 3% (naloxone) |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 97-187 L (buprenorphine) |
| **Dialyzable** | Unknown | **Metabolism** | Buprenorphine, hepatic, major substrate of CYP3A4/5; naloxone: hepatic via glucuronidation |
| **Pregnancy Category** | C | **Elimination** | 30% renal elimination with half-life of 33 h (buprenorphine); half-life of 6 h (naloxone) |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

**Medication Safety Issues: Buprenorphine/Naloxone**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | Yes, medication guide required | No | No |

### Drug Interactions: Buprenorphine/Naloxone

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Barbiturates, benzodiazepines, centrally acting muscle relaxants, opioids, phenothiazines | Additive CNS depression | Monitor and consider dose adjustments |
| Opioid agonists/antagonists, opioid antagonists | Precipitation of withdrawal symptoms | Avoid concurrent use with opioids |
| CYP3A4/5 inducers | Increased buprenorphine metabolism reduces buprenorphine effectiveness | Monitor and consider dose increases of buprenorphine |
| CYP3A4/5 inhibitors | Decreased buprenorphine metabolism increases risk of buprenorphine toxicity | Monitor and consider dose decreases of buprenorphine |

### Adverse Reactions: Buprenorphine/Naloxone

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Vasodilation, sweating, headaches, insomnia, constipation, GI distress, opioid withdrawal, dizziness | Dyspnea, respiratory depression, glossodynia | Stevens-Johnson syndrome, physical dependence, tolerance, elevated liver functions tests, seizures |

**Efficacy Monitoring Parameters.** Urine drug screening tests that are negative for illicit drugs. Relief of signs and symptoms associated with narcotic addiction.

**Toxicity Monitoring Parameters.** Severe skin rash, excessive drowsiness, decreased breathing, severe constipation.

**Key Patient Counseling Points.** Use a stool softener and/or laxative for preventing constipation. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol and other CNS depressants. Do not crush or swallow the sublingual tablet. Place the tablet under the tongue until it is dissolved. If you take 2 or more tablets at a time, place all of the tablets under the tongue together. If this is uncomfortable, place 2 tablets at a time under the tongue and repeat the process until all tablets have been taken. If you are using the sublingual film, place the film under the tongue until it is dissolved. If you need to take an additional film, place the new film on the opposite side from the first film. Do not chew, swallow, or move the film after placing it under the tongue. If using the buccal film, press and hold film to moistened cheek for 5 s with finger. If you need an additional film, place on the inside of other cheek. Do not use more than 2 buccal films simultaneously.

**Clinical Pearls.** Taking opioids will result in precipitation of withdrawal symptoms. The opioid agonist properties of buprenorphine are limited by a ceiling effect which occurs at higher doses. The strength of sublingual films and tablets are not interchangeable. For example, one 8 mg film is not equivalent to 4 films of 2 mg each. Do not substitute multiple smaller dose films to equal a larger dose. Recommended as a component of therapy including counseling and psychosocial support. Not recommended for treatment of dependence on long-acting opiates or methadone; useful for withdrawal of short-acting opiates and heroin.



https://kat.cr/user/Blink99/

# BUPROPION: Wellbutrin, Zyban, Various



**Class:** Monocyclic Antidepressant

**Dosage Forms. Oral Tablet (Immediate Release):** 75 mg, 100 mg; **Oral Tablet (Sustained Release 12 h):** 100 mg, 150 mg, 200 mg; **Oral Tablet (Hydrochloride, Extended Release 24 h):** 150 mg, 300 mg, 450 mg; **Oral Tablet (Hydrobromide. Extended Release 24 h):** 174 mg, 348 mg, 522 mg

Sandoz generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Depression: Immediate release, 100 mg po bid × 3 d, increase to 100 mg po tid (*max* 450 mg/d); Sustained release, 150 mg po daily in the morning × 3 d, then increase to 150 mg po bid (*max* 200 mg bid); Extended release, 150 mg po daily × 3 d, then increase to 300 mg po daily (*max* 450 mg/d)
2. Seasonal affective disorder (SAD): 150 or 174 mg once daily in the morning, may titrate to 300 or 348 mg once daily in the morning
3. Smoking cessation assistance: Sustained release, 150 mg po daily in the morning × 3 d, then 150 mg po bid (*max* 300 mg/d) for 7-12 wk; begin treatment 1 wk prior to smoking quit date

**Off-Label Uses.** None

**MOA.** Bupropion is a monocyclic antidepressant, unique as a mild dopamine and norepinephrine uptake inhibitor with no direct effect on serotonin receptors or MAO.

**Drug Characteristics: Bupropion**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Mild to moderate: reduce frequency and/or dose. Severe liver disease: *max* dose 75 mg daily | **Absorption** | Food has minimal effect on absorption |
| **Dose Adjustment Renal** | Reduce frequency and/or dose | **Distribution** | Vd = 19-21 L/kg; 84% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, 10-15%; major substrate of CYP2B6; inhibitor of CYP2D6 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 87% and 10% in feces, with a half-life of 14-37 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Seizure disorder; history of anorexia/bulimia; use of MAOI within 14 d; patients undergoing abrupt discontinuation of ethanol, benzodiazepines, barbiturates, or antiepileptics | **Black Box Warnings** | Suicidality |

### Medication Safety Issues: Bupropion

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| SR and XL | BuPROPion | SR and XL formulations | No | BusPIRone | No |

### Drug Interactions: Bupropion

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Alcohol | Increased risk of seizures | Avoid concomitant use |
| CYP3A4/5 inducers | Increased bupropion metabolism reduces bupropion effectiveness | Monitor and consider dose increases of bupropion |
| CYP3A4/5 inhibitors | Decreased bupropion metabolism increases risk of bupropion toxicity | Monitor and consider dose decreases of bupropion |
| CYP2D6 substrates | Decreased metabolism or activation of prodrugs requiring CYP2D6 | Avoid concurrent use if substrate is narrow therapeutic index, otherwise consider dose modification |

### Adverse Reactions: Bupropion

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Agitation, constipation, dizziness, headache, insomnia, nausea, tachyarrhythmia, tremor, xerostomia | Anxiety, arthralgia, confusion, hostile behavior, hypertension, myalgia, pruritus, rash, urticaria | Cardiac dysrhythmia, mania, seizure, suicidal thoughts, wide QRS complex |

**Efficacy Monitoring Parameters.** Improvement in depressive symptoms, may require 4-6 wk. Abstinence from tobacco products.

**Toxicity Monitoring Parameters.** Worsening of depression, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases. BP and heart rate in patients using concomitant nicotine replacement therapy.

**Key Patient Counseling Points.** Avoid alcohol, CNS depressants, and activities requiring mental alertness. Take at the same time each day and at bedtime if possible. If taking the extended-release tablet, the tablet shell may remain intact and be visible in the stool.

**Clinical Pearls.** Not FDA approved for use in children. Depression, suicidal ideation, attempts, and suicides occur in patients with and without preexisting psychiatric disease. When switching patients from immediate- or sustained-release tablets to extended-release tablets, give the same total daily dose when possible. Medication safety guide required.



https://kat.cr/user/Blink99/

# BUSPIRONE: BuSpar, Various



**Class:** Antianxiety

**Dosage Forms. Oral Tablet:** 5 mg, 7.5 mg, 10 mg, 15 mg, 30 mg

Teva generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Anxiety: Adults, 5 mg po bid-tid or 7.5 mg po bid, may titrate to 20-30 mg/d in 2-3 divided doses (*max* 60 mg/d)

**Off-Label Uses.**

1. Anxiety: Children, 5 mg/d po, may titrate to 15 mg po bid (*max* 50 mg/d)
2. Depression: Adults, 5 mg po tid, may titrate to 40-55 mg/d in 2-3 divided doses (*max* 90 mg/d)

**MOA.** Buspirone is the first of a class of selective serotonin-5-$HT_{1A}$ receptor partial agonists. It also has some effect on dopamine-$D_2$ auto-receptors and, like antidepressants, can down-regulate β-adrenergic receptors. Unlike benzodiazepines, it lacks amnestic, anticonvulsant, muscle relaxant, and hypnotic effects. Its exact anxiolytic mechanism of action is complex and not clearly defined.

**Drug Characteristics: Buspirone**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Use lower initial doses and increase gradually as needed and tolerated | **Absorption** | F = 90%; food increases AUC and Cmax |
| **Dose Adjustment Renal** | Use lower initial doses and increase gradually as needed and tolerated | **Distribution** | Vd = 5.3 L/kg; 86% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic; major substrate of CYP3A4/5 |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 29-63% (primarily as metabolites), with a half-life of 2-3 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

**Medication Safety Issues: Buspirone**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | BusPIRone | No | No | BuPROPion | No |

### Drug Interactions: Buspirone

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Linezolid, SSRIs, St. John's wort | Increased risk of serotonin syndrome | Monitor for symptoms (hypertension, hyperthermia, myoclonus, mental status changes) |
| CYP3A4/5 inducers | Increased buspirone metabolism reduces buspirone effectiveness | Monitor and consider dose increases of buspirone |
| CYP3A4/5 inhibitors | Decreased buspirone metabolism increases risk of buspirone toxicity | Monitor and consider dose decreases of buspirone |

### Adverse Reactions: Buspirone

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Dizziness | Asthenia, confusion, diarrhea, excitement, feeling nervous, fatigue, headache, hostile behavior, nausea | Mania, psychiatric disorder |

**Efficacy Monitoring Parameters.** Reduction in symptoms of anxiety.

**Toxicity Monitoring Parameters.** Signs and symptoms of withdrawal upon abrupt dose reduction or discontinuation.

**Key Patient Counseling Points.** Patient should avoid activities requiring mental alertness or coordination until drug effects are realized. Advise patient that symptomatic improvement may not be seen for a few weeks. Advise patient against sudden discontinuation of drug. Patient may take with or without food, but should always take drug consistently. Patient should not drink alcohol or large amounts of grapefruit juice while taking this drug. Avoid concomitant use with MAOI.

**Clinical Pearls.** Safety and efficacy not established in pediatric patients <18 y of age.



https://kat.cr/user/Blink99/

# CANDESARTAN: Atacand, Various

**Class:** Angiotensin II Receptor Antagonist

**Dosage Forms. Oral Tablet:** 4 mg, 8 mg, 16 mg, and 32 mg

AstraZeneca pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Heart failure: 4 mg po daily, may titrate to 32 mg/d po
2. Hypertension: Adults, 16 mg po daily or in 2 divided doses, may titrate to 32 mg po daily; Children 1-5 y of age, 0.2 mg/kg po daily, may titrate to 0.4 mg/kg daily; Children 6-16 y of age and <50 kg, 4-8 mg po daily, may titrate to 32 mg daily; Children 6-16 y of age and ≥50 kg, 8-16 mg po daily, may titrate to 32 mg daily

**Off-Label Uses.** None

**MOA.** Candesartan is a selective, reversible, competitive antagonist of the angiotensin II receptor type 1 (AT1).

**Drug Characteristics: Candesartan**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Decrease dose in patients with moderate hepatic impairment | **Absorption** | F = 15%, food does not affect absorption |
| **Dose Adjustment Renal** | CrCl 15-60 mL/min, 8 mg po daily | **Distribution** | Vd = 0.13 L; >99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Parent compound bioactivated during absorption via ester hydrolysis within intestinal wall to candesartan |
| **Pregnancy Category** | D | **Elimination** | Renal elimination is 33% and fecal elimination is 67% with a half-life of 5-10 h (metabolite) |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to candesartan or other ARB, pregnancy | **Black Box Warnings** | Pregnancy |

**Medication Safety Issues: Candesartan**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Antacid | No |

## Drug Interactions: Candesartan

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Potassium-sparing diuretics | Increased risk of hypotension, hyperkalemia | Avoid concurrent use or monitor BP and serum potassium levels |
| Eplerenone | Increased risk of hyperkalemia | Avoid concurrent use or monitor serum potassium levels |
| Potassium supplements | Increased risk of hyperkalemia and cardiac arrhythmias | Avoid concurrent use or monitor serum potassium levels |
| NSAIDs | Decreased antihypertensive and natriuretic effect of candesartan, increased risk of nephrotoxicity | Avoid concurrent use or monitor BP and SCr |
| Diuretics | Increased risk of postural hypotension due to hypovolemia | Monitor BP |

## Adverse Reactions: Candesartan

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Hypotension | Back pain, constipation, dizziness, dyspepsia, f ushing, hyperkalemia, nephrotoxicity, tachycardia | Angioedema, birth defects, hepatotoxicity, rhabdomyolysis |

**Efficacy Monitoring Parameters.** Decreased BP, resolution of heart failure; may require 3-6 wk to obtain therapeutic response.

**Toxicity Monitoring Parameters.** Report signs/symptoms of hypotension, tachycardia. Baseline and periodic sodium, potassium, total bicarbonate, BUN, SCr, and urinalysis prior to initiating therapy.

**Key Patient Counseling Points.** Avoid pregnancy. Use potassium supplements or salt substitutes only under medical supervision. May cause dizziness that may worsen if dehydrated. Seek care if angioedema, excessive fluid loss, hyperkalemia, reduction in urination, or jaundice occurs.

**Clinical Pearls.** Not indicated for use in children <1 y of age. Observe volume-depleted patient for hypotension with first dose. May cause progressive renal impairment and acute renal failure; those with preexisting renal impairment, heart failure, or diabetes are at increased risk.



https://kat.cr/user/Blink99/

# CARBAMAZEPINE: Tegretol, Various



**Class:** Anticonvulsant

**Dosage Forms.** **Oral Tablet:** 200 mg; **Tablet, Chewable:** 100 mg; **Oral Tablet, Extended Release:** 100 mg, 200 mg, 400 mg; **Oral Suspension:** 100 mg/5 mL; **Oral Capsule, Extended Release:** 100 mg, 200 mg, 300 mg

Taro generic 200 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Bipolar disease, acute manic and mixed episodes: 200 mg po bid, may titrate to 1600 mg/d po
2. Epilepsy, partial, generalized, and mixed types: Adults, 200 mg po bid, may titrate to 1200 mg po daily; Children <6 y of age, 10-20 mg/kg/d po in 2-3 divided doses, may titrate to 250-350 mg/d po; Children 6-12 y of age, 100 mg po bid, may titrate to 800 mg po daily
3. Trigeminal neuralgia: Regular release, 100 mg po q12h, may titrate to 1200 mg po daily prn for pain control

**Off-Label Uses.**

1. Neuropathic pain: 50-100 mg po bid in combination with opioids, may titrate to 1200 mg/d po

**MOA.** Carbamazepine acts presynaptically to block firing of action potentials, which decreases the release of excitatory neurotransmitters, and postsynaptically by blocking high-frequency repetitive discharge initiated at cell bodies.

**Drug Characteristics: Carbamazepine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Avoid | **Absorption** | F = 89%; no effect of food on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 0.59-2 L/kg; 75-90% protein bound |
| **Dialyzable** | Yes | **Metabolism** | Hepatic; major substrate of CYP3A4/5; strong inducer of CYP1A2, 2B6, 2C19, 2C8, 2C9, 3A4/5 and P-glycoprotein |
| **Pregnancy Category** | D | **Elimination** | Renal elimination 72%, with an initial half-life of 25-65 h, then 12-17 h after 3-5 wk due to autoinduction |
| **Lactation** | Compatible | **Pharmacogenetics** | Serious and sometimes fatal dermatologic reactions are more likely in patients with the inherited allelic variant HLA-B*1502. Avoid in individuals with this genotype |
| **Contraindications** | Hypersensitivity to carbamazepine, history of bone marrow depression, MAOIs, nefazodone | **Black Box Warnings** | Agranulocytosis; aplastic anemia; dermatological reactions (especially in Asians); screen for HLA-B*1502 |

## Medication Safety Issues: Carbamazepine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| XR | CarBAMazepine, TEGretol | Do not crush or chew ER tablets or capsules | No | OXcarbazepine, Toradol | No |

## Drug Interactions: Carbamazepine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Acetaminophen | Increased risk of hepatotoxicity | Monitor LFTs |
| CYP3A4/5 inducers | Increased carbamazepine metabolism reduces carbamazepine effectiveness | Monitor and consider dose increases of carbamazepine |
| CYP3A4/5 inhibitors | Decreased carbamazepine metabolism increases risk of carbamazepine toxicity | Monitor and consider dose decreases of carbamazepine |
| CYP1A2, 2B6, 2C19, 2C8, 2C9, 3A4/5 and P-glycoprotein substrates | Carbamazepine increases metabolism of substrates drugs, lowers plasma concentration, and decreases substrate drug activity | Avoid concurrent use, or monitor substrate drug and consider dose increase |
| Ergocalciferol | Increased catabolism of vitamin D | Monitor vitamin D levels and supplement |
| Diuretics | Increased risk of hyponatremia | Monitor electrolytes |
| MAOIs | Increased risk or ergotism | Contraindicated |
| Nefazodone | Inhibition of carbamazepine metabolism, induction of nefazodone metabolism | Contraindicated |
| Warfarin | Decreased anticoagulant effectiveness | Monitor INR |

## Adverse Reactions: Carbamazepine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Hyponatremia | Blurred vision, confusion, hypocalcaemia, nausea, nystagmus, somnolence | Cardiac dysrhythmia, hepatitis, nephrotoxicity, pancreatitis, pancytopenia, Stevens-Johnson syndrome, syncope, toxic epidermal necrolysis |

**Efficacy Monitoring Parameters.** Reduction in number of seizures, decreased pain, therapeutic concentrations for epilepsy: 4-12 mcg/mL.

**Toxicity Monitoring Parameters.** Emergence or worsening of depression, suicidal behavior or ideation, or unusual changes in behavior; baseline CBC, serum sodium, LFTs, complete urinalysis, and BUN; thyroid function test at baseline and during therapy, eye examinations at baseline and during therapy.

**Key Patient Counseling Points.** May decrease effectiveness of oral contraceptives; use an alternative form of birth control. Avoid activities requiring mental alertness or coordination until drug effects are realized. Take with food, but not alcohol, grapefruit, or grapefruit juice. Avoid abrupt discontinuation.

**Clinical Pearls.** Carbamazepine is a drug of first choice for seizure disorder due to equivalent activity and decreased toxicity compared to other anti-seizure medications. Suspension is dosed 3-4 times per day.



https://kat.cr/user/Blink99/

# CARBIDOPA/LEVODOPA: Sinemet, Various



**Class:** Antiparkinsonian

**Dosage Forms.** **Oral Tablet, Immediate Release:** (Carbidopa/Levodopa) 10 mg/100 mg, 25 mg/100 mg, 25 mg/250 mg; **Oral Tablet, Extended Release:** (Carbidopa/Levodopa) 25 mg/100 mg, 50 mg/200 mg; **Orally Disintegrating Tablet:** (Carbidopa/Levodopa) 10 mg/100 mg, 25 mg/100 mg, 25 mg/250 mg

25 mg/100 mg

25 mg/250 mg

Teva generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Parkinson disease: Immediate release, 25 mg/100 mg po tid, increasing dose to therapeutic response; Extended release, 50 mg/200 mg po bid, separate doses by at least 6 h; patients generally treated with 400-1600 mg of levodopa per day; *max* 200 mg of carbidopa and 2000 mg of levodopa

**Off-Label Uses.**

1. Restless legs syndrome: 25 mg/100 mg po qhs, may repeat dose if awakening within 2 h

**MOA.** When levodopa is administered orally, it is rapidly decarboxylated to dopamine in extracerebral tissues so that only a small portion of a given dose is transported unchanged to the CNS. For this reason, when given alone, large doses of levodopa are required for adequate therapeutic effect. However, these doses often result in nausea and other adverse reactions. Carbidopa inhibits decarboxylation of circulating levodopa, preventing nausea and allowing more levodopa to reach the CNS. Carbidopa does not cross the blood-brain barrier and does not affect the metabolism of levodopa within the CNS.

**Drug Characteristics: Carbidopa/Levodopa**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Carbidopa F = 60%; levodopa F = 70-75% |
| **Dose Adjustment Renal** | Not required | **Distribution** | CSF concentrations of levodopa are 10-20% of plasma levels |
| **Dialyzable** | Not dialyzable | **Metabolism** | Levodopa undergoes extensive decarboxylation to dopamine in the gut wall, liver, and kidney; when given with carbidopa, peripheral decarboxylation of levodopa is blocked, increasing availability of levodopa for brain transport |
| **Pregnancy Category** | C | **Elimination** | Carbidopa renal elimination is 30% with a half-life of 1-2 h; levodopa renal elimination is 70-80% with a half-life of 45-90 min |
| **Lactation** | Avoid; may inhibit lactation | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to carbidopa or levodopa, narrow-angle glaucoma | **Black Box Warnings** | None |

### Medication Safety Issues: Carbidopa/Levodopa

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| CR | No | Do not crush CR or oral disintegrating products | No | Serevent | No |

### Drug Interactions: Carbidopa/Levodopa

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Dopamine $D_2$ receptor antagonists (isoniazid) | Reduction in therapeutic effect of levodopa | Increase dose of carbidopa/levodopa |
| Linezolid | Unknown; serotonin toxicity with severe hypertension | Concurrent use contraindicated; must wait at least 2 wk after discontinuing linezolid before initiating carbidopa/levodopa |
| MAOIs | Severe hypertension | Concurrent use contraindicated; must wait at least 2 wk after discontinuing MAOI before initiating carbidopa/levodopa |
| Phenytoin | Phenytoin reverses the effects of levodopa in Parkinson disease | Increase dose of carbidopa/levodopa |

### Adverse Reactions: Carbidopa/Levodopa

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Dyskinesia | Nausea | Orthostatic hypotension, neuroleptic malignant syndrome |

**Efficacy Monitoring Parameters.** Reduction in symptoms of Parkinson disease (extrapyramidal movements, rigidity, tremor, gait disturbances).

**Toxicity Monitoring Parameters.** Seek medical attention if GI bleeding and dyskinesia occur; monitor IOP in glaucoma patients who take this product.

**Key Patient Counseling Points.** Patients using concomitant antihypertensive may be at increased risk for postural hypotension. If you are using the oral disintegrating tabs, place on top of the tongue; does not require water or swallowing.

**Clinical Pearls.** Since levodopa competes with certain amino acids for transport across the gut wall, the absorption of levodopa may be impaired in some patients on a high protein diet. Parkinson disease is a progressive, neurodegenerative disorder of the extrapyramidal nervous system affecting the mobility and control of the skeletal muscular system. Its characteristic features include resting tremor, rigidity, and bradykinetic movements. Similar symptoms can occur (known as "parkinsonism") due to manganese or carbon monoxide intoxication, after encephalitic conditions, and idiopathically. All are treated with levodopa/carbidopa at the same doses as used for Parkinson disease.



https://kat.cr/user/Blink99/

# CARISOPRODOL: Soma, Various



**Class:** Centrally Acting Skeletal Muscle Relaxant. C-IV

**Dosage Forms. Oral Tablet:** 250 mg, 350 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Disorder of musculoskeletal system: 250-350 mg po tid and hs

**Off-Label Uses.** None

**MOA.** Carisoprodol blocks interneuronal activity in descending reticular formation and spinal cord, resulting in muscle relaxation.

Qualitest generic 350 mg pictured

## Drug Characteristics: Carisoprodol

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Use lower doses initially and increase dose carefully in patients with hepatic failure | **Absorption** | Unknown |
| **Dose Adjustment Renal** | Not required | **Distribution** | Unknown |
| **Dialyzable** | Yes | **Metabolism** | Hepatic; major substrate of CYP2C19 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is slight with a half-life of 8 h |
| **Lactation** | Avoid | **Pharmacogenetics** | CYP2C19 poor metabolizers at increased risk of toxicity |
| **Contraindications** | Hypersensitivity to carisoprodol or meprobamate, acute intermittent porphyria | **Black Box Warnings** | None |

## Medication Safety Issues: Carisoprodol

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | Avoid. Most muscle relaxants poorly tolerated by older adults, because of anticholinergic adverse effects, sedation, increased risk of fractures. |

### Drug Interactions: Carisoprodol

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP2C19 inducers | Increased carisoprodol metabolism reduces carisoprodol effectiveness | Monitor and consider dose increases of carisoprodol |
| CYP2C19 inhibitors | Decreased carisoprodol metabolism increases risk of carisoprodol toxicity | Monitor and consider dose decreases of carisoprodol |
| CNS depressants (opioids, benzodiazepines, alcohol) | Additive sedative effects | Avoid concurrent use or monitor carefully for signs of toxicity |

### Adverse Reactions: Carisoprodol

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Drowsiness, dizziness | Headache | Seizure, drug dependence, withdrawal symptoms upon discontinuation after chronic use |

**Efficacy Monitoring Parameters.** Reduction in pain and muscle spasms.

**Toxicity Monitoring Parameters.** Seek medical attention if idiosyncratic symptoms such as extreme weakness, transient quadriplegia, dizziness, confusion occur within minutes or hours after first dose.

**Key Patient Counseling Points.** Patients should avoid activities requiring mental alertness or coordination until drug effects are known, as drug may cause dizziness or sedative effects. Patients withdrawing from prolonged therapy should be monitored carefully for withdrawal symptoms, including seizures.

**Clinical Pearls.** Carisoprodol is used for the relief of discomfort associated with acute, painful musculoskeletal conditions in adults and should be used for only short periods (up to 2 or 3 wk). The drug was approved by the FDA in 1959 and limited pharmacologic and pharmacokinetic data are available.



https://kat.cr/user/Blink99/

# CARVEDILOL: Coreg, Coreg CR, Various

**Class:** α/β-Adrenergic Blocker

**Dosage Forms. Oral Tablet:** 3.125 mg, 6.25 mg, 12.5 mg, 25 mg; **Oral Capsule, Extended Release:** 10 mg, 20 mg, 40 mg, 80 mg

Teva generic pictured



## Common FDA Label Indication, Dosing, and Titration.

1. Heart failure: Tablets, 3.125 mg po bid, *max* 25 mg po bid for patients weighing <85 kg, 50 mg po bid for patients weighing >85 kg; Extended-release capsule, 10 mg po daily in the morning, *max* 80 mg po daily
2. Hypertension: Tablet, 6.25 mg po bid; *max* 25 mg po bid; Extended-release capsule, 20 mg po daily in the morning, *max* 80 mg po daily
3. Impaired left ventricular function, myocardial infarction: Tablet, 3.125-6.25 mg po bid, may titrate to 25 mg po bid; Extended-release capsule, 10-20 mg po daily in the morning, *max* 80 mg po daily

## Off-Label Uses.

1. Angina pectoris: 25-50 mg po bid
2. Cardiac dysrhythmia: 6.25 mg po bid, may titrate to 50 mg po bid

**MOA.** Carvedilol is a selective $\alpha_1$- and nonselective β-adrenergic blocker that decreases AV nodal conduction in supraventricular tachycardias and blockade of catecholamine-induced dysrhythmias.

## Drug Characteristics: Carvedilol

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Avoid use in patients with hepatic impairment; contraindicated in severe liver dysfunction | **Absorption** | F = 25-35%; food significantly increases AUC and Cmax for extended-release product |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 115 L; >95% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic 98%; major substrate of CYP2D6, P-glycoprotein; inhibitor of P-glycoprotein |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 16% and 60% in feces, with a half-life of 6-10 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | CYP2D6 poor metabolizers with higher plasma levels, consider lower initial dose |
| **Contraindications** | Hypersensitivity, bronchial asthma, severe sinus bradycardia, 2nd- or 3rd-degree AV block, sick sinus syndrome, overt heart failure, cardiogenic shock, severe hepatic impairment | **Black Box Warnings** | None |

## Medication Safety Issues: Carvedilol

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| CR | No | No | No | Corgard, Cortef, Cozaar | No |

## Drug Interactions: Carvedilol

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Calcium channel blockers, quinidine, amiodarone, dronedarone | Increased risk of bradycardia, atrioventricular block, sinus arrest | Avoid concurrent use in patients with sick sinus syndrome or AV block |
| P-glycoprotein inducers | Increased carvedilol metabolism reduces carvedilol effectiveness | Monitor and consider dose increases of carvedilol |
| CYP2D6, P-glycoprotein inhibitors | Decreased carvedilol metabolism increases risk of carvedilol toxicity | Monitor and consider dose decreases of carvedilol |
| P-glycoprotein substrates | Carvedilol inhibits metabolism of substrates resulting in increased risk of substrate toxicity | Monitor and consider dose decreases of substrates |
| Insulin, oral hypoglycemic agents | May enhance the hypoglycemic effect of sulfonylureas, may also mask hypoglycemia | Monitor blood glucose levels |
| NSAIDs | Decreased antihypertensive effect of carvedilol | Avoid concurrent use or monitor BP |

## Adverse Reactions: Carvedilol

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Cold extremities, dizziness, erectile dysfunction, fatigue, hypotension, weight gain | Arthralgia, bradyarrhythmias, bronchospasm, diarrhea, hyperglycemia, dyspnea, depression, headache, nausea, somnolence, syncope, vomiting | Heart failure, hepatotoxicity, Stevens-Johnson syndrome |

**Efficacy Monitoring Parameters.** Decreased BP, reduction in chest pain, decreased number of weekly angina attacks, reduction in use of prophylactic nitroglycerin to relieve chest pain, improvement in signs/symptoms of heart failure.

**Toxicity Monitoring Parameters.** Signs/symptoms of heart failure, decreased HR, bronchospasm, increased blood glucose levels in diabetic patients, and hepatotoxicity.

**Key Patient Counseling Points.** Take carvedilol with food or milk. Report signs/symptoms of heart failure, bradyarrhythmias, bronchospasm, hepatotoxicity, hypotension, syncope, or exacerbation of angina with initial dosing and dose changes. Avoid alcohol. Avoid abrupt discontinuation, may cause rebound hypertension. Avoid driving, using machinery, or doing anything else that could be dangerous if not alert. Diabetic patients carefully follow blood sugar levels as β-blockers may mask symptoms of hypoglycemia.

**Clinical Pearls.** Safety and efficacy not established in pediatric patients. Reduce dose with bradycardia (<55 beats/min).



https://kat.cr/user/Blink99/

# CEFDINIR: Omnicef, Various

**Class:** Third-Generation Cephalosporin

**Dosage Forms.** **Powder for Oral Suspension:** 125 mg/5 mL, 250 mg/5 mL; **Oral Capsule:** 300 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Acute otitis media, pharyngitis, tonsillitis: Children 6 mo through 12 y, 7 mg/kg po bid × 5-10 d or 14 mg/kg po daily x 10 d; *max* 600 mg/d; Adults, 300 mg po bid × 5-10 d
2. Bronchitis, acute, secondary bacterial infection: Adults and Children >12 y of age, 300 mg po bid × 5-10 d
3. Community-acquired pneumonia, uncomplicated skin, and/or subcutaneous tissue infection: 300 mg po bid × 10 d

**Off-Label Uses.** None

**MOA.** Cefdinir is a third-generation cephalosporin with activity against a number of gram-positive and gram-negative bacteria including β-lactamase–producing strains.

Aurobindo generic 300 mg pictured

C

## Drug Characteristics: Cefdinir

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 25%, food decreases absorption by 30% |
| **Dose Adjustment Renal** | CrCl <30 mL/min, decrease interval to daily | **Distribution** | Lung, maxillary sinus, middle ear fluid, skin, sputum |
| **Dialyzable** | Administer after hemodialysis and decrease interval to every other day | **Metabolism** | Not metabolized |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 18% with a half-life of 2 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to cephalosporin | **Black Box Warnings** | None |

## Medication Safety Issues: Cefdinir

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | No |

### Drug Interactions: Cefdinir

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Antacids, iron, vitamins | Decreased absorption | Separate administration by 2 h |

### Adverse Reactions: Cefdinir

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Diarrhea | Nausea and vomiting, vaginitis, headache | Increased liver enzymes, hypersensitivity |

**Efficacy Monitoring Parameters.** Resolution of infection.

**Toxicity Monitoring Parameters.** Seek medical attention if severe diarrhea.

**Key Patient Counseling Points.** Complete full course of therapy. For the suspension, shake well and can be stored at room temperature. Note short expiration after reconstitution. Avoid mixing suspension with food or beverages, but food can be taken afterward. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner. Separate administration of antacids, iron, and vitamins by 2 h.

**Clinical Pearls.** May resume normal activities after 24 h of antibiotics and if afebrile. Approximately 10% of patients allergic to penicillin are also allergic to cephalosporin; use with caution in penicillin-allergic patients.



https://kat.cr/user/Blink99/

# CEFUROXIME: Ceftin, Various



**Class:** Second-Generation Cephalosporin

**Dosage Forms.** **Powder for Oral Suspension:** 125 mg/5 mL, 250 mg/5 mL; **Oral Tablet:** 125 mg, 250 mg, 500 mg

Northstar Rx generic 500 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Acute infective exacerbation of COPD, uncomplicated skin and/or subcutaneous tissue infection, acute bacterial maxillary sinusitis, uncomplicated urinary tract infection: Adults, 250-500 mg po bid × 10 d
2. Acute otitis media: Children who are able to swallow tablets, 250 mg po bid × 10 d
3. Bronchitis, acute, secondary bacterial infection: Adults and Children >12 y of age, 250-500 mg po bid × 5-10 d
4. Gonorrhea, uncomplicated: 1 g po × 1 dose
5. Impetigo: Children 3 mo to 12 y of age, suspension 30 mg/kg/d po in 2 divided doses × 10 d, *max* 1 g/d
6. Lyme disease: 500 mg po bid × 14-21 d
7. Pharyngitis, tonsillitis: Adults: 250 mg po bid × 10 d; Children 3 mo to 12 y of age, suspension 20 mg/kg/d po in 2 divided doses for 10 d, *max* 500 mg/d

**Off-Label Uses.** None

**MOA.** Cefuroxime is a second-generation cephalosporin whose activity is better than cefazolin but less than cefotaxime, against *H. influenzae*, including β-lactamase–producing strains. The activity of cefuroxime against *S. aureus* is slightly less than that of cefazolin. Its activity against anaerobes is poor, similar to the first-generation cephalosporins.

**Drug Characteristics: Cefuroxime**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 37%, food increases absorption to 52%, suspension must be taken with food; tablets can be taken without regard to food |
| **Dose Adjustment Renal** | CrCl = 10-30 mL/min, administer full dose every 24 h; CrCl ≤10 mL/min, administer full dose every 48 h | **Distribution** | Aqueous humor, bronchial secretions, ear fluid, placenta, sinus |
| **Dialyzable** | Dialyzable by both hemodialysis and peritoneal dialysis | **Metabolism** | Cefuroxime is rapidly hydrolyzed by plasma and GI esterases |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 50% with a half-life of 2 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to cephalosporins | **Black Box Warnings** | None |

### Medication Safety Issues: Cefuroxime

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Do not crush or chew tablets due to persistent bitter taste | No | Cefzil, Cipro | No |

### Drug Interactions: Cefuroxime

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Ethinyl estradiol and other estrogen-based birth control products | Alters intestinal flora which, in turn, reduces the enterohepatic circulation of estrogen metabolites; decreased efficacy of birth control | Use an alternative form of birth control |

### Adverse Reactions: Cefuroxime

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Diarrhea | Nausea and vomiting, vaginitis, increased liver enzymes | Stevens-Johnson syndrome, hepatotoxicity, severe hypersensitivity, anemia, neutropenia, pancytopenia, seizure |

**Efficacy Monitoring Parameters.** Resolution of infection.

**Toxicity Monitoring Parameters.** Yellowing of the eyes, blistering skin rash or extreme fatigue, unusual bruising or bleeding, shortness of breath.

**Key Patient Counseling Points.** Seek medical attention if rash develops. Complete full course of therapy. For the suspension, shake well and store in the refrigerator. Note short expiration after reconstitution. Avoid mixing suspension with food or beverages, but food can be taken afterward. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner.

**Clinical Pearls.** May resume normal activities after 24 h of antibiotics if afebrile. Approximately 10% of patients allergic to penicillins are also allergic to cephalosporins; use with caution in penicillin-allergic patients. Dosing of suspension and tablets are not interchangeable. Also available in injectable formulation.



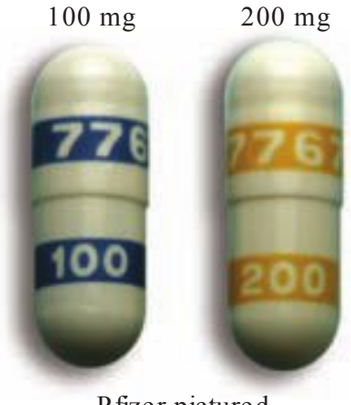
https://kat.cr/user/Blink99/

# CELECOXIB: Celebrex



**Class:** Cyclooxygenase-2 Inhibitor

**Dosage Forms. Oral Capsule:** 50 mg, 100 mg, 200 mg, 400 mg



Pfizer pictured

**Common FDA Label Indication and Dosing.**

1. Osteoarthritis: 100 mg po bid or 200 mg po daily
2. Rheumatoid arthritis: Adults, 100-200 mg po bid; Children >2 y of age, 10-25 kg, 50 mg po bid, >25 kg, 100 mg po bid
3. Ankylosing spondylitis: 100 mg po bid
4. Acute pain, primary dysmenorrhea: 200 mg po bid prn

**Off-Label Uses.**

1. Gout: 400 mg po bid × 7 d

**MOA.** Inhibition of the COX-2 enzyme isoform is thought to be responsible for the anti-inflammatory effects of NSAIDs, whereas inhibition of COX-1 results in GI and possibly other side effects.

**Drug Characteristics: Celecoxib**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Moderate: reduce dose by 50%; severe: avoid use | **Absorption** | Well absorbed, food enhances absorption |
| **Dose Adjustment Renal** | CrCl <30 mL/min: avoid use | **Distribution** | Vd = 400 L; 97% protein bound |
| **Dialyzable** | Unknown | **Metabolism** | Hepatic 97%; major substrate of CYP2C9; moderate inhibitor of CYP2C8 and 2D6 |
| **Pregnancy Category** | D | **Elimination** | 27% renal elimination with a half-life of 11 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | Consider dose reduction of 50% in CYP2C9 poor metabolizers |
| **Contraindications** | Asthma, urticaria, or allergic-type reaction following aspirin or other NSAID administration; CABG surgery, treatment of perioperative pain, hypersensitivity to sulfonamides | **Black Box Warnings** | GI toxicity, cardiotoxicity, CABG |

**Medication Safety Issues: Celecoxib**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | CeleBREX | No | No | CeleXA, Cerebyx, Cervarix, Clarinex | No |

### Drug Interactions: Celecoxib

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Aspirin, SSRIs | Additive GI toxicity | Monitor for GI toxicity |
| Angiotensin II receptor blockers, thiazide diuretics | Decreased diuretic and antihypertensive efficacy via decreased renal prostaglandin production | Monitor and consider alternative therapy |
| CYP2C9 inducers | Increased celecoxib metabolism reduces celecoxib effectiveness | Monitor and consider dose increases of celecoxib |
| CYP2C9 inhibitors | Decreased celecoxib metabolism increases risk of celecoxib toxicity | Monitor and consider dose decreases of celecoxib |
| CYP2D6 and 2C8 substrates | Decreased metabolism and increased toxicity of substrates | Monitor and consider substrate dose reduction |
| Lithium | Increased lithium levels, unknown mechanism | Monitor lithium concentrations and adjust |
| Pemetrexed | Decreased renal clearance and increased toxicity of pemetrexed | Avoid NSAIDs in combination with pemetrexed in patients with renal dysfunction |
| Warfarin | Both substrates for CYP2C9, competitive metabolism | Monitor INR and adjust warfarin dose |

### Adverse Reactions: Celecoxib

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Hypertension, headaches, GI distress, diarrhea | Myocardial infarction, bronchospasm | Stevens-Johnson syndrome, GI ulcers and bleeding, thrombosis, elevated liver functions, acute renal failure |

**Efficacy Monitoring Parameters.** Decreased pain and improved range of motion, regression of colonic polyps on colonoscopy.

**Toxicity Monitoring Parameters.** CBC, LFTs, SCr, fecal occult blood tests, BP, severe skin rash, black tarry stools, swelling or weight gain, severe pain, yellowing of eyes of skin, change in urination.

**Key Patient Counseling Points.** Take with food or milk to decrease GI upset. May open capsule and pour into a teaspoon of applesauce.

**Clinical Pearls.** Elderly patients are at increased risk of GI ulceration. Patients with underlying cardiac dysfunction are at increased risk for cardiovascular effects. Celecoxib has less risk of GI effects than other NSAIDs, but increased cardiovascular toxicity.



https://kat.cr/user/Blink99/

# CEPHALEXIN: Keflex, Various



**Class:** First-Generation Cephalosporin

**Dosage Forms.** **Powder for Oral Suspension:** 125 mg/5 mL, 250 mg/5 mL; **Oral Tablet:** 250 mg, 500 mg; **Oral Capsule:** 250 mg, 500 mg, 750 mg

Teva generic 500 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Infection of skin and/or subcutaneous tissue: Adults, 500 mg po q12h; Children, 25-50 mg/kg/d po divided q12h
2. Osteomyelitis: Adults, 250 mg-1 g po q6h; Children, 25-100 mg/kg/d po divided q6h, *max* 4 g/d
3. Otitis media, respiratory tract infection, urinary tract infection: Adults, 250 mg-1 g po q6h; Children, 25-100 mg/kg/d po divided q6h, *max* 4 g/d
4. Streptococcal pharyngitis: Adults, 500 mg po q12h × 10 d; Children, 25-50 mg/kg/d po divided q6h × 10 d, *max* 4 g/d

**Off-Label Uses.**

1. Bacterial endocarditis; prophylaxis for high-risk patients; dental, respiratory, or infected skin/skin structure or musculoskeletal tissue procedures: Adults, 2 g po 30-60 min prior to procedure; Children, 50 mg/kg 30-60 min prior to procedure

**MOA.** Cephalexin is a first-generation cephalosporin that inhibits bacterial wall synthesis of actively dividing cells by binding to one or more penicillin-binding proteins (PBPs). Most gram-positive bacteria, including non-penicillinase and penicillinase-producing staphylococci, and streptococci. Activity against gram-negative bacteria is less than that observed with the second- and third-generation cephalosporins and is primarily restricted to *E. coli*, *Klebsiella*, and *P. mirabilis*.

**Drug Characteristics: Cephalexin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 90%, food has little effect on absorption |
| **Dose Adjustment Renal** | CrCl <50 mL/min, 500 mg q12h | **Distribution** | Bile, joints, placenta, sputum |
| **Dialyzable** | Dialyzable by both hemodialysis and peritoneal dialysis | **Metabolism** | Not metabolized |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 69-100% with a half-life of 1 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to cephalosporins | **Black Box Warnings** | None |

### Medication Safety Issues: Cephalexin

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Cefaclor, ceFAZolin, ciprofloxacin, Valtrex | No |

### Drug Interactions: Cephalexin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Cholestyramine | Cholestyramine may bind to and decrease absorption of cephalexin | Administer cephalexin 1 h before or 6 h after cholestyramine |
| Metformin | Cephalexin may decrease metformin renal excretion leading to increased metformin toxicity | Use with caution; increase monitoring for metformin toxicity |

### Adverse Reactions: Cephalexin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Nausea and vomiting | Stevens-Johnson syndrome, renal failure, severe hypersensitivity, anemia, neutropenia, seizure |

**Efficacy Monitoring Parameters.** Resolution of signs and symptoms of infection.

**Toxicity Monitoring Parameters.** Seek medical attention if decreased urination, blistering skin rash or extreme fatigue, unusual bruising or bleeding, shortness of breath.

**Key Patient Counseling Points.** Seek medical attention if rash develops. Complete full course of therapy. For the suspension, shake well and store in the refrigerator. Note short expiration after reconstitution. Avoid mixing suspension with food or beverages, but food can be taken afterward. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner.

**Clinical Pearls.** May resume normal activities after 24 h of antibiotics and if afebrile. Approximately 10% of patients allergic to penicillins are also allergic to cephalosporins; use with caution in penicillin-allergic patients.



https://kat.cr/user/Blink99/

# CETIRIZINE: Zyrtec, Various



**Class:** Antihistamine

**Dosage Forms.** **Oral Tablet:** 5 mg, 10 mg; **Oral Tablet, Chewable:** 5 mg, 10 mg; **Oral Capsule:** 10 mg; **Oral Solution:** 1 mg/mL; **Oral Syrup:** 1 mg/mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Perennial or seasonal allergic rhinitis: Children 6-23 mo of age, 2.5 mg po daily; Children 2-5 y of age, 2.5-5 mg po daily; Children ≥6 y of age and Adults, 5-10 mg po daily
2. Urticaria, chronic: Children 6-23 mo of age, 2.5 mg po daily; Children 2-5 y of age, 2.5-5 mg po daily; Children ≥6 y of age and Adults, 5-10 mg po daily

**Off-Label Uses.**

1. Atopic dermatitis: Children 6-23 mo of age, 2.5 mg po daily; Children 2-5 y of age, 2.5-5 mg po daily; Children ≥6 y of age and Adults, 5-10 mg po daily

**MOA.** Cetirizine is a low-sedating, long-acting $H_1$-receptor antagonist that is a metabolite of hydroxyzine. Cetirizine competitively inhibits the interaction of histamine with $H_1$ receptors, thereby preventing the allergic response.

**Drug Characteristics: Cetirizine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Chronic liver failure, 5 mg po daily | **Absorption** | F = 70%, limited effect of food on absorption |
| **Dose Adjustment Renal** | CrCl <30 mL/min, 5 mg po daily | **Distribution** | Vd = 0.5-0.8 L/kg with 90% protein binding |
| **Dialyzable** | Yes | **Metabolism** | Limited hepatic; substrate of P-glycoprotein |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 70% with a half-life of 8.3 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to cetirizine or hydroxyzine | **Black Box Warnings** | None |

Sunmark 1 mg/mL generic solution pictured

### Medication Safety Issues: Cetirizine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| ZyrTEC-D | ZyrTEC | No | No | ZyrTEC Itchy Eye (ketotifen), Zantac | No |

### Drug Interactions: Cetirizine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CNS depressants (opioids, benzodiazepines, alcohol) | Possible increase in sedation effects | Use concurrently with caution |
| P-glycoprotein inducers | Increased cetirizine metabolism reduces cetirizine effectiveness | Monitor and consider dose increases of cetirizine |
| P-glycoprotein inhibitors | Decreased cetirizine metabolism increases risk of cetirizine toxicity | Monitor and consider dose decreases of cetirizine |

### Adverse Reactions: Cetirizine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Drowsiness | Sedation, headache, dry mouth, fatigue, and nausea | |

**Efficacy Monitoring Parameters.** Improvement in rhinitis or urticaria symptoms.

**Toxicity Monitoring Parameters.** Seek medical attention for signs of severe CNS toxicity.

**Key Patient Counseling Points.** Patients should avoid activities requiring mental alertness or coordination until drug effects are known, as drug may cause dizziness or sedative effects.

**Clinical Pearls.** Product is available in several nonprescription dosage forms.



https://kat.cr/user/Blink99/

# CHLORHEXIDINE: Peridex, Hibiclens, Various



**Class:** Antibacterial Cleansing Agent

**Dosage Forms.** **Liquid Oral Rinse:** 0.12%; **Topical Solution:** 2%, 4%

**Common FDA Label Indication, Dosing, and Titration.**

1. Gingivitis: 15 mL oral rinse (undiluted, 0.12%), swish 30 s and spit bid (morning and evening) after tooth brushing
2. Skin or wound cleansing: Rinse area to be cleansed, apply minimum amount of solution necessary to cover skin or wound area, and wash gently; then rinse

**Off-Label Uses.**

1. Burn, prevention of nosocomial infectious disease: Rinse area to be cleansed, apply minimum amount of 4% solution necessary to cover skin or wound area, and wash gently; then rinse
2. Oropharyngeal decontamination, to reduce risk of ventilator-associated pneumonia in critically ill patients: 15 mL oral rinse (undiluted, 0.12%), swab oral area q8h

**MOA.** Chlorhexidine, a polybiguanide, is an antiseptic and antimicrobial drug with bactericidal activity. The bactericidal effect of chlorhexidine is a result of the binding of this cationic molecule to negatively charged bacterial cell walls and extracellular microbial complexes.

Xttrium generic pictured

**Drug Characteristics: Chlorhexidine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Not absorbed |
| **Dose Adjustment Renal** | Not required | **Distribution** | Not absorbed |
| **Dialyzable** | Unknown | **Metabolism** | Not absorbed |
| **Pregnancy Category** | C | **Elimination** | Not absorbed |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to chlorhexidine | **Black Box Warnings** | None |

**Medication Safety Issues: Chlorhexidine**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Precedex | No |

**Drug Interactions: Chlorhexidine.** None

**Adverse Reactions: Chlorhexidine**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Tooth aches and discolored teeth with oral rinse | GI irritation | Allergic reactions, skin irritation |

**Efficacy Monitoring Parameters.** Oral rinse: resolution of gingivitis. Topical: no signs of bacterial infection (redness, pruritus, burning, swelling).

**Toxicity Monitoring Parameters.** Tooth discoloration, skin irritation.

**Key Patient Counseling Points.** For oral rinse, measure out 1/2 fluid ounce (15 mL) as marked in the cap which comes with the bottle, swish the solution in mouth for at least 30 s; do not swallow. Wait several hours after use of chlorhexidine to eat or drink. Likely to cause tooth discoloration, which can be removed by dental cleaning. For topical product, use only on unbroken skin, do not swallow, or get in the eyes, ears, mouth, nose, genital area, or anal area. Contains large amounts of alcohol (70%) and are flammable. Apply the medicine in a well-ventilated place. Do not cover the treated area until the medicine is completely dry. This is usually 3 min or longer for hairless skin. If you must apply the medicine to a hairy area of the body, wipe the area with a towel to remove extra medicine.

**Clinical Pearls.** Not for use in children. Several nonprescription products also available.



https://kat.cr/user/Blink99/

# CHLORTHALIDONE: Hygroton, Thalitone, Various



**Class:** Thiazide Diuretic

**Dosage Forms. Oral Tablet:** 25 mg, 50 mg, 100 mg

Mylan generic 25 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Hypertension: Adults, 25 mg po daily, may titrate to *max* of 100 mg po daily
2. Edema: 50 mg po daily, may titrate to *max* of 200 mg po daily; heart failure–associated edema, 12.5-25 mg po daily, may titrate to *max* of 100 po daily

**Off-Label Uses.**

1. Hypertension: Children, 0.3 mg/kg po daily, may titrate to *max* of 2 mg/kg/d or 50 mg/d, whichever is less
2. Calcium nephrolithiasis, prevention of recurrent kidney stones: 25 mg po daily

**MOA.** Chlorthalidone increases sodium and chloride excretion by interfering with their reabsorption in the cortical-diluting segment of the nephron.

**Drug Characteristics: Chlorthalidone**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 65%, food has no effect on absorption |
| **Dose Adjustment Renal** | CrCl <10 mL/min: increase dosing interval to q48h | **Distribution** | Vd = 3-13 L/kg; protein binding 75% |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic |
| **Pregnancy Category** | B | **Elimination** | Renal elimination 50-74%, half-life of 40-60 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to chlorthalidone or sulfonamides; anuria | **Black Box Warnings** | None |

**Medication Safety Issues: Chlorthalidone**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | No |

### Drug Interactions: Chlorthalidone

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| NSAIDs | Decreased antihypertensive effect of chlorthalidone | Avoid concurrent use or monitor BP |
| Calcium channel blockers, quinidine | Increased risk of hypotension and/or bradycardia and atrioventricular block | Avoid concurrent use |
| Digoxin | Increased risk of AV block | Monitor HR, ECG, and serum digoxin concentrations |
| ACE-Is | Increased risk of postural hypotension (first dose) | Start with low dose of ACE-I and monitor BP |
| Dofetilide | Increased risk of ventricular arrhythmias (torsades de pointes) due to hypokalemia, hypomagnesemia | Avoid concurrent use |

### Adverse Reactions: Chlorthalidone

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Dizziness, hypotension, hyperuricemia | Anorexia, diarrhea, headache, hypokalemia, hyponatremia, nausea, orthostatic hypotension, rash | Heart failure, pancreatitis |

**Efficacy Monitoring Parameters.** Decreased BP, swelling, edema.

**Toxicity Monitoring Parameters.** Signs/symptoms of heart failure, decreased HR. Monitor serum electrolytes, uric acid, and renal function at baseline and periodically.

**Key Patient Counseling Points.** Instruct patient to report signs/symptoms of dyspnea, hypotension, gout, or heart failure. Avoid alcohol and NSAIDs. Avoid abrupt discontinuation. This medicine may cause dizziness. Avoid driving, using machinery, or doing anything else that could be dangerous if not alert. Instruct patient to rise slowly from sitting/supine position, as drug may cause orthostatic hypotension. Instruct patient to eat high-potassium foods during therapy.

**Clinical Pearls.** Chlorthalidone is not FDA approved for use in children, but it is included in guidelines and can be used off label.



https://kat.cr/user/Blink99/

# CIPROFLOXACIN ORAL: Cipro, Cipro XR, Various

**Class:** Fluoroquinolone Antibiotic

**Dosage Forms.** **Microcapsules for Oral Suspension:** 250 mg/5 mL, 500 mg/5 mL; **Oral Tablet:** 100 mg, 250 mg, 500 mg, 750 mg; **Oral Tablet, Extended Release:** 500 mg, 1000 mg

Northstar Rx generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Anthrax, postexposure prophylaxis: Adults, 500 mg po q12h × at least 60 d, Children, 15 mg/kg po bid × at least 60 d, *max* 500 mg/dose
2. Bacterial prostatitis, chronic: 500 mg po q12h × 28 d
3. Bronchitis, lower respiratory tract infection, infection of bone, skin, or soft tissue, sinusitis: 500-750 mg po q12h × 7-14 d
4. Urinary tract infectious disease: 250-500 mg po q12h or 500 mg (extended release) q24h × 3 d

**Off-Label Uses.**

1. Chancroid: 500 mg po bid × 3 d
2. Traveler's diarrhea: 750 mg po as a single dose (mild); 500 mg po bid × 3 d (severe)

**MOA:** Ciprofloxacin is a fluoroquinolone that inhibits bacterial DNA gyrase. It is highly active against aerobic, gram-negative bacilli.

**Drug Characteristics: Ciprofloxacin Oral**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 60-80%, minor food effect |
| **Dose Adjustment Renal** | CrCl 30-50 mL/min, 250-500 mg q12h; CrCl 5-29 mL/min, 250-500 mg q18h | **Distribution** | Widespread (bile, CSF, gynecologic tissues, liver, lung, prostate, peritoneum, synovial fluid, sputum, etc) |
| **Dialyzable** | Dialyzable by both hemodialysis and peritoneal dialysis. Give 250-500 mg q24h after dialysis | **Metabolism** | Not metabolized; substrate of P-glycoprotein; strong inhibitor of CYP1A2 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 30-57% with a half-life of 3-6 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | Serious and sometimes fatal hemolytic reactions may occur in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency |
| **Contraindications** | Hypersensitivity to ciprofloxacin or other quinolones, concomitant tizanidine | **Black Box Warnings** | Myasthenia gravis, tendon inflammation and rupture |

**Medication Safety Issues: Ciprofloxacin Oral**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| XR | No | Do not crush Cipro XR | No | Ceftin, cephalexin | No |

### Drug Interactions: Ciprof oxacin Oral

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Diabetic agents | Hypoglycemic or hyperglycemic episodes, mechanism unknown | Avoid concurrent use; monitor FPG and consider dose adjustments of antidiabetic agent |
| Aluminum, calcium, and magnesium-containing antacids, calcium fortified foods, didanosine, iron, sevelamer | Decreased absorption of ciprof oxacin caused by chelation | Take ciprof oxacin 2 h before or 6 h after |
| Corticosteroids | Increased risk of tendon rupture | Counsel patients to discontinue ciprof oxacin and seek medical attention if tendon pain or rupture |
| CYP1A2 substrates | Ciprof oxacin inhibits CYP1A2 reducing substrate metabolism and increased substrate toxicity | Monitor for toxicity and consider dose reductions of substrates |
| Warfarin | Increased risk of bleeding | Increased monitoring of INR and warfarin adjustments |
| P-glycoprotein inducers | Increased ciprof oxacin metabolism reduces ciprof oxacin effectiveness | Monitor and consider dose increases of ciprof oxacin |
| P-glycoprotein inhibitors | Decreased ciprof oxacin metabolism increases risk of ciprof oxacin toxicity | Monitor and consider dose decreases of ciprof oxacin |

### Adverse Reactions: Ciprof oxacin Oral

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Tooth discoloration in infants | Nausea and vomiting, rash, myalgia, arthralgia, tendinitis, headache | Stevens-Johnson syndrome, renal failure, severe hypersensitivity, anemia, neutropenia, thrombocytopenia, seizure, cardiac effects, liver failure, myasthenia gravis, tendon rupture, renal failure, psychosis, QT prolongation |

**Efficacy Monitoring Parameters.** Resolution of signs and symptoms of infection.

**Toxicity Monitoring Parameters.** Baseline SCr. If obtained, levels should be between 0.5 and 5 mcg/mL.

**Key Patient Counseling Points.** Seek medical attention if decreased urination, yellowing of eyes, blistering skin rash or extreme fatigue, unusual bruising or bleeding, shortness of breath or chest pain, tendon pain. Take with or without food, but not with milk or other dairy products. Take ciprofloxacin at least 2 h before or 6 h after antacids, sucralfate, or mineral supplements and multivitamins with calcium, iron, or zinc. If using the suspension, shake well before use; suspension may be stored at room temperature.

**Clinical Pearls.** Not approved in children <18 y of age except for anthrax and complicated UTIs. Requires medication guide when dispensed. Also available in injectable, otic, and ophthalmic formulations.



https://kat.cr/user/Blink99/

# CIPROFLOXACIN OTIC: Cipro HC, Cetraxal, Various



**Class:** Fluoroquinolone Antibiotic

**Dosage Forms. Otic Solution:** 0.2%

**Common FDA Label Indication, Dosing, and Titration.**

1. Otitis externa, acute: Adults and Children >1 y of age, 0.25 mL (entire single-use container) into affected ear(s) bid (approximately q12h) × 7 d

**Off-Label Uses.** None

**MOA.** Ciprofloxacin is a fluoroquinolone that inhibits bacterial DNA gyrase, an enzyme responsible for the unwinding of DNA for transcription and subsequent supercoiling of DNA for packaging into chromosomal subunits. It is highly active against aerobic, gram-negative bacilli, especially Enterobacteriaceae, with MICs often <0.1 mg/L. It is also active against some strains of *P. aeruginosa* and *Staphylococcus* spp., with an MIC of 0.5-1 mg/L. However, recent reports indicate increasing resistance to this agent in *S. aureus*. It has poor activity against streptococci and anaerobes.

Alcon pictured

## Drug Characteristics: Ciprofloxacin Otic

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Not systemically absorbed |
| **Dose Adjustment Renal** | Not required | **Distribution** | Not systemically absorbed |
| **Dialyzable** | Not absorbed | **Metabolism** | Not systemically absorbed |
| **Pregnancy Category** | C | **Elimination** | Not systemically absorbed |
| **Lactation** | Unknown if ciprofloxacin otic solution is excreted into breast milk. Weigh risks and benefits | **Pharmacogenetics** | None known that affect otic solution administration |
| **Contraindications** | Hypersensitivity to ciprofloxacin or other quinolones | **Black Box Warnings** | None |

## Medication Safety Issues: Ciprofloxacin Otic

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | CefTRIAXone, cephalexin | No |

**Drug Interactions: Ciprofloxacin Otic.** None known

**Adverse Reactions: Ciprof oxacin Otic**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Application site pain and itching, fungal ear superinfection | Hypersensitivity reactions |

**Efficacy Monitoring Parameters.** Resolution of signs and symptoms of infection. Cultures may be required if infection does not improve within 1 wk of therapy.

**Toxicity Monitoring Parameters.** Ear pain, local hypersensitivity reaction, secondary fungal infections.

**Key Patient Counseling Points.** Warm solution by holding container in hands for at least 1 min before administering. Patient should lie with affected ear upward; position should be maintained for at least 1 min after instillation; repeat in the opposite ear if necessary.

**Clinical Pearls.** Ciprofloxacin otic is not approved in children <1 y of age. Not for ophthalmologic use, otic use only. Also available as injectable, ophthalmic, and oral formulations.



https://kat.cr/user/Blink99/

# CITALOPRAM: Celexa, Various

**Class:** SSRI Antidepressant

**Dosage Forms. Oral Tablet:** 10 mg, 20 mg, 40 mg; **Oral Solution:** 10 mg/5 mL

Sun Pharmaceuticals generic 40 mg pictured

Greenstone generic 20 mg pictured

Blu Pharmaceuticals generic 10 mg pictured

C

**Common FDA Label Indication, Dosing, and Titration.**

1. Depression: 20 mg po daily, may titrate to 40 mg po daily

**Off-Label Uses.**

1. OCD: 20 mg po daily, may titrate to 40 mg/d
2. Panic disorder: 20-30 mg po daily, may titrate to 40 mg po daily

**MOA.** Citalopram is a bicyclic antidepressant that is a selective and potent inhibitor of presynaptic reuptake of serotonin (an SSRI). It does not affect reuptake of norepinephrine or dopamine and has a relative lack of affinity for muscarinic, histamine, $\alpha_1$- and $\alpha_2$-adrenergic, and serotonin receptors.

**Drug Characteristics: Citalopram**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | *Max* dose 20 mg po daily in hepatic impairment | **Absorption** | F = 80%; no effect of food on absorption |
| **Dose Adjustment Renal** | Use with caution in severe renal impairment | **Distribution** | Vd = 12 L/kg; 80% protein bound |
| **Dialyzable** | Not dialyzed | **Metabolism** | Hepatic >90%; substrate of CYP2C19 and 3A4/5 |
| **Pregnancy Category** | C | **Elimination** | Fecal elimination is 20%, renal elimination is 20% (12-13% unchanged), with a half-life of 33-37 h |
| **Lactation** | Avoid | **Pharmacogenetics** | CYP2C19 poor metabolizers, *max* dose 20 mg/d |
| **Contraindications** | Hypersensitivity, concomitant use of pimozide, MAOIs | **Black Box Warnings** | Suicidal ideation; not approved for use in children |

**Medication Safety Issues: Citalopram**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | CeleXA | No | No | CeleBREX, ZyPREXA | No |

## Drug Interactions: Citalopram

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Anticoagulants, antiplatelet drugs, NSAIDs | Increased risk of bleeding | Monitor for bleeding |
| Dextroamphetamine, triptans, linezolid, lithium, MAOIs | Increased risk of serotonin syndrome | Monitor closely for symptoms of serotonin syndrome (restlessness, hyperthermia, hyperref exia, incoordination), do not use MAOIs |
| CYP2C19 and CYP3A4/5 inducers | Increased citalopram metabolism reduces citalopram effectiveness | Monitor and consider dose increases of citalopram |
| CYP2C19 and CYP3A4/5 inhibitors | Decreased citalopram metabolism increases risk of citalopram toxicity | Monitor and consider dose decreases of citalopram |

## Adverse Reactions: Citalopram

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Constipation, dizziness, headache, insomnia, nausea, sedation, xerostomia | Agitation, anxiety, diaphoresis, diarrhea, disorder of ejaculation, fatigue, impotence, reduced libido, tremor | Prolonged QT interval, serotonin syndrome, suicidal thoughts, torsades de pointes, agranulocytosis |

**Efficacy Monitoring Parameters.** Improvement in symptoms of depression, panic disorder, OCD.

**Toxicity Monitoring Parameters.** Worsening of mental health symptoms, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases; signs/symptoms of abnormal bleeding.

**Key Patient Counseling Points.** Avoid activities requiring mental alertness or coordination until drug effects are realized. Symptomatic improvement may not be seen for several weeks. Report worsening depression, suicidal ideation, unusual changes in behavior, or unusual bleeding. Avoid abrupt discontinuation, may precipitate withdrawal symptoms. Do not drink alcohol or use NSAIDs or aspirin while taking this drug.

**Clinical Pearls.** If intolerable withdrawal symptoms occur following a decrease in dose or therapy discontinuation, may need to resume the previous dose and taper at a more gradual rate. Medication guide required when dispensing.



https://kat.cr/user/Blink99/

# CLARITHROMYCIN: Biaxin, Various



**Class:** Macrolide Antibiotic

**Dosage Forms.** **Oral Tablet:** 250 mg, 500 mg; **Oral Suspension:** 125 mg/5 mL; 250 mg/5 mL; **Oral Tablet, Extended Release:** 500 mg

Dava generic 500 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Acute infective exacerbation of COPD: 250-500 mg po bid × 7-14 d
2. Community-acquired pneumonia, skin infection, sinusitis, pharyngitis: Adults, 250 mg po bid × 7-14 d or extended-release tablets, 1000 mg po daily for 7 d; Children ≥6 mo of age, 15 mg/kg/d divided q12h × 10 d
3. Disseminated infection due to *M. avium*-intracellulare group, prophylaxis-HIV infection, primary prevention and treatment: 500 mg po bid
4. *H. pylori* GI tract infection: 500 mg, bid × 10-14 d in combination with various other antibiotics and PPIs

**Off-Label Uses.**

1. Bacterial endocarditis prophylaxis for high-risk patients; dental, respiratory, or infected skin/skin structure or musculoskeletal tissue procedures: Adults, 500 mg po 30-60 min prior to procedure; Children, 15 mg/kg po 30-60 min prior to procedure

**MOA.** Clarithromycin binds to the 50S ribosomal subunit of the 70S ribosome of susceptible organisms, thereby inhibiting bacterial RNA-dependent protein synthesis.

**Drug Characteristics: Clarithromycin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 50%, extended release should be taken with food, immediate release can be taken without regard to food |
| **Dose Adjustment Renal** | CrCl <30 mL/min, reduce dose by 50% or increase interval to q24h | **Distribution** | Gastric tissue, lung, ear f uid, prostate, sputum, soft tissue |
| **Dialyzable** | Unknown | **Metabolism** | Hepatic; substrate of CYP3A4/5 to active metabolites, inhibitor of CYP3A4/5, P-glycoprotein |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 20-40% with a half-life of 5-7 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to any macrolide or ketolide antibiotic; concomitant cisapride, pimozide, astemizole, terfenadine, ergotamine, or dihydroergotamine | **Black Box Warnings** | None |

**Medication Safety Issues: Clarithromycin**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| XL | No | Do not crush XL formulation | No | Claritin | No |

### Drug Interactions: Clarithromycin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Drugs known to prolong the QT interval | Increased risk of cardiotoxicity via additive QT prolongation | Avoid concurrent use or consider monitoring ECG |
| CYP3A4/5, P-glycoprotein substrates | Inhibition of CYP3A4/5, P-glycoprotein by clarithromycin reduces substrate metabolism and increases substrate toxicity | Monitor for toxicity and consider dose reductions of substrates; do not use substrates if narrow therapeutic index or if known to prolong QT interval |
| CYP3A4/5 inducers | Increased clarithromycin metabolism reduces clarithromycin effectiveness | Monitor and consider dose increases of clarithromycin |
| CYP3A4/5 inhibitors | Decreased clarithromycin metabolism increases risk of clarithromycin toxicity | Monitor and consider dose decreases of clarithromycin |
| Digoxin | Increased bioavailability and digoxin toxicity | Caution with concurrent use |
| Sulfonylureas | Increased risk of hypoglycemia | Use with caution and increase blood glucose monitoring |
| SSRIs | Increased risk of serotonin syndrome | Consider dose reduction of SSRI |
| Warfarin | Increased risk of bleeding via inhibition of warfarin metabolism | Monitor INR closely |

### Adverse Reactions: Clarithromycin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Taste disturbance | Headache, diarrhea, nausea, vomiting, rash | QT prolongation, Stevens-Johnson syndrome, anemia, neutropenia, thrombocytopenia, severe hypersensitivity, myasthenic crisis, elevated LFTs, hallucinations, nephrotoxicity |

**Efficacy Monitoring Parameters.** Resolution of signs and symptoms of infection.

**Toxicity Monitoring Parameters.** Seek medical attention if heart palpitations, blistering skin rash, unusual bruising or bleeding, yellowing of skin or eyes, or extreme fatigue.

**Key Patient Counseling Points.** Complete full course of therapy. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with healthcare practitioner.

**Clinical Pearls.** Use with caution in severe renal, hepatic, or cardiac disease. Extended-release and immediate-release formulations are not interchangeable. Multiple drug interactions. *Max* dose in children, 1 g/d.



https://kat.cr/user/Blink99/

# CLINDAMYCIN ORAL: Cleocin, Various

**Class:** Lincosamide Antibiotic

**Dosage Forms.** **Oral Capsule:** 75 mg, 150 mg, 300 mg; **Granules for Oral Solution:** 75 mg/5 mL

Greenstone generic 300 mg pictured



**Common FDA Label Indication, Dosing, and Titration.**

1. Bacterial infectious disease, susceptible infections due to anaerobic organisms, staphylococci, streptococci, pneumococci: Adults, 150-450 mg po q6h; Children, 8-20 mg/kg/d po divided q6-8h
2. Infection of skin and/or subcutaneous tissue: Adults, 150-450 mg po q6h; Children, 8-20 mg/kg/d po divided q6-8h
3. Infectious disease of abdomen: Adults, 150-450 mg po q6h; Children, 8-20 mg/kg/d po divided q6-8h
4. Lower respiratory tract infection: Adults, 150-450 mg po q6h; Children, 8-20 mg/kg/d po divided q6-8h
5. Pelvic inflammatory disease: Adults, 150-450 mg po q6h; Children, 8-20 mg/kg/d po divided q6-8h
6. Septicemia: Adults, 150-450 mg po q6h; Children, 8-20 mg/kg/d po divided q6-8h

**Off-Label Uses.**

1. Bacterial vaginosis, oral treatment, pregnant women with symptomatic disease: 300 mg po bid × 7 d
2. Streptococcal pharyngitis, penicillin-allergic patients: Children, 20 mg/kg/d po in 3 divided doses (*max* 1.8 g/d)

**MOA.** Clindamycin is a semisynthetic 7-chloro-7-deoxylincomycin derivative that is active against most gram-positive organisms except enterococci and *C. difficile*. Gram-negative aerobes are resistant, but most anaerobes are sensitive. It inhibits bacterial protein synthesis by binding to the 50S ribosomal subunit; it is bactericidal or bacteriostatic depending on the concentration, organism, and inoculums.

**Drug Characteristics: Clindamycin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 90%, no food effect |
| **Dose Adjustment Renal** | If CrCl <30 mL/min, reduce dose by 50% or double interval | **Distribution** | Appendix, bone, gastric tissue, head and neck, sputum, peritoneal f uid, uterus |
| **Dialyzable** | Unknown | **Metabolism** | Minor hepatic |
| **Pregnancy Category** | B | **Elimination** | Renal elimination 5-28% with a half-life of 1.5-5 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to clindamycin | **Black Box Warnings** | Colitis |

### Medication Safety Issues: Clindamycin

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| Pediatric | No | Do not open capsules | No | Bleomycin, Clinoril, Claritin, clarithromycin | No |

### Drug Interactions: Clindamycin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Atracurium and nondepolarizing muscle relaxants | Clindamycin may have added effect on muscle contractility | Monitor for excessive neuromuscular blockade, consider dose reduction of muscle relaxant |
| Cyclosporine | Decreased bioavailability of cyclosporine; mechanism unknown | Monitor cyclosporine levels and consider dose adjustments |
| Erythromycin | Competition for the same binding site decreased antibiotic effect; theoretical additive effects on QT prolongation | Avoid concurrent use |

### Adverse Reactions: Clindamycin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Diarrhea, nausea, vomiting, rash | QT prolongation, Stevens-Johnson syndrome, pseudomembranous colitis, esophagitis |

**Efficacy Monitoring Parameters.** Resolution of signs and symptoms of infection.

**Toxicity Monitoring Parameters.** Seek medical attention if heart palpitations, blistering skin rash, or profuse watery diarrhea.

**Key Patient Counseling Points.** Complete full course of therapy. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with healthcare practitioner. Take with full glass of water. Remain upright for 30 min after dose to minimize risk of GI ulceration.

**Clinical Pearls.** May resume normal activities after 24 h of antibiotics and if afebrile. Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*–associated diarrhea, which has been observed >2 m postantibiotic treatment. Also available as injectable, topical, and vaginal formulations. Common antibiotic for anaerobes infections above the diaphragm. Potential alternative in patients with gram-positive infection and allergy to penicillin (immediate-type hypersensitivity reactions).



https://kat.cr/user/Blink99/

# CLINDAMYCIN TOPICAL: Cleocin T, Various

**Class:** Lincosamide Antibiotic

**Dosage Forms.** **Topical Foam:** 1%; **Topical Solution:** 1%; **Topical Gel:** 1%; **Topical Pad:** 1%; **Topical Lotion:** 1%

**Common FDA Label Indication, Dosing, and Titration.**

1. Acne vulgaris: Topical solution, lotion, gel; apply thin-film bid to affected areas; Foam: apply once daily to affected areas

**Off-Label Uses.**

1. Acneiform eruptions induced by epidermal growth factor receptor inhibitors: Topical gel or lotion; apply thin-film bid to affected areas

**MOA.** Clindamycin is a semisynthetic 7-chloro-7-deoxylincomycin derivative that is active against most gram-positive organisms except enterococci and *C. difficile*. Gram-negative aerobes are resistant, but most anaerobes are sensitive. It inhibits bacterial protein synthesis by binding to the 50S ribosomal subunit; it is bactericidal or bacteriostatic depending on the concentration, organism, and inoculums.

**Drug Characteristics: Clindamycin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Not systemically absorbed |
| **Dose Adjustment Renal** | Not required | **Distribution** | Not systemically absorbed |
| **Dialyzable** | Not systemically absorbed | **Metabolism** | Not systemically absorbed |
| **Pregnancy Category** | B | **Elimination** | Not systemically absorbed |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

1% Solution

1% Gel

Fougera generic pictured

**Medication Safety Issues: Clindamycin**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| T | No | No | No | Bleomycin, Clinoril, Claritin, clarithromycin | No |

**Drug Interactions: Clindamycin.** None known

**Adverse Reactions: Clindamycin**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Dry skin | Itching pruritus, rash | |

**Efficacy Monitoring Parameters.** Resolution of acne lesions.

**Toxicity Monitoring Parameters.** Seek medical attention if blistering skin rash.

**Key Patient Counseling Points.** Wash and dry face prior to application. Use on skin only, avoid eyes and mucous membranes, avoid cut or broken skin. Shake well before use. Liquid is flammable; avoid smoking while applying or exposure to heat or open flame. For the foam, apply to tissue and use that to apply to face.

**Clinical Pearls.** May have increased sensitivity to sun; may use sunscreen but wait 1-2 h after applying clindamycin topical solution. Also available as injectable, oral, and vaginal formulations.



https://kat.cr/user/Blink99/

# CLOBAZAM: Onfi

**Class:** Anticonvulsant. C-IV

**Dosage Forms. Oral Tablet:** 5 mg, 10 mg, 20 mg; **Oral Suspension:** 2.5 mg/mL

Lundbeck 5 mg pictured



**Common FDA Label Indication, Dosing, and Titration.**

1. Lennox-Gastaut syndrome: Children ≥2 y of age and ≤30 kg, 5 mg po daily, may titrate to 20 mg po daily; Adults and Children ≥2 y of age and >30 kg, 10 mg po daily, may titrate to 40 mg po daily

**Off-Label Uses.**

1. Alcohol withdrawal syndrome: 0.3-0.9 mg/kg/d po × 1 wk
2. Anxiety: 20-80 mg po daily (single or divided doses) × 5-14 d

**MOA.** Clobazam is a benzodiazepine. The exact mechanism of action for clobazam is not known, but is thought to involve potentiation of neurotransmission resulting from binding at the benzodiazepine site of the $GABA_A$ receptor.

**Drug Characteristics: Clobazam**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Initial dose no higher than 5 mg po daily; titrate slowly to *max* of 40 mg po daily | **Absorption** | F = 87%, no effect of food on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 100 L; 90% protein bound |
| **Dialyzable** | Hemodialysis has no effect on plasma concentration of parent or metabolite | **Metabolism** | Extensive hepatic; substrate of CYP2C19, P-glycoprotein to active metabolite (norclobazam); inhibits CYP2D6, UGT1A4, UGT1A6, UGT2B4 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 82% with a half-life of 36-42 h for parent, 71-82 h for metabolite |
| **Lactation** | Compatible (small amounts expressed in breast milk) | **Pharmacogenetics** | Use with caution and reduce dose in CYP2C19 poor metabolizers |
| **Contraindications** | Hypersensitivity to clobazam | **Black Box Warnings** | None |

**Medication Safety Issues: Clobazam**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | cloBAZam | No | No | clonazePAM | No |

## Drug Interactions: Clobazam

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP2C19, P-glycoprotein inducers | Increased clobazam metabolism reduces clobazam effectiveness | Monitor and consider dose increases of clobazam |
| CYP2C19, P-glycoprotein inhibitors | Decreased clobazam metabolism increases risk of clobazam toxicity | Monitor and consider dose decreases of clobazam |
| CYP2D6, UGT1A4, UGT1A6, UGT2B4 substrates | Decreased substrate metabolism may result in substrate toxicity | Monitor and consider decreasing dose of substrate |
| Alcohol, opioids, and other CNS depressants | Additive CNS and respiratory depression | Avoid if possible and consider dose reductions of both agents |
| Phenytoin, fosphenytoin | Decreased metabolism of phenytoin | Monitor for phenytoin toxicity, reduce dose if necessary |

## Adverse Reactions: Clobazam

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Constipation, drooling, ataxia, lethargy, respiratory infections, somnolence, fever | Dysarthria, insomnia, sedation, aggressive behavior, couth | Depression, Stevens-Johnson syndrome, suicidal attempts, toxic epidermal necrolysis |

**Efficacy Monitoring Parameters.** Decrease in the frequency of seizures. Reduction in anxiety.

**Toxicity Monitoring Parameters.** Signs and symptoms of CNS depression, suicidal thoughts or behaviors, unusual changes in mood or behavior. Seek medical attention immediately if rash occurs, as significant risk of Stevens-Johnson syndrome.

**Key Patient Counseling Points.** Often causes lethargy and somnolence. Avoid alcohol while using. Avoid activities requiring mental alertness.

**Clinical Pearls.** Not indicated for children <2 y of age. Many drug-drug interactions; monitor concurrent drug use carefully. Medication guide required when dispensing.



https://kat.cr/user/Blink99/

# CLOBETASOL: Temovate, Various



**Class:** Topical Corticosteroid

**Dosage Forms. Cream:** 0.05%; **Ointment:** 0.05%; **Topical Solution:** 0.05%; **Aerosol Foam:** 0.05%; **Gel:** 0.05%; **Shampoo:** 0.05%

**Common FDA Label Indication, Dosing, and Titration.**

1. Skin disorders, corticosteroid responsive: Children ≥12 y of age and Adults, apply thin layer topically to affected area bid for a *max* of 2 wk
2. Plaque psoriasis: Children >12 y of age and adults, apply thin layer topically to affected area bid for a *max* of 2-4 wk

**Off-Label Uses.**

1. Oral lichen planus: Apply thin layer topically bid with antimycotics

**MOA.** Clobetasol has anti-inflammatory, antipruritic, and vasoconstrictive properties. Corticosteroids are thought to act by the induction of phospholipase A2 inhibitory proteins, lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor, arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A2.

Taro generic 0.05% cream pictured

## Drug Characteristics: Clobetasol

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Minimal absorption unless covering large surface area or covering areas lacking skin integrity |
| **Dose Adjustment Renal** | Not required | **Distribution** | Not absorbed |
| **Dialyzable** | Unknown | **Metabolism** | Not absorbed |
| **Pregnancy Category** | C | **Elimination** | Not absorbed |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

## Medication Safety Issues: Clobetasol

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | No |

**Drug Interactions: Clobetasol.** None known

**Adverse Reactions: Clobetasol**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Burning sensation, stinging, pruritus at site of administration, headache | Hypothalamic axis (HPA) suppression has been reported when used with occlusive dressings, over larger surface areas |

**Efficacy Monitoring Parameters.** Improvement in clinical signs of skin disorder.

**Toxicity Monitoring Parameters.** Seek medical attention if severe skin irritation or symptoms worsen after administration.

**Key Patient Counseling Points.** Apply thin layer to affected area of skin. Skin should be clean and intact at site of application. Avoid contact with eyes and do not ingest by mouth. Avoid occlusive dressings or tight-fitting clothes over site of administration.

**Clinical Pearls.** Various dosage forms (foams, gels, shampoos, etc) available. Very high-potency corticosteroid. Application to large surface areas, prolonged use, and occlusive dressings may increase risk of systemic absorption and toxicity. Pediatric patients are more susceptible to systemic absorption.



https://kat.cr/user/Blink99/

# CLONAZEPAM: Klonopin, Various

Teva generic pictured

**Class:** Benzodiazepine. C-IV

**Dosage Forms.** **Oral Tablet:** 0.5 mg, 1 mg, 2 mg; **Oral Tablet, Disintegrating:** 0.125 mg, 0.25 mg, 0.5 mg, 1 mg, 2 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Panic disorder: 0.25 mg po bid, may titrate by 0.125-0.25 mg po bid every 3 d to a *max* total daily dose of 1-4 mg (divided into 2-3 daily doses)
2. Seizure: Children ≥10 y of age or ≥30 kg and Adults, 0.5 mg po tid, may titrate by 0.125-0.25 mg po bid every 3 d to a *max* of 1-4 mg/d (divided into 2-3 daily doses); Children <10 y of age or <30 kg, 0.01-0.03 mg/kg/d po divided into 2-3 daily doses, may titrate by 0.25-0.5 mg po every 3 d to *max* of 0.1-0.2 mg/kg/d (divided into 3 daily doses)

**Off-Label Uses.**

1. Restless legs syndrome: 0.5-2 mg po qhs

**MOA.** Enhances the postsynaptic effect of the inhibitory neurotransmitter, γ-aminobutyric acid (GABA).

**Drug Characteristics: Clonazepam**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Decrease usual dose by 50% | **Absorption** | F = 90%, no effect of food on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 1.5-3 L; 85% protein bound |
| **Dialyzable** | Supplemental dose not required | **Metabolism** | Hepatic; substrate of CYP3A4/5 |
| **Pregnancy Category** | D | **Elimination** | Renal elimination is 1% with a half-life of 30-40 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to benzodiazepines, narrow-angle glaucoma, liver disease | **Black Box Warnings** | None |

### Medication Safety Issues: Clonazepam

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | ClonazePAM | Oral disintegrating tablets | No | cloBAZam, cloNIDine, clorazepate, cloZAPine, LORazepam | Avoid benzodiazepines (any type) for treatment of insomnia, agitation, or delirium. |

### Drug Interactions: Clonazepam

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Alfentanil, opioids, and other respiratory depressants | Additive respiratory depression | Avoid if possible and consider dose reductions of both agents |
| CYP3A4/5 inducers | Increased clonazepam metabolism reduces clonazepam effectiveness | Monitor and consider dose increases of clonazepam |
| CYP3A4/5 inhibitors | Decreased clonazepam metabolism increases risk of clonazepam toxicity | Monitor and consider dose decreases of clonazepam |
| Theophylline | Decreased clonazepam effectiveness via inhibition of adenosine receptors | Monitor and consider dose increases for clonazepam |

### Adverse Reactions: Clonazepam

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Ataxia, lethargy, somnolence, weight gain | Tachycardia, palpitations, nausea and vomiting, blurred vision | Seizures, mania, depression, withdrawal symptoms |

**Efficacy Monitoring Parameters.** Reduction in anxiety symptoms or seizures.

**Toxicity Monitoring Parameters.** Seek medical attention if severe drowsiness, slow or rapid heartbeat or skipped beats, thoughts of suicide.

**Key Patient Counseling Points.** May cause drowsiness; avoid driving or other tasks requiring motor coordination. Allow orally disintegrating tablet to dissolve on your tongue. Avoid alcohol.

**Clinical Pearls.** Consider dose reductions of benzodiazepine in hepatic impairment. Use caution in elderly, appear more sensitive to the effects; dose reductions of 50% have been recommended. Use CNS depressants with caution, may have additive effects. Avoid abrupt discontinuation after chronic use, may cause seizures. Medication guide required when dispensing. Higher abuse potential among benzodiazepines.



https://kat.cr/user/Blink99/

# CLONIDINE: Catapres, Various

**Class:** $\alpha_2$-Adrenergic Agonist

**Dosage Forms.** **Oral Tablet:** 0.1 mg, 0.2 mg, 0.3 mg; **Oral Tablet, Extended Release:** 0.1 mg, 0.2 mg; **Transdermal Patch:** 0.1 mg/24 h, 0.2 mg/24 h, 0.3 mg/24 h

Actavis generic pictured

C

**Common FDA Label Indication, Dosing, and Titration.**

1. Attention-deficit hyperactivity disorder: Children >6 y of age, 0.1 mg extended-release tablet po qhs, may titrate in increments of 0.1 mg/d at weekly intervals to desired effect; give doses >0.1 mg/d in 2 divided doses; *max* dose 0.4 mg/d
2. Essential hypertension: 0.1 mg/d transdermal patch applied every 7 d, may titrate by 0.1 mg/d transdermal patch increments every 1-2 wk; *max* 0.6 mg/d every 7 d
3. Hypertension: 0.1 mg po bid, may titrate by 0.1 mg/d at weekly intervals, to 0.2-0.6 mg in 2 divided doses, *max* 2.4 mg/d

**Off-Label Uses.**

1. Hot sweats: 0.1 mg/d transdermal patch every 7 d or 0.2 mg po daily
2. Nicotine dependence: 0.1-0.2 mg/24 h transdermal patch daily or 0.1-0.45 mg po daily
3. Spasticity: 0.05-0.4 mg po daily in divided doses

**MOA.** Clonidine stimulates postsynaptic $\alpha_2$-adrenergic receptors in the CNS by activating inhibitory neurons to decrease sympathetic outflow. Clonidine is not a complete agonist, so some of its effects might result from antagonist actions at presynaptic $\alpha$-receptors. These actions reduce peripheral vascular resistance, renal vascular resistance, HR, and BP.

**Drug Characteristics: Clonidine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 75-100% immediate-release tablet, F = 60% patch; no effect of food on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 2.9 L/kg; 20-40% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic metabolism, unknown pathway |
| **Pregnancy Category** | C | **Elimination** | Renal elimination of clonidine is 40-60% with a half-life of 12.5-16 h (41 h in patients with renal disease) |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | Epidural use |

### Medication Safety Issues: Clonidine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| TTS | CloNIDine | Extended-release tablets | No | Clomid, clomiPHENE, clonazePAM, cloZAPine, KlonoPIN, quiNIDine | Avoid clonidine as a first-line antihypertensive. High risk of adverse CNS effects; may cause bradycardia and orthostatic hypotension. |

### Drug Interactions: Clonidine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| NSAIDs | Decreased antihypertensive effect of clonidine | Avoid concurrent use or monitor BP |
| TCAs | Decreased antihypertensive effect of clonidine by increasing release of norepinephrine | Avoid concurrent use or monitor BP |
| Beta-blockers, calcium channel blockers | Increased risk of hypotension and sinus bradycardia | Avoid concurrent use or monitor BP and HR |
| Cyclosporine | Increased risk of cyclosporine toxicity | Monitor serum cyclosporine levels |

### Adverse Reactions: Clonidine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Feeling nervous, headache, somnolence, erythema (patch), xerostomia | Bradycardia, constipation, contact dermatitis (patch), fatigue, hypotension, increased body temperature, irritability, nausea, palpitations, rash, rebound hypertension, sedation, tachycardia, urticaria | AV block |

**Efficacy Monitoring Parameters.** Decreased BP or improvement of mental and behavioral symptoms of ADHD.

**Toxicity Monitoring Parameters.** Rebound hypertension, increased HR, palpitations, syncope.

**Key Patient Counseling Points.** Avoid alcohol, CNS depressants. Caution with driving and other tasks requiring alertness. Swallow extended-release tablet whole, may be taken with or without food. Apply patch to hairless area of intact skin on upper outer arm or chest; rotate patch location. If patch loosens during the 7-d wearing, secure adhesive cover. Report signs/symptoms of hypotension, exacerbation of angina peripheral edema, fatigue, hypotension, or hepatic dysfunction with initial dosing and dose changes. Avoid abrupt discontinuation to avoid rebound hypertension.

**Clinical Pearls.** Safety and efficacy of the immediate-release tablet for the treatment of hypertension not established in children. Extended-release tablets and immediate-release tablet formulation are not interchangeable. Injectable formulation available for epidural infusion (pain management).



https://kat.cr/user/Blink99/

# CLOPIDOGREL: Plavix, Various

**Class:** Platelet Aggregation Inhibitor

**Dosage Forms.** **Oral Tablet:** 75 mg, 300 mg

Bristol-Myers Squibb/Sanofi Aventis
75 mg pictured

C

**Common FDA Label Indication, Dosing, and Titration.**

1. Acute ST and non–ST segment elevation myocardial infarction: 300-600 mg po loading dose, followed by 75 mg po daily (in combination with aspirin for those not at risk of bleeding)
2. Thrombosis prevention in arteriosclerotic vascular disease, following stroke, in peripheral arterial occlusive disease: 75 mg po daily

**Off-Label Uses.**

1. Thrombosis prevention in atrial fibrillation or following percutaneous coronary intervention: 75 mg po daily (in combination with aspirin for those not at risk of bleeding)

**MOA.** Clopidogrel is an antiplatelet agent that prevents platelet aggregation by direct inhibition of ADP binding to receptor sites, inhibiting subsequent activation of the glycoprotein IIb/IIIa complex. This action is irreversible; therefore, platelets exposed to clopidogrel are inhibited for their life spans.

**Drug Characteristics: Clopidogrel**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 50%; no effect of food on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | 93% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Prodrug, requires activation by CYP2C19; substrate of CYP2C19, inhibitor of CYP2B6, CYP2C8 |
| **Pregnancy Category** | B | **Elimination** | Renal elimination of clopidogrel is 50% with a half-life of 6 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | CYP2C19 poor metabolizers; increased risk of cardiovascular events due to reduced efficacy of clopidogrel; consider alternative treatment or a higher dose |
| **Contraindications** | Hypersensitivity to clopidogrel and active bleeding | **Black Box Warnings** | Reduced CYP2C19 function |

**Medication Safety Issues: Clopidogrel**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Elavil, Paxil, Pradaxa | No |

## Drug Interactions: Clopidogrel

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Amiodarone, azole antifungals, calcium channel blockers, cimetidine, fluoxetine, fluvoxamine, PPIs | Decreased platelet inhibitory effect of clopidogrel | Avoid concurrent use or monitor for signs/symptoms of thrombus formation |
| Aspirin, cilostazol, direct thrombin inhibitors, fibrinolytics, fondaparinux, low-molecular-weight heparin, NSAIDs, SSRIs, ticlopidine, unfractionated heparin, warfarin | Increased risk of bleeding | Monitor for signs/symptoms of bleeding |
| CYP2B6, CYP2C8 substrates | Reduced metabolism of substrates via inhibition of CYP2B6, CYP2C8 | Monitor and consider substrate dose reductions |
| CYP2C19 inducers | Increased clopidogrel activation increases clopidogrel toxicity | Monitor and consider decreasing dose of clopidogrel |
| CYP2C19 inhibitors | Decreased clopidogrel activation decreases clopidogrel efficacy | Monitor and consider increasing dose of clopidogrel |

## Adverse Reactions: Clopidogrel

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Arthralgia, backache, epistaxis, gastritis, headache, hypertension, pruritus | Agranulocytosis, Stevens-Johnson syndrome, GI hemorrhage, GI ulcer, pancytopenia, thrombotic thrombocytopenic purpura |

**Efficacy Monitoring Parameters.** Prevention of thrombotic events.

**Toxicity Monitoring Parameters.** Signs/symptoms of bleeding, especially with concomitant anticoagulant therapy.

**Key Patient Counseling Points.** Report signs/symptoms of bleeding, especially if used concomitantly with anticoagulant therapy. Do not stop therapy abruptly without first talking with prescriber to minimize the risk of re-thrombosis, particularly after stent placement. Clopidogrel should be discontinued 5 d prior to elective surgery, if an antiplatelet effect is not desired.

**Clinical Pearls.** Safety and efficacy not established in pediatric patients. Clopidogrel effectiveness is dependent on its activation to an active metabolite by CYP2C19. In patients who are CYP2C19 poor metabolizers or taking concurrent CYP2C19 inhibitors, clopidogrel at recommended doses forms less of the active metabolite and has a smaller effect on platelet function. Compared with normal metabolizers, poor CYP2C19 metabolizers with acute coronary syndrome, or undergoing percutaneous coronary intervention treated with clopidogrel at recommended doses, exhibit higher cardiovascular event rates. Consider alternative treatment or a higher dose in CYP2C19 poor metabolizers.



https://kat.cr/user/Blink99/

# CLOTRIMAZOLE/BETAMETHASONE: Lotrisone, Various



**Class:** Anti-infective/Anti-inflammatory Combination

**Dosage Forms. Topical Cream:** (Clotrimazole/Betamethasone) 1%/0.05%**, Topical Lotion:** (Clotrimazole/Betamethasone) 1%/0.05%

**Common FDA Label Indication, Dosing, and Titration.**

1. Tinea: Adults and children >12 y, apply to affected area bid, for a *max* of 2 wk (for tinea corporis or tinea cruris) or 4 wk (for tinea pedis)

**Off-Label Uses.** None

**MOA.** Clotrimazole inhibits biosynthesis of ergosterol or other sterols, damaging the fungal cell wall membrane and altering its permeability. Betamethasone dipropionate is a corticosteroid that stimulates synthesis of enzymes thought to be responsible for anti-inflammatory effects.

Taro generic 1%/0.05% cream pictured

## Drug Characteristics: Betamethasone/Clotrimazole

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Minimal absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Minimal absorption |
| **Dialyzable** | Unknown | **Metabolism** | Minimal absorption |
| **Pregnancy Category** | C | **Elimination** | Minimal absorption |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to clotrimazole or betamethasone | **Black Box Warnings** | None |

## Medication Safety Issues: Betamethasone/Clotrimazole

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Co-trimoxazole | No |

**Drug Interactions: Betamethasone/Clotrimazole.** None known

**Adverse Reactions: Betamethasone/Clotrimazole**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Dry skin | Rash, HPA suppression has been reported in children, therefore not recommended in children <12 y of age |

**Efficacy Monitoring Parameters.** Resolution of erythema and pruritus. Improvement in erythema and pruritus usually occurs within 3-5 d. If no improvement is seen after 1 wk of treatment for tinea cruris or tinea corporis, or after 2 wk of treatment for tinea pedis, then the diagnosis should be reviewed.

**Toxicity Monitoring Parameters.** Seek medical attention if severe skin irritation or rash. Various cortisol tests could be utilized to evaluate HPA suppression.

**Key Patient Counseling Points.** Apply thin layer to affected area. If using lotion, shake well before use.

**Clinical Pearls.** Patients receiving the combination therapy show an earlier, better clinical response than patients treated with clotrimazole cream or betamethasone cream alone. Cure rates with clotrimazole/betamethasone are at least as good or better as compared to clotrimazole alone. Do not use with occlusive dressings or on larger areas. This can lead to systemic absorption of betamethasone and HPA suppression.



https://kat.cr/user/Blink99/

# CODEINE: Tylenol with Codeine, Various

**Class:** Opioid. C-II (when in combination with acetaminophen, C-III)

**Dosage Forms. Oral Tablet (Codeine Alone):** 15 mg, 30 mg, 60 mg; **Oral Solution (Codeine Alone):** 30 mg/5 mL; **Oral Tablet (With Acetaminophen):** Acetaminophen/Codeine 300 mg/15 mg, Acetaminophen/Codeine 300 mg/30 mg, Acetaminophen/Codeine 300 mg/60 mg; **Oral Elixir, Oral Solution (With Acetaminophen):** Acetaminophen/Codeine 120 mg/12 mg per 5 mL

300 mg/30 mg

Teva generic pictured

C

**Common FDA Label Indication, Dosing, and Titration.**

1. Pain: Adults, 15-60 mg po q4h prn; with acetaminophen 300-1000 mg (*max* 4000 mg/d); Children 3-6 y of age, 12 mg po 3-4 times a day prn, with acetaminophen 120 mg/dose; Children 7-10 y of age, 24 mg po 3-4 times a day prn, with acetaminophen 240 mg/dose

**Off-Label Uses.** None

**MOA.** Codeine is 3-methoxymorphine, a phenanthrene opioid with very low affinity for opioid receptors. Its analgesic activity appears to result from conversion to morphine.

**Drug Characteristics: Codeine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Avoid chronic use in hepatic impairment | **Absorption** | Well absorbed; food has no effect on absorption |
| **Dose Adjustment Renal** | Codeine: CrCl 10-50 mL/min, 75% of dose; CrCl <10 mL/min, 50% of dose | **Distribution** | Vd = 2.6 L/kg; 7-25% protein bound |
| **Dialyzable** | Unknown | **Metabolism** | Codeine is a prodrug that requires activation by CYP2D6 to morphine; substrate of CYP2D6 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination approaches 100% with a half-life of 2-4 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | CYP2D6 variants with altered response |
| **Contraindications** | Hypersensitivity to codeine | **Black Box Warnings** | Hepatotoxicity |

**Medication Safety Issues: Codeine**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| Tylenol 3 and Tylenol | No | No | Yes (opioids) | Cardene, Lodine | No |

### Drug Interactions: Codeine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Alcohol, opioids, and other CNS depressants | Additive CNS and respiratory depression | Avoid if possible and consider dose reductions of both agents |
| Buprenorphine, opioid agonists/ antagonists, opioid antagonists | Precipitation of withdrawal symptoms | Avoid concurrent use with opioids |
| CYP2D6 inhibitors | Decreased effectiveness of codeine; prevents conversion of codeine to active metabolite, morphine | Monitor and consider increasing dose of codeine or choose alternative analgesic agent |

### Adverse Reactions: Codeine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Nausea, vomiting, constipation, somnolence | Pruritus, euphoria, dizziness | Stevens-Johnson syndrome, GI bleeding, elevated liver functions, thrombocytopenia, physical dependence, tolerance, respiratory depression |

**Efficacy Monitoring Parameters.** Decreased pain.

**Toxicity Monitoring Parameters.** LFTs, SCr, if chronic use; severe skin rash, black tarry stools, excessive drowsiness, yellowing of eyes of skin, change in urination.

**Key Patient Counseling Points.** If using chronically, use a stool softener and/or laxative for preventing constipation. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol.

**Clinical Pearls.** Use caution in elderly, appear more sensitive to the effects. Use of CNS depressants with caution, may have additive effects. Tolerance and physical dependence may occur, avoid abrupt discontinuation. Oral solution contains 7% alcohol. Patients with multiple CYP2D6 gene copies metabolize codeine more rapidly (ultrarapid metabolism), whereas patients who lack functional CYP2D6 genes do not metabolize codeine to morphine and do not experience analgesic effects. Multiple CYP2D6 gene copies occur in 4-5% of Caucasians and is absent in 5-10% of the Caucasian population. In ultrarapid metabolizers, pediatric deaths post-tonsillectomy have been reported. CYP2D6 inhibitors, especially SSRIs, may also prevent activation of codeine to morphine. Codeine also available in combination with guaifenesin for cough.



https://kat.cr/user/Blink99/

# COLCHICINE: Colcyrs, Various

**Class:** Antigout

**Dosage Forms.** **Oral Tablet:** 0.6 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Gout, acute: 1.2 mg po at the first sign of a flare followed by 0.6 mg 1 h later; *max* 1.8 mg over 1 h
2. Gout, prophylaxis: 0.6 mg po daily to bid, *max* of 1.2 mg/d or onset of diarrhea
3. Familial Mediterranean fever: Children 4-6 y of age, 0.3-1.8 mg po daily; Children 6-12 y, 0.9-1.8 mg po daily; Children ≥12 y of age and Adults, 1.2-2.4 mg po daily, increase or decrease dose in increments of 0.3 mg/d

West-ward generic 0.6 mg pictured

C

**Off-Label Uses.**

1. Amyloidosis: 0.6 mg po bid
2. Constipation: 0.6 mg po q30 min until onset of diarrhea

**MOA.** Exact mechanism unknown. In patients with gout, may interrupt the cycle of monosodium urate crystal deposition in joint tissues and the resultant inflammatory response that initiates and sustains an acute attack. Colchicine also inhibits urate crystal deposition, which is enhanced by a low pH in the tissues, probably by inhibiting oxidation of glucose and subsequent lactic acid production in leukocytes.

**Drug Characteristics: Colchicine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Severe hepatic failure, do not repeat gout f are courses more than once every 2 wk | **Absorption** | F = 45%, no effect of food on absorption |
| **Dose Adjustment Renal** | CrCl <30 mL/min, for gout f are, do not repeat course more than once every 2 wk | **Distribution** | Vd = 5-8 L/kg, 39% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Partial hepatic; substrate of CYP3A4/5, P-glycoprotein |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 40-65% with a half-life of 26-32 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to colchicine; concurrent use with strong CYP3A4/5 inhibitors in patients with renal or hepatic failure | **Black Box Warnings** | None |

### Medication Safety Issues: Colchicine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Cortrosyn | No |

### Drug Interactions: Colchicine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5, P-glycoprotein inducers | Increased colchicine metabolism reduces colchicine effectiveness | Monitor and consider dose increases of colchicine |
| CYP3A4/5, P-glycoprotein inhibitors | Decreased colchicine metabolism increases risk of colchicine toxicity | Monitor and consider dose decreases of colchicine, particularly if renal or hepatic dysfunction exists |
| Lipid-lowering agents (fibrates, statins) | Coadministration of colchicine and lipid-lowering agents may result in myopathy and rhabdomyolysis; mechanism unknown | Avoid concurrent use |

### Adverse Reactions: Colchicine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Diarrhea, nausea | Vomiting | Agranulocytosis, rhabdomyolysiss |

**Efficacy Monitoring Parameters.** Resolution of clinical signs and symptoms of gout (pain, stiffness, swelling).

**Toxicity Monitoring Parameters.** CBC, alkaline phosphatase at baseline and periodically during treatment. Instruct patients to discontinue the medication immediately and seek medical attention if signs and symptoms of agranulocytosis (severe neutropenia), or myotoxicity (including rhabdomyolysis). Monitor renal and hepatic function.

**Key Patient Counseling Points.** Instruct patient on appropriate dosing strategy for gout flares (dosing to symptom relief or onset of adverse effects, particularly diarrhea).

**Clinical Pearls.** Colchicine is a natural alkaloid found in plants such as the autumn crocus (*Colchicum autumnale*) and glory lily (*Gloriosa superba*). Medication guide required with dispensing.



https://kat.cr/user/Blink99/

# COLESEVELAM: Welchol

**Class:** Hypolipidemic, Bile Acid Sequestrant

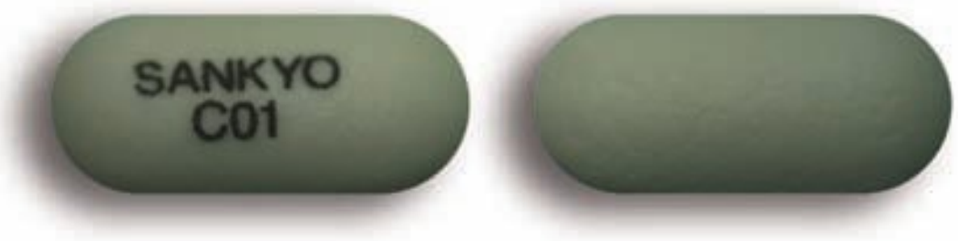
**Dosage Forms.** **Oral Tablet:** 625 mg; **Granules for Oral Suspension:** 3.75 g/packet

**Common FDA Label Indication, Dosing, and Titration.**

1. Primary hyperlipidemia: 1875 mg (3 tablets or 1.875 g powder packet) po bid or 3750 mg (6 tablets or 3.75 g powder packet) po daily

**Off-Label Uses.**

1. Familial hypercholesterolemia: 1875 mg (3 tablets or 1.875 g powder packet) po bid or 3750 mg (6 tablets or 3.75 g powder packet) po daily



Daichi-Sankyo 625 mg pictured

C

**MOA.** Colesevelam is a nonabsorbed, polymeric, lipid-lowering agent that binds intestinal bile acids, resulting in the increased clearance of LDL-cholesterol and a reduction in total cholesterol. Unlike cholestyramine and colestipol, colesevelam is not an anion exchange resin but binds bile acids and impedes their reabsorption.

**Drug Characteristics: Colesevelam**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Not absorbed |
| **Dose Adjustment Renal** | Not required | **Distribution** | Not absorbed |
| **Dialyzable** | Not dialyzable | **Metabolism** | Not absorbed |
| **Pregnancy Category** | B | **Elimination** | Fecal elimination is >99% and renal elimination is 0.05% |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | History of bowel obstruction, hypertriglyceridemia-induced pancreatitis; serum triglyceride level >500 mg/dL | **Black Box Warnings** | None |

**Medication Safety Issues: Colesevelam**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Tablets (use granules instead) | No | No | No |

### Drug Interactions: Colesevelam

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Antidiabetic drugs, diltiazem, ezetimibe, fibrates, levothyroxine, mycophenolate, oral contraceptives | Decreased bioavailability of colesevelam due to binding and decreased absorption | Take drug 4 h prior to colesevelam |
| Cyclosporine, phenytoin | Decreased bioavailability of cyclosporine and phenytoin due to binding and decreased absorption | Take drug 4 h prior to colesevelam; monitor drug serum levels |
| Warfarin | Decreased bioavailability of warfarin due to binding and decreased absorption | Take warfarin 4 h prior to colesevelam; monitor INR values |

### Adverse Reactions: Colesevelam

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Constipation | Asthenia, nasopharyngitis, myalgia, nausea, hypertension, hypertriglyceridemia, hypoglycemia | Pancreatitis, bowel obstruction |

**Efficacy Monitoring Parameters.** Reduction in total cholesterol, LDL-cholesterol, and triglycerides levels; increase in HDL-cholesterol levels.

**Toxicity Monitoring Parameters.** Signs/symptoms of GI side effects, vitamin A, D, E, or K deficiencies.

**Key Patient Counseling Points.** Should be used together with diet and exercise to lower cholesterol levels. Empty contents of powder packet into a glass and mix with 120-240 mL of water; stir well and drink. Oral suspension should not be taken in its dry form. Take with a meal. Tablet should be swallowed with liquid (water, milk, or juice). May be dosed concomitantly with an HMG-CoA reductase inhibitor.

**Clinical Pearls.** Safety and efficacy not established in pediatric patients <10 y of age or in premenarcheal girls. Patients with difficulty swallowing should use oral suspension instead of tablets.



https://kat.cr/user/Blink99/

# CONJUGATED ESTROGENS: Premarin

**Class:** Estrogen Hormone

**Dosage Forms. Oral Tablet:** 0.3 mg, 0.45 mg, 0.625 mg, 0.9 mg, 1.25 mg

Wyeth pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Abnormal vasomotor function (menopause), atrophy of vagina or vulva, postmenopausal osteoporosis prophylaxis, female hypogonadism syndrome: 0.3 mg po daily, continuously or cyclically; adjust dose to individual response
2. Primary ovarian failure: 1.25 mg po daily cyclically (3 wk on, 1 wk off); adjust dose to individual response

**Off-Label Uses.** None

**MOA.** Estrogens are largely responsible for the development and maintenance of the female reproductive system and secondary sexual characteristics. The primary source of estrogen in normally cycling adult women is the ovarian follicle. After menopause, most endogenous estrogen is produced by conversion of androstenedione to estrone by peripheral tissues. Estrogens act through binding to nuclear receptors in estrogen-responsive tissues. Circulating estrogens modulate the pituitary secretion of the gonadotropins, luteinizing hormone (LH), and follicle-stimulating hormone (FSH), through a negative-feedback mechanism. Estrogens act to reduce the elevated levels of these gonadotropins seen in postmenopausal women.

**Drug Characteristics: Conjugated Estrogens**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Avoid in severe liver dysfunction | **Absorption** | Well absorbed, no effect of food on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Largely distributed; bound to sex hormone proteins |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic; substrate of CYP3A4/5 and 1A2 |
| **Pregnancy Category** | X | **Elimination** | Primary renal elimination with a half-life of 26 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity, undiagnosed abnormal genital bleeding, history of estrogen- or progesterone-dependent neoplasia, active or history of deep vein thrombosis or pulmonary embolism, severe liver dysfunction, known or suspected pregnancy | **Black Box Warnings** | Breast cancer, cardiovascular disease, endometrial cancer, dementia risks |

### Medication Safety Issues: Conjugated Estrogens

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Primaxin, Provera, Remeron | Avoid oral and topical patch. |

### Drug Interactions: Conjugated Estrogens

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5, 1A2 inducers | Increased estrogen metabolism reduces estrogen effectiveness | Monitor and consider dose increases of estrogen |
| CYP3A4/5, 1A2 inhibitors | Decreased estrogen metabolism increases risk of estrogen toxicity | Monitor and consider dose decreases of estrogen |
| Levothyroxine | Estrogen increases serum thyroxine-binding globulin, reducing free thyroxine resulting in hypothyroid effects | Measure TSH and adjust dose if necessary |

### Adverse Reactions: Conjugated Estrogens

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Weight change, headache, migraine, depression, disorder of menstruation, breast pain | Edema, vasodilation, abdominal pain, hirsutism, diarrhea, nausea, stomach cramps, vomiting, backache | Heart disease, hypertension, myocardial infarction, breast cancer, diabetes mellitus, hypercalcemia, venous thromboembolism, anaphylaxis, cerebrovascular accident, cervical cancer, malignant neoplasm of endometrium of corpus uteri, ovarian cancer, pulmonary embolism |

**Efficacy Monitoring Parameters.** Resolution of clinical signs of abnormal bleeding or hot flashes or other symptoms, prevention of osteoporosis.

**Toxicity Monitoring Parameters.** Monitor BMD; conduct diagnostic evaluation to rule out malignancy in the event of persistent or recurring vaginal bleeding.

**Key Patient Counseling Points.** Discuss potential long-term adverse effects of hormone therapy including myocardial infarction, stroke, deep vein thrombosis, pulmonary embolism, and breast cancer. Take at bedtime to minimize side effects. Take with or without meals.

**Clinical Pearls.** Injectable and vaginal cream is also available for other indications requiring estrogen replacement therapy. Combination of estrogens and progestins should not be used for the prevention of cardiovascular disease. Increased risk (over placebo) of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and DVT has been shown in postmenopausal women. Because of these risks, estrogens with or without progestins should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman. In postmenopausal women with a uterus, a progestin (eg, medroxyprogesterone) should be added to estrogen to reduce the risk of endometrial cancer. Increased incidence of dementia was observed in women ≥65 y of age taking estrogens. Also available in combination with bazedoxifene (Duavee) for osteoporosis prevention and vasomotor symptoms.



https://kat.cr/user/Blink99/

# CYANOCOBALAMIN: Cobolin-M, Various



**Class:** Essential B Vitamin ($B_{12}$)

**Dosage Forms. Injection Solution:** 1000 mcg/mL; **Mucous Membrane Lozenge/Troche:** 50 mcg, 100 mcg, 250 mcg, 500 mcg; **Oral Tablet:** 50 mcg, 100 mcg, 250 mcg, 500 mcg, 1 mg; **Oral Tablet, Extended Release:** 1 mg; **Sublingual Tablet:** 2.5 mg; **Nasal Solution:** 500 mcg/0.1 mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Cobalamin deficiency, normal absorption: Oral, 1000 mcg po daily; Nasal, 500 mcg in 1 nostril once weekly
2. Cobalamin deficiency, malabsorption: 100 mcg IM or deep subq injection daily for 6-7 d, then 100 mcg monthly for life

**Off-Label Uses.** None

**MOA.** $B_{12}$ is required for the synthesis of the amino acid methionine from homocysteine. A deficiency of $B_{12}$ results in hyperhomocysteinemia and a decrease in methionine. Since methionine is required for DNA synthesis, $B_{12}$ deficiency also results in decreased DNA synthesis, which presents clinically as macrocytic anemia when red blood cells are unable to extrude their nucleus.

**Drug Characteristics: Cyanocobalamin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Oral: Absorption is poor and requires intrinsic factor, patients without intrinsic factor require IM supplementation; IM: approaches 100% |
| **Dose Adjustment Renal** | Not required | **Distribution** | Stored in the liver and most tissues |
| **Dialyzable** | Not dialyzable | **Metabolism** | Enterohepatic cycling occurs |
| **Pregnancy Category** | C | **Elimination** | Dose dependent, renal 50-98% with 100-1000 mcg IM dose |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to cyanocobalamin or cobalt | **Black Box Warnings** | None |

American Regent 1000 mcg/mL generic pictured

**Medication Safety Issues: Cyanocobalamin**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | ER product | No | No | No |

**Drug Interactions: Cyanocobalamin.** None known

**Adverse Reactions: Cyanocobalamin**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Injection site pain, arthralgia, fatigue, dizziness, headache | Edema | Anaphylaxis, worsening of heart failure, angioedema |

**Efficacy Monitoring Parameters.** Baseline and periodic $B_{12}$ and folic acid levels, intrinsic factor, normalization of MCV, normalization of Hgb, resolution of symptoms of anemia (fatigue, shortness of breath).

**Toxicity Monitoring Parameters.** Seek medical attention if severe shortness of breath, swelling, skin rash, or hives.

**Key Patient Counseling Points.** May require several weeks for maximum effect. Take extended-release products with food. Avoid alcohol as it inhibits the absorption of $B_{12}$.

**Clinical Pearls.** Drugs that interfere with folate metabolism (methotrexate, hydroxyurea, pemetrexed) will cause an elevated MCV in the absence of vitamin B deficiency. Patients on pemetrexed receive $B_{12}$ to prevent toxicity. Metformin decreases $B_{12}$ concentrations.



https://kat.cr/user/Blink99/

# CYCLOBENZAPRINE: Flexeril, Various

**Class:** Centrally Acting Skeletal Muscle Relaxant

**Dosage Forms.** **Oral Tablet:** 5 mg, 7.5 mg, 10 mg; **Oral Capsule, Extended Release:** 15 mg, 30 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Skeletal muscle spasm: 5 mg po tid; may titrate to 10 mg po tid, may treat up to 2-3 wk

**Off-Label Uses.**

1. Temporomandibular joint disorder, 10 mg po daily × 3 wk

**MOA.** Cyclobenzaprine relieves skeletal muscle spasm of local origin without interfering with muscle function. It is ineffective in muscle spasm due to CNS disease. Evidence suggests that the net effect of cyclobenzaprine is a reduction in tonic somatic motor activity, influencing both gamma (γ) and alpha (α) motor systems.

Mylan generic 10 mg pictured



## Drug Characteristics: Cyclobenzaprine

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Mild hepatic dysfunction, 5 mg po daily; moderate, severe hepatic dysfunction, avoid | **Absorption** | F = 33-55%, no effect of food on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | 93% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic; substrate of CYP1A2 |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 50% with a half-life of 18 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to cyclobenzaprine, concomitant MAOI use, heart failure, acute coronary phase of AMI, heart block | **Black Box Warnings** | None |

## Medication Safety Issues: Cyclobenzaprine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Extended-release capsules | No | CycloSERINE, Floxin | Avoid. Most muscle relaxants poorly tolerated by older adults, because of anticholinergic adverse effects, sedation, increased risk of fractures. |

### Drug Interactions: Cyclobenzaprine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP1A2 inducers | Increased cyclobenzaprine metabolism reduces cyclobenzaprine effectiveness | Monitor and consider dose increases of cyclobenzaprine |
| CYP1A2 inhibitors | Decreased cyclobenzaprine metabolism increases risk of cyclobenzaprine toxicity | Monitor and consider dose decreases of cyclobenzaprine |
| CNS depressants (opioids, benzodiazepines, alcohol) | Additive sedative effects | Avoid concurrent use or monitor carefully for signs of toxicity |

### Adverse Reactions: Cyclobenzaprine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Xerostomia, headache, drowsiness | Constipation, indigestion, nausea, pharyngeal dryness, asthenia, dizziness, confusion, blurred vision | Cardiac dysrhythmia, cholestasis, hepatitis, jaundice, anaphylaxis, immune hypersensitivity reaction |

**Efficacy Monitoring Parameters.** Reduction in pain and muscle spasms.

**Toxicity Monitoring Parameters.** Seek medical attention if symptoms of hepatic failure occur during therapy with this agent.

**Key Patient Counseling Points.** Patients should avoid activities requiring mental alertness or coordination until drug effects are known, as drug may cause dizziness or sedative effects. Take extended-release capsule same time each day.

**Clinical Pearls.** Cyclobenzaprine is used for the relief of discomfort associated with acute, painful musculoskeletal conditions in adults and should be used for only short periods (up to 2-3 wk). Should be used with caution in patients with glaucoma, increased IOP, urinary retention, etc, as cyclobenzaprine has anticholinergic-like effects. Avoid use in elderly, may be more sensitive to effects.



https://kat.cr/user/Blink99/

# CYCLOSPORINE OPHTHALMIC: Restasis



**Class:** Calcineurin Inhibitor

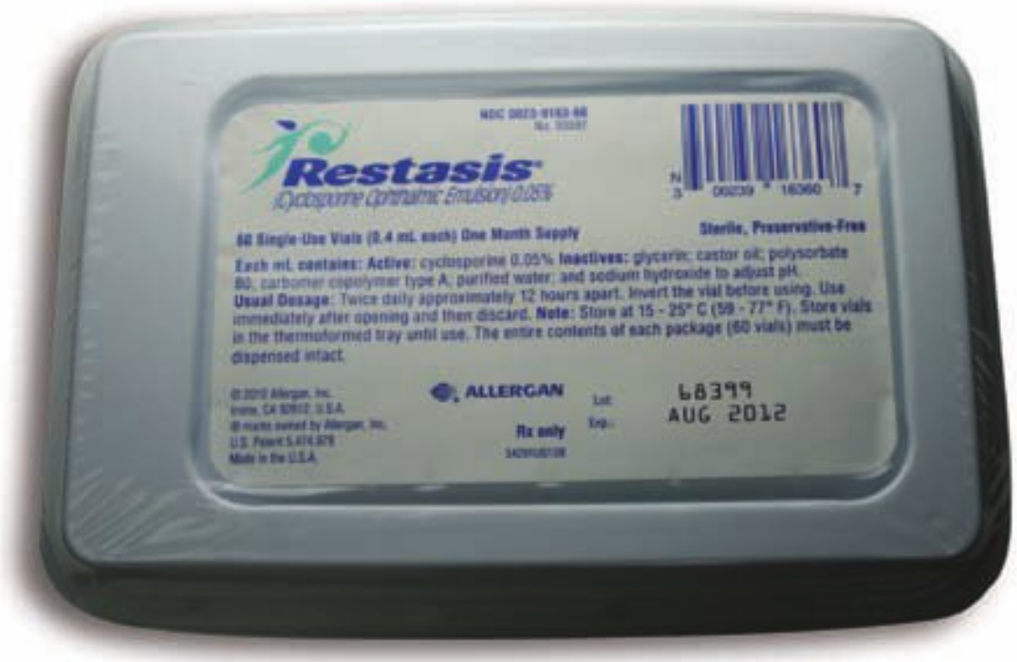
**Dosage Forms. Ophthalmic Emulsion:** 0.5%

**Common FDA Label Indication, Dosing, and Titration.**

1. Keratoconjunctivitis sicca, when associated ocular inflammation results in scanty tear production: 1 drop in affected eye(s) q12h

**Off-Label Uses.** None

**MOA.** Ocular inflammation associated with keratoconjunctivitis sicca results in reduced tear production. Cyclosporin binds to cyclophilin, which inhibits the antigenic response of helper T lymphocytes which reduces the production of interleukin-2 and suppresses interferon-γ. Inhibition of the immune response limits inflammation.




Allergan 0.05% emulsion pictured

## Drug Characteristics: Cyclosporine Ophthalmic

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Minimal absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Minimal absorption |
| **Dialyzable** | Not dialyzable | **Metabolism** | Minimal absorption |
| **Pregnancy Category** | C | **Elimination** | Minimal absorption |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to cyclosporine, active ocular infection | **Black Box Warnings** | None |

## Medication Safety Issues: Cyclosporine Ophthalmic

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | CycloSPORINE | No | No | CycloSERINE | No |

**Drug Interactions: Cyclosporine Ophthalmic.** None known

**Adverse Reactions: Cyclosporine Ophthalmic**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Burning sensation in eye | Conjunctivitis, blurred vision | Hypersensitivity |

**Efficacy Monitoring Parameters.** Improved tear production.

**Toxicity Monitoring Parameters.** Severe burning of the eye, active ocular infection.

**Key Patient Counseling Points.** This medicine comes in single-use packages. After you open a single-use package, use the medicine right away. Mix the medicine well just before using it. To do this, turn the single-use package upside down a few times. Remove contact lenses before using this medicine. Wait at least 15 min before inserting contact lenses after using the medicine. May be used with artificial tears as long as there is 15-min interval in between.

**Clinical Pearls.** Not for use in children <16 y of age. Oral formulation available for transplant rejection prevention.



https://kat.cr/user/Blink99/

# DABIGATRAN: Pradaxa

**Class:** Anticoagulant

**Dosage Forms. Oral Capsule:** 75 mg, 150 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Treatment and prevention of initial or recurrent deep venous thrombosis and pulmonary embolism: 150 mg po bid (after 5-10 d treatment with parenteral anticoagulant)
2. Prevention of stroke and systemic embolism in patient with nonvalvular atrial fibrillation: 150 mg po bid

**Off-Label Uses.**

1. Prevention of thromboembolism after orthopedic surgery: 150 mg po bid

**MOA.** Dabigatran is a competitive, direct thrombin inhibitor. Because thrombin enables the conversion of fibrinogen into fibrin during the coagulation cascade, its inhibition prevents the development of a thrombus. Both free and clot-bound thrombin and thrombin-induced platelet aggregation are inhibited.

Boehringer-Ingelheim
150 mg pictured

**Drug Characteristics: Dabigatran**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 3-7%, no effect of food on absorption |
| **Dose Adjustment Renal** | CrCl 15-30 mL/min, 75 mg po bid; CrCl <15 mL/min, avoid use | **Distribution** | Vd = 50-70 L; 35% protein bound |
| **Dialyzable** | Use in ESRD should be avoided; hemodialysis removes 60% of drug in 2-3 h | **Metabolism** | Extensive hepatic metabolism but not by CYP; substrate of P-glycoprotein |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 80% with a half-life of 12-17 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Active bleeding, prosthetic heart valve | **Black Box Warnings** | Use in elderly; risk of stroke at discontinuation; spinal epidural hematoma |

**Medication Safety Issues: Dabigatran**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Do not open; F increased 75% when capsule opened | Yes | Plavix | No |

### Drug Interactions: Dabigatran

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| P-glycoprotein inducers | Increased dabigatran metabolism reduces dabigatran effectiveness | Monitor and consider dose increases of dabigatran |
| P-glycoprotein inhibitors | Decreased dabigatran metabolism increases risk of dabigatran toxicity | If concurrent P-glycoprotein inhibitor and CrCl 30-50 mL/min, reduce dabigatran dose to 75 mg po bid; avoid concurrent use if CrCl <30 mL/min |
| Antiplatelet agents, NSAIDs, anticoagulants | Additive risk of bleeding | Avoid concurrent use or monitor carefully and adjust dose if necessary |

### Adverse Reactions: Dabigatran

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Bleeding | Gastritis, GERD | Major bleeding, MI, intracranial hemorrhage |

**Efficacy Monitoring Parameters.** Prevention of clotting or recurrence of clotting. The aPTT assay can be used as a qualitative indicator of anticoagulation status.

**Toxicity Monitoring Parameters.** Monitor for signs and symptoms of bleeding; evaluate renal function. Not recommended in valvular heart disease.

**Key Patient Counseling Points.** May be given with or without food. Do not open capsules. Treatment must be suspended prior to surgical procedures, using protocols provided in the product package insert. Increased risk of stroke on discontinuation.

**Clinical Pearls.** Detailed dosing conversion protocols used to convert patients from warfarin or parenteral anticoagulants to dabigatran are available in the product package insert. Dispense in manufacturer original bottle and discard remaining doses 4 mo after opening. Guidelines recommend against use in advanced liver disease or CrCl <15 mL/min. Medication guide required at dispensing.



https://kat.cr/user/Blink99/

# DARBEPOETIN: Aranesp



**Class:** Hematopoietic

**Dosage Forms.** **Injection Solution, Vial:** 25 mcg/mL, 40 mcg/mL, 60 mcg/mL, 100 mcg/mL, 200 mcg/mL, 300 mcg/mL, 500 mcg/mL; **Injectable Solution, Prefilled Syringe:** 25 mcg/0.42 mL, 40 mcg/0.4 mL, 60 mcg/0.3 mL, 100 mcg/0.5 mL, 150 mcg/0.3 mL, 150 mcg/0.75 mL, 200 mcg/0.4 mL, 300 mcg/0.6 mL

Amgen 100 mcg/0.5 mL pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Anemia due to chemotherapy: 2.25 mcg/kg sq weekly; or 500 mcg sq every 3 wk; dose adjusted based on changes in Hgb levels
2. Anemia of chronic kidney disease: Patients not on dialysis, 0.45 mcg/kg IV or sq once every 4 wk; Patients on dialysis 45, mcg/kg IV or sq once weekly or 0.75 mcg/kg IV or sq once every 2 wk; dose adjusted based on changes in Hgb levels

**Off-Label Uses.**

1. Anemia associated with myelodysplastic syndrome: 150-300 mcg sq weekly

**MOA.** Darbepoetin alfa is a hyperglycosylated analogue of recombinant human erythropoietin. It binds to the erythropoietin receptor on erythroid progenitor cells, stimulating production/differentiation of mature red cells.

**Drug Characteristics: Darbepoetin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 37%, food has no effect on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 52 mL/kg |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatically metabolized via galactose receptors |
| **Pregnancy Category** | C | **Elimination** | Minimal renal elimination with a half-life of 46 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to darbepoetin, uncontrolled hypertension | **Black Box Warnings** | Increased CV, stroke, mortality risk; cancer recurrence; REMS program |

**Medication Safety Issues: Darbepoetin**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Aricept, dalteparin, epoetin | No |

**Drug Interactions:** **Darbepoetin.** None

**Adverse Reactions: Darbepoetin**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Edema, hypertension, diarrhea, injection site thrombosis, myalgia, fatigue | Thromboembolism, myocardial infarction | Pure red cell aplasia, immune hypersensitivity, seizures, tumor progression |

**Efficacy Monitoring Parameters.** For anemia, titrate dose to avoid transfusion (usually target is to keep Hgb >9 g/dL) but discontinue if Hgb >10 g/dL. For renal failure, titrate to keep Hgb between 10 and 11 g/dL. Iron studies to ensure adequate iron stores, transferring saturation >20% and ferritin >100 mg/mL.

**Toxicity Monitoring Parameters.** BP; weight to monitor edema; SCr in renal failure patients; signs and symptoms of thrombosis; cancer progression. Rapid rise in hemoglobin, >1 g/dL >2 wk may increase the risk for cardiovascular events.

**Key Patient Counseling Points.** Do not shake, dilute, or expose to light. Refrigerate. Do not combine remainders from different syringes; each syringe is for single use. May require several weeks for maximum effect.

**Clinical Pearls.** Typically administered in hospital infusion and dialysis clinics. In cancer patients with certain tumor types (eg, breast, non-small cell lung, head and neck, etc), epoetin and darbepoetin shortened overall survival, and/or increased risk of tumor progression or recurrence in some clinical studies. Discontinue after the completion of the chemotherapy course and if no response after 8 wk of therapy. Hospitals and health-care professionals who prescribe and/or dispense darbepoetin to patients with cancer must enroll and comply with the ESA (erythropoiesis-stimulating agent) APPRISE oncology program at www.esa-apprise.com. Renal failure patients experienced greater risks for death, stroke, and serious cardiovascular events when administered ESAs to target Hgb levels of 11 g/dL or higher in clinical studies. Not for initial use in children, typically started on erythropoietin and converted to darbepoetin.



https://kat.cr/user/Blink99/

# DARIFENACIN: Enablex

**Class:** Urinary Antispasmodic

**Dosage Forms.** **Oral Tablet, Extended Release:** 7.5 mg, 15 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Overactive bladder: 7.5 mg po daily, may titrate to 15 mg po daily

**Off-Label Uses.** None

**MOA.** Darifenacin is a competitive muscarinic receptor antagonist. Muscarinic receptors play an important role in several major cholinergically mediated functions, including contractions of the urinary bladder smooth muscle and stimulation of salivary secretion.

Warner Chilcott 15 mg pictured

D

## Drug Characteristics: Darifenacin

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Child-Pugh B or C, do not exceed 7.5 mg po daily | **Absorption** | F = 15-25%, no effect of food on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 163 L |
| **Dialyzable** | Unknown | **Metabolism** | Extensive hepatic; substrate of CYP3A4/5; inhibits CYP2D6 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 60% with a half-life of 13-19 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to darifenacin, gastric retention, glaucoma, urinary retention | **Black Box Warnings** | None |

## Medication Safety Issues: Darifenacin

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Do not crush or chew | No | Solifenacin | No |

### Drug Interactions: Darifenacin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inducers | Increased darifenacin metabolism reduces darifenacin effectiveness | Monitor and consider dose increases of darifenacin |
| CYP3A4/5 inhibitors | Decreased darifenacin metabolism increases risk of darifenacin toxicity | Monitor and consider dose decreases of darifenacin; *max* dose 7.5 mg/d |
| CYP2D6 substrates | Inhibition of CYP2D6-mediated metabolism can raise concentrations of substrates | Avoid concurrent use or monitor carefully for signs of substrate toxicity |
| Anticholinergic agents | Additive anticholinergic adverse effects | Avoid concurrent use or monitor carefully for adverse effects |

### Adverse Reactions: Darifenacin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Constipation, xerostomia, blurred vision | Abdominal pain, indigestion, urinary retention, dizziness | Angioedema |

**Efficacy Monitoring Parameters.** Resolution of clinical signs of bladder spasticity, incontinence, urinary urgency and frequency.

**Toxicity Monitoring Parameters.** Severe anticholinergic effects (dry mouth, cognitive impairment, constipation, vision changes).

**Key Patient Counseling Points.** This drug may cause anticholinergic effects, including constipation, urinary retention, blurred vision, constipation, dyspepsia, or xerostomia. Heat prostration (due to decreased sweating) can occur when used in a hot environment. Can be taken with or without food.

**Clinical Pearls.** May note decline in cognitive function, especially in elderly patients.



https://kat.cr/user/Blink99/

# DESVENLAFAXINE: Pristiq, Various

**Class:** Serotonin/Norepinephrine Reuptake Inhibitor

**Dosage Forms. Oral Tablet, Extended Release:** 50 mg, 100 mg

Pfizer 50 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Depression: 50 mg po daily

**Off-Label Uses.**

1. Menopausal flushing: 100 mg po daily

**MOA.** Desvenlafaxine is a potent reuptake inhibitor of serotonin and norepinephrine, like many TCAs, but lacks effects on muscarinic, α-adrenergic, or histamine receptors.



**Drug Characteristics: Desvenlafaxine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Moderate to severe impairment, *max* dose, 100 mg po daily | **Absorption** | F = 80%; no effect of food on absorption |
| **Dose Adjustment Renal** | CrCl = 30-50 mL/min, *max* 50 mg po daily; CrCl <30 mL/min, *max* 50 mg po qod | **Distribution** | Vd = 3.4 L/kg; 30% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic metabolism via conjugation |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 45% as unchanged drug, with a half-life of 10-11 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to desvenlafaxine or venlafaxine; MAOI use | **Black Box Warnings** | Suicidality; not for use in children; not for bipolar disorder |

**Medication Safety Issues: Desvenlafaxine**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | ER tablets | No | Prilosec | No |

### Drug Interactions: Desvenlafaxine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Anticoagulants, antiplatelet drugs, NSAIDs | Increased risk of bleeding | Monitor for bleeding |
| Triptans, SSRIs, tramadol | Increased risk of serotonin syndrome | Monitor closely for symptoms of serotonin syndrome (restlessness, hyperthermia, hyperref exia) |
| Linezolid, metoclopramide, MAOI | Increased risk of serotonin syndrome | Concurrent use contraindicated |

### Adverse Reactions: Desvenlafaxine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Diaphoresis, dizziness, headache, nausea, xerostomia | Anxiety, bleeding, blurred vision, constipation, diarrhea, disorder of ejaculation, fatigue, feeling nervous, hypertension, hyponatremia, insomnia, loss of appetite, proteinuria, serum cholesterol raised, sexual dysfunction, somnolence, tremor, vomiting, weight loss | GI hemorrhage, serotonin syndrome, suicidal thoughts |

**Efficacy Monitoring Parameters.** Improvement in symptoms of depression (suicidal thoughts or intent, change in appetite, lack of energy, change in sleep patterns, etc).

**Toxicity Monitoring Parameters.** Worsening of depression, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases; signs/symptoms of abnormal bleeding, monitor BP, LFT, and serum cholesterol levels, in case of severe impairment at baseline and periodically during therapy; signs/symptoms of hyponatremia, especially in patients on concomitant diuretics, volume-depleted patients, and elderly. Monitor renal function.

**Key Patient Counseling Points.** Take with food, but avoid alcohol. Symptomatic improvement may not be evident for a few weeks. Do not discontinue drug abruptly, as this may precipitate withdrawal symptoms such as dysphoric mood, irritability, and agitation. Avoid activities requiring mental alertness or coordination until drug effects are realized, as this medicine may cause dizziness or somnolence.

**Clinical Pearls.** Safety and efficacy not established in children. Medication guide required at dispensing.



https://kat.cr/user/Blink99/

# DEXAMETHASONE ORAL: Decadron, Various

**Class:** Adrenal Corticosteroid

**Dosage Forms. Oral Tablet:** 0.5 mg, 0.75 mg, 1 mg, 1.5 mg, 2 mg, 4 mg, 6 mg; **Oral Solution:** 0.5 mg/5 mL; **Oral Elixir:** 0.5 mg/5 mL

Roxane generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

Dosing for indications listed below: Adults, 0.75-9 mg/d po; Children, 0.02-0.3 mg/kg/d in 3-4 divided doses; for all patients, adjust dose according to patient response

1. Allergic states (eg, asthma, etc)
2. Dermatologic diseases (eg, exfoliative erythroderma, etc)
3. Endocrine disorders (eg, adrenocortical insufficiency, etc)
4. GI diseases (eg, regional enteritis, ulcerative colitis, etc)
5. Hematologic disorders (eg, acquired hemolytic anemia, etc)
6. Neoplastic diseases (eg, palliative management of leukemias and lymphomas, etc)
7. Nervous system (eg, multiple sclerosis, cerebral edema, etc)
8. Renal diseases (eg, idiopathic nephrotic syndrome, systemic lupus erythematosus, etc)
9. Respiratory diseases (eg, idiopathic eosinophilic pneumonia, etc)
10. Rheumatic disorders (eg, rheumatoid arthritis, etc)

**Off-Label Uses.**

1. Chemotherapy-induced nausea and vomiting: 20 mg IV before chemotherapy, 8 mg IV or po bid × 3 d after chemotherapy

**MOA.** Glucocorticosteroids are naturally occurring, and synthetic adrenocortical steroids cause varied metabolic effects, modify the body's immune responses to diverse stimuli and are used primarily for their anti-inflammatory effects in disorders of many organ systems.

**Drug Characteristics: Dexamethasone Oral**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Adjust dose to response | **Absorption** | F = 85% |
| **Dose Adjustment Renal** | Adjust dose to response | **Distribution** | Vd = 2 L/kg |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic; substrate of CYP3A4/5; inhibitor of P-glycoprotein; inducer of CYP3A4/5 and P-glycoprotein |
| **Pregnancy Category** | C | **Elimination** | Primarily renal elimination with a half-life of 2-2.5 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to glucocorticosteroids; concurrent use of live vaccines; fungal infections | **Black Box Warnings** | None |

## Medication Safety Issues: Dexamethasone Oral

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Methadone | No |

## Drug Interactions: Dexamethasone Oral

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inducers | Increased dexamethasone metabolism reduces dexamethasone effectiveness | Monitor and consider dose increases of dexamethasone |
| CYP3A4/5 inhibitors | Decreased dexamethasone metabolism increases risk of dexamethasone toxicity | Monitor and consider dose decreases of dexamethasone |
| CYP3A4/5 substrates | Induced metabolism of CYP3A4/5 substrates results in increased metabolism and loss of substrate effectiveness | Monitor and consider substrate dose increases |
| P-glycoprotein substrates | Metabolism of substrates may be inhibited or induced | Monitor and consider substrate dose increase or decrease depending on therapeutic effect |
| Fluoroquinolones | Concurrent use of steroids and fluoroquinolones can increase risk of tendon rupture, especially in elderly | Avoid concurrent use, or monitor carefully for tendon rupture |
| Phenytoin | Phenytoin increases dexamethasone metabolism; dexamethasone can increase or decrease phenytoin metabolism | Monitor dexamethasone efficacy and phenytoin concentrations |
| Warfarin | Steroids can either increase or decrease INR in patients taking warfarin | Monitor INR carefully |

## Adverse Reactions: Dexamethasone Oral

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| GI upset | Hypertension, atrophic condition of skin, impaired skin healing, osteoporosis, depression, euphoria, pulmonary tuberculosis, hyperglycemia | Primary adrenocortical insufficiency, Cushing syndrome, decreased body growth, increased risk of infection |

**Efficacy Monitoring Parameters.** Improvement or resolution of clinical signs and symptoms; monitor for decrease in ESR, or improvement of PFT.

**Toxicity Monitoring Parameters.** Monitor for signs of hyperglycemia, leukocytosis, osteoporosis, and adrenocortical insufficiency and infection; frequency and severity of adverse effects are dependent on the length of treatment and dose.

**Key Patient Counseling Points.** For short-term treatment, inform patients to take doses with meals to prevent GI upset. For high dose or longer-term treatment, inform patients to monitor for signs of hyperglycemia, osteoporosis, adrenocortical insufficiency, and infection. Patient may experience insomnia, anxiety, aggression at higher doses.

**Clinical Pearls.** Available in a wide variety of dosage forms for various indications, including injectable, topical, otic, and ophthalmic preparations. Use lowest effective and discontinue as soon as possible to avoid serious long-term adverse effects. Use with caution in patient with history of diabetes.



https://kat.cr/user/Blink99/

# DEXLANSOPRAZOLE: Dexilant

**Class:** Proton Pump Inhibitor

**Dosage Forms. Oral Capsule, Delayed Release:** 30 mg, 60 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Erosive esophagitis, treatment: 60 mg po daily × 8 wk; thereafter may continue 30 mg po daily × 6 mo
2. Symptomatic gastroesophageal reflux disease: 30 mg po daily × 4 wk

**Off-Label Uses.** None.

**MOA.** Lansoprazole is a proton pump inhibitor (PPI) that, when protonated in the secretory canaliculi of the parietal cells, covalently binds to $H^+/K^+$-ATPase (proton pump), which is the final pathway for acid secretion.

## Drug Characteristics: Dexlansoprazole

| | | | |
|---|---|---|---|
| Dose Adjustment Hepatic | Child-Pugh class B: *max* 30 mg po daily; Child-Pugh class C: avoid. | **Absorption** | Well absorbed after oral administration |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 40.3 L; 96-99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic by multiple pathways including CYP2C19 and CYP3A4/5, but CYP inhibitors/inducers do not produce clinically relevant interactions |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 50.7%; fecal 47.6% with a half-life of 1-2 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None |
| **Contraindications** | Hypersensitivity to dexlansoprazole or other PPI | **Black Box Warnings** | None |

## Medication Safety Issues: Dexlansoprazole

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | If capsules are opened, granules should not be chewed | No | Aripiprazole, lansoprazole | No |

### Drug Interactions: Dexlansoprazole

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| pH-dependent drugs | As lansoprazole lowers gastric pH, absorption of drugs that require acid environment is reduced | Avoid concurrent use |

### Adverse Reactions: Dexlansoprazole

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Diarrhea, abdominal pain, nausea, f atulence, vomiting | Stevens-Johnson syndrome, rhabdomyolysis, acute interstitial nephritis, *C. diff cile* diarrhea, hypomagnesemia, myocardial infarction |

**Efficacy Monitoring Parameters.** Resolution of GI discomfort.

**Toxicity Monitoring Parameters.** Seek medical attention if severe headache or blistering skin rash occurs. Prolonged duration of therapy may increase risk of *C. difficile* infection in a hospitalized patient.

**Key Patient Counseling Points.** May be taken without regard to meals. Should not be taken with antacids.

**Clinical Pearls.** Other PPI and $H_2$ antagonists available OTC; warn patients not to take multiple products concurrently to avoid additive risk of adverse effects. Increased risk of bone fracture with long-term use, use with caution in those with osteoporosis. Medication guide required at dispensing. Unlike lansoprazole, does not interact with clopidogrel or CYP inhibitors/inducers.



https://kat.cr/user/Blink99/

# DEXMETHYLPHENIDATE: Focalin, Various

**Class:** CNS Stimulant. C-II

**Dosage Forms.** **Oral Tablet:** 2.5 mg, 5 mg, 10 mg; **Oral Capsule, Extended Release:** 5 mg, 10 mg, 15 mg, 20 mg, 25 mg, 30 mg, 35 mg, 40 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Attention-deficit hyperactivity disorder, methylphenidate-naive patients: Adults, immediate release 2.5 mg po bid (*max* 20 mg po daily) or extended release 10 mg po daily (*max* of 40 mg/d); Children ≥ 6 y of age, immediate release 2.5 mg po bid (*max* 20 mg po daily) or extended release 5 mg po daily (*max* of 30 mg/d)
2. Attention-deficit hyperactivity disorder currently using methylphenidate: Adults and Children ≥ 6 y of age, one-half the total daily dose of extended-release racemic methylphenidate; patients currently using dexmethylphenidate immediate release may be switched to the same daily dose of dexmethylphenidate extended release

Novartis pictured

**Off-Label Uses.** None

**MOA.** Amphetamines are noncatecholamine sympathomimetic amines with CNS stimulant activity. Amphetamines are thought to block the reuptake of norepinephrine and dopamine into the presynaptic neuron and increase the release of these monoamines into the extraneuronal space.

**Drug Characteristics: Dexmethylphenidate**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 22-25%, minimal food effect |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 2.6 L/kg |
| **Dialyzable** | Unknown | **Metabolism** | Extensive via de-esterification |
| **Pregnancy Category** | C | **Elimination** | Minimal renal elimination with a half-life of 3 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to amphetamines, MAOI use, drug dependence, glaucoma, tics, or history of Tourette syndrome | **Black Box Warnings** | Tolerance and dependence; risk of psychosis |

**Medication Safety Issues: Dexmethylphenidate**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| XL | No | Extended-release capsule, but may open | No | Methadone, Folotyn | No |

### Drug Interactions: Dexmethylphenidate

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| TCAs | Enhanced amphetamine effects from the release of norepinephrine (hypertension, CNS stimulation) | Avoid concurrent use |
| MAOIs | Hypertensive crisis | Contraindicated within 14 d |

### Adverse Reactions: Dexmethylphenidate

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Weight loss, loss of appetite, headache, insomnia, restlessness | Anxiety, tachycardia | Seizures, spasmodic movement, anemia, thrombocytopenia, psychosis, mania, drug dependence, priapism |

**Efficacy Monitoring Parameters.** Resolution of signs of ADHD (improved attention span and reduced impulsivity).

**Toxicity Monitoring Parameters.** Monitor BP, HR, weight, CBC. Seek medical attention if chest pain, seizures, heart palpitations, change in behavior or personality, hostility. Growth rate in children.

**Key Patient Counseling Points.** Avoid late evening doses due to resulting insomnia. If you cannot swallow the extended-release capsule, you may open it and pour the medicine into a small amount of soft food such as applesauce. Stir this mixture well and swallow it without chewing.

**Clinical Pearls.** Dexmethylphenidate is the d-enantiomer of methylphenidate. Amphetamines have a high potential for abuse, and administration for prolonged periods of time may lead to drug dependence and should be avoided. Misuse of amphetamines may cause sudden death and serious cardiovascular adverse events.



https://kat.cr/user/Blink99/

# DIAZEPAM: Valium, Various

**Class:** Benzodiazepine. C-IV

**Dosage Forms.** **Oral Tablet:** 2 mg, 5 mg, 10 mg; **Oral Solution:** 1 mg/mL, 5 mg/mL; **Rectal Gel:** 20 mg/5 mL

10 mg

5 mg

2 mg

Teva generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Alcohol withdrawal syndrome: 10 mg po tid-qid in first 24 h, then 5 mg po tid-qid prn
2. Anxiety: Adults, 2-10 mg po bid-qid; Children, 1-2.5 mg po tid-qid
3. Seizure, adjunct: Adults, 2-10 mg po bid-qid; Children, 1-2.5 mg po tid-qid

**Off-Label Uses.**

1. Benzodiazepine withdrawal syndrome: 10 mg po tid-qid in first 24 h, then 5 mg po tid-qid prn

**MOA.** Enhanced postsynaptic effect of the inhibitory neurotransmitter, γ-aminobutyric acid (GABA)

**Drug Characteristics: Diazepam**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Decrease dose by 50% | **Absorption** | F = 98%, no effect of food on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 1 L/kg; 99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic; substrate of CYP2C19 and CYP3A4/5 |
| **Pregnancy Category** | D | **Elimination** | Renal elimination is 75% with a half-life of 24-48 h |
| **Lactation** | Avoid | **Pharmacogenetics** | Use with caution in CYP2C19 poor metabolizers |
| **Contraindications** | Hypersensitivity to benzodiazepines, narrow-angle glaucoma, severe liver disease, myasthenia gravis, sleep apnea, respiratory insufficiency, children <6 mo | **Black Box Warnings** | None |

### Medication Safety Issues: Diazepam

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | LORazepam | Avoid benzodiazepines (any type) for treatment of insomnia, agitation, or delirium. |

### Drug Interactions: Diazepam

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Alfentanil, opioids, and other respiratory depressants | Additive respiratory depression | Avoid if possible and consider dose reductions of both agents |
| CYP2C19, CYP3A4/5 inducers | Increased diazepam metabolism reduces diazepam effectiveness | Monitor and consider dose increases of diazepam |
| CYP2C19, CYP3A4/5 inhibitors | Decreased diazepam metabolism increases risk of diazepam toxicity | Monitor and consider dose decreases of diazepam |
| Ethinyl estradiol and other estrogen-based birth control products | Inhibition of diazepam metabolism and additional toxicity | Use with caution |
| Digoxin | Reduced renal clearance of digoxin and increased digoxin toxicity | Monitor digoxin levels and consider dose reductions |

### Adverse Reactions: Diazepam

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Drowsiness, impaired motor coordination | Confusion, ataxia, nausea and vomiting, blurred vision | Seizures, mania, depression, withdrawal symptoms, elevated liver function tests |

**Efficacy Monitoring Parameters.** Reduction in anxiety symptoms, alcohol withdrawal symptoms, or seizures.

**Toxicity Monitoring Parameters.** Severe drowsiness, thoughts of suicide, yellowing of eyes, seizures.

**Key Patient Counseling Points.** May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol.

**Clinical Pearls.** Use caution in elderly, appear more sensitive to the effects; dose reductions of 50% have been recommended. Use CNS depressants concurrently with caution, may have additive effects. Avoid abrupt discontinuation after chronic use, may cause seizures. Long-acting benzodiazepines have increased risk of physical and psychological dependence when compared to short acting.



https://kat.cr/user/Blink99/

# DICLOFENAC: Voltaren, Various

**Class:** NSAID

**Dosage Forms.** **Oral Tablet:** 50 mg; **Oral Tablet, Extended Release:** 25 mg, 50 mg, 75 mg, 100 mg; **Oral Capsule:** 18 mg, 25 mg, 35 mg; **Powder for Oral Solution:** 50 mg

Sandoz generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Pain: Immediate-release tablet or capsule only, 18-50 mg po tid
2. Dysmenorrhea: Immediate-release tablets only, 50 mg po tid
3. Migraine: Powder for solution only, 50 mg po once
4. Osteoarthritis: 100 mg extended release po daily or bid
5. Rheumatoid arthritis: 100 mg extended release daily or bid

**Off-Label Uses.** None

**MOA.** Nonselective inhibitor of cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2)

**Drug Characteristics: Diclofenac**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 50%, minimal food effect |
| **Dose Adjustment Renal** | CrCl <30 mL/min, avoid use | **Distribution** | Vd = 1.3 L/kg |
| **Dialyzable** | Unknown | **Metabolism** | Hepatic; minor substrate of multiple CYP pathways |
| **Pregnancy Category** | C, <30 wk gestation; D, ≥30 wk gestation | **Elimination** | Renal elimination is 65% with a half-life of 2 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to diclofenac, concurrent ketorolac, pentoxifylline use, asthma, allergic-type reaction following other NSAID use, CABG | **Black Box Warnings** | Cardiovascular, GI risk, CABG |

**Medication Safety Issues: Diclofenac**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| XR | No | XR should not be crushed | No | Diflucan | Avoid chronic use unless other alternatives are not effective and patient can take gastroprotective agent. |

### Drug Interactions: Diclofenac

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Aspirin, low-molecular-weight heparins, SSRIs, NSAIDs, pentoxifylline | Additive GI toxicity and increased risk of bleeding | Concurrent ketorolac, pentoxifylline contraindicated; others, monitor for GI toxicity |
| ACEIs, ARBs, beta-blockers, loop and thiazide diuretics | Decreased diuretic and antihypertensive efficacy via decreased renal prostaglandin production | Monitor and consider alternative therapy |
| Cholestyramine | Decreased absorption of diclofenac | Separate administration by 1-2 h |
| Most CYP inducers | Increased diclofenac metabolism reduces diclofenac effectiveness | Consider dose increases of diclofenac |
| Most CYP inhibitors | Decreased diclofenac metabolism increases risk of diclofenac toxicity | Consider dose decreases of diclofenac |
| Cyclosporine, tacrolimus | Increased risk of cyclosporine, tacrolimus toxicity, unknown mechanism | Monitor cyclosporine and tacrolimus levels and consider dose adjustments |
| Pemetrexed | Decreased renal clearance and increased toxicity of pemetrexed | Avoid concurrent use in patients with renal dysfunction |
| Sulfonylureas | Increased risk of hypoglycemia via inhibition of sulfonylurea metabolism | Monitor FPG and adjust as necessary |
| Warfarin | Both substrates for CYP2C9, competitive metabolism | Monitor INR and adjust warfarin dose |

### Adverse Reactions: Diclofenac

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Headaches, GI distress | GI ulcers | Stevens-Johnson syndrome, GI bleeding, thrombosis, elevated liver functions, acute renal failure, myocardial infarction, aplastic anemia, hemolytic anemia |

**Efficacy Monitoring Parameters.** Decreased pain and improved range of motion.

**Toxicity Monitoring Parameters.** Monitor CBC, LFTs, SCr, fecal occult blood tests, severe skin rash, black tarry stools, chest pain, yellowing of eyes or skin, and change in urination.

**Key Patient Counseling Points.** Take with food or milk to decrease GI upset.

**Clinical Pearls.** Elderly patients are at increased risk of GI ulceration. Patients with underlying cardiac dysfunction are at increased risk of cardiovascular effects. Use lowest dose for shortest period of time to minimize toxicity. Available in both sodium and potassium salts, in combination with misoprostol, and in ophthalmic and topical products. Medication guide required at dispensing.



https://kat.cr/user/Blink99/

# DICYCLOMINE: Bentyl, Various

**Class:** Antimuscarinic

**Dosage Forms.** **Oral Capsule:** 10 mg; **Oral Tablet:** 20 mg; **Oral Syrup:** 10 mg/5 mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Irritable bowel syndrome: Children 6 mo-2 y of age, 5 mg po tid-qid; Children 2-12 y of age, 10 mg po tid, may titrate to 40 mg/d; Adults, 20 mg po qid, may titrate to 40 mg po qid

Watson generic 20 mg pictured

Mylan generic 10 mg pictured

**Off-Label Uses.** None

**MOA.** Dicyclomine relieves smooth muscle spasm of the GI tract via a specific anticholinergic effect (antimuscarinic) at the acetylcholine-receptor sites and a direct effect on smooth muscle (musculotropic).



## Drug Characteristics: Dicyclomine

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Well absorbed, minimal food effect |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 3.65 L/kg |
| **Dialyzable** | Unknown | **Metabolism** | Minimal |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 80% with a half-life of 2 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to dicyclomine, age <6 mo, breastfeeding, GI obstruction, glaucoma, myasthenia gravis, obstructive uropathy, reflux esophagitis, severe ulcerative colitis, toxic megacolon, unstable cardiovascular state in acute hemorrhage | **Black Box Warnings** | None |

## Medication Safety Issues: Dicyclomine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | DiphenhydrAMINE, doxycycline | Avoid except in short-term palliative care to decrease oral secretions. Highly anticholinergic, uncertain effectiveness. |

**Drug Interactions: Dicyclomine**

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Agents with anticholinergic effects | Additive anticholinergic adverse effects can result | Avoid concurrent use or monitor carefully for adverse effects |

**Adverse Reactions: Dicyclomine**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Decreased sweating, xerostomia, GI distress, blurred vision, dizziness, constipation, drowsiness | Tachycardia, urinary retention | Psychosis, euphoria, anaphylaxis, drug dependence |

**Efficacy Monitoring Parameters.** Improved bowel function, decreased flatulence, diarrhea.

**Toxicity Monitoring Parameters.** Rapid heart beat, severe dizziness, unusual thoughts, shortness of breath, or severe rash.

**Key Patient Counseling Points.** May cause drowsiness; avoid driving and operating heavy equipment. Heat prostration (due to decreased sweating) can occur when used in a hot environment.

**Clinical Pearls.** There are reports that administration of dicyclomine to infants has been followed by serious respiratory symptoms (dyspnea, shortness of breath, breathlessness, respiratory collapse, apnea, asphyxia), seizures, syncope, pulse rate fluctuations, muscular hypotonia, and coma. Death has been reported.



https://kat.cr/user/Blink99/

# DIGOXIN: Lanoxin, Various

**Class:** Digitalis Glycoside

**Dosage Forms.** **Oral Tablet:** 62.5 mcg, 125 mcg, 187.5 mcg, 250 mcg; **Oral Solution:** 0.05 mg/mL

West-ward generic 0.125 mg pictured

Jerome Stevens Pharmaceuticals generic 0.25 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Atrial fibrillation: Loading dose of 0.25 mg po q2h to a total dose of 1.5 mg, then 0.125-0.375 mg po daily
2. Heart failure: Premature infant, loading dose of 20 mcg/kg, then 5 mcg/kg/d; Full-term infant to children 2 mo of age, loading dose of 30 mcg/kg, then 8-10 mcg/kg/d; Children 2-23 mo of age, loading dose of 40-50 mcg/kg, then 10-12 mcg/kg/d; Children 2-10 y of age, loading dose of 30-40 mcg/kg (solution), then 8-10 mcg/kg/d; Children >10 y of age, loading dose of 0.75-1.5 mg/kg, then 0.125-0.5 mg/kg po; Adults, loading dose of 0.5-0.75 mg po once, followed by 0.125-0.375 mg po q6-8h to achieve response, followed by 0.125-0.5 mg po daily
3. Supraventricular tachyarrhythmia: Loading dose of 0.75-1.5 mg po (divided into 3 doses, ½ of total dose initially, followed by ¼ of total dose at 6-8 h intervals later), then 0.125-0.5 mg po daily

**Off-Label Uses.**

1. Fetal tachycardia, supraventricular tachycardia: 0.125-0.375 mg po daily (administered to mother)

**MOA.** Digitalis glycosides exert positive inotropic effects through improved availability of calcium to myocardial contractile elements, thereby increasing cardiac output in heart failure. Antiarrhythmic actions are caused primarily by an increase in AV nodal refractory period via increased vagal tone, sympathetic withdrawal, and direct mechanisms.

**Drug Characteristics: Digoxin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 60-80% (tablet); food reduces absorption rate |
| **Dose Adjustment Renal** | Mild-to-moderate renal impairment, 0.125 mg po daily; severe renal impairment, 0.0625 mg po daily; titrate q2wk | **Distribution** | Vd = 4-7 L/kg; 25% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Modest hepatic; substrate of P-glycoprotein |
| **Pregnancy Category** | C | **Elimination** | Renal elimination (unchanged) is 57-80% with a half-life of 1.3-2.2 d |
| **Lactation** | Compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to digoxin, ventricular fibrillation | **Black Box Warnings** | None |

## Medication Safety Issues: Digoxin

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | Yes | Desoxyn, doxepin | Avoid >0.125 mg/d. In heart failure, higher dosages associated with no additional benefit and may increase risk of toxicity. |

## Drug Interactions: Digoxin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Beta-blockers | Increased risk of bradycardia and AV block | Monitor heart rate and ECG |
| Diuretics | Increased risk of digoxin toxicity due to potassium depletion | Monitor potassium and supplement if necessary |
| P-glycoprotein inducers | Increased digoxin metabolism reduces digoxin effectiveness | Monitor and consider dose increases of digoxin |
| P-glycoprotein inhibitors | Decreased digoxin metabolism increases risk of digoxin toxicity | Monitor and consider dose decreases of digoxin |
| Antacids, bile acid sequestrants, sucralfate | Decreased digoxin absorption and decreased efficacy | Avoid concurrent use or give digoxin 1-2 h before medications that decrease absorption |

## Adverse Reactions: Digoxin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Anorexia, confusion, diarrhea, dizziness, ECG changes, headache, nausea, rash, reduced color discrimination, visual disturbances, vomiting, weakness | Cardiac dysrhythmias, psychosis, seizures |

**Efficacy Monitoring Parameters.** ECG, decreased heart rate, improvement in signs/symptoms of heart failure; therapeutic serum range 0.8-2 ng/mL.

**Toxicity Monitoring Parameters.** ECG for cardiac dysrhythmia, excessive bradycardia; SCr, and serum electrolytes (especially potassium, magnesium, calcium).

**Key Patient Counseling Points.** Take after morning meals (and after evening meals if giving in divided doses). Report signs/symptoms of bradycardia. Do not discontinue drug suddenly.

**Clinical Pearls.** Tablet and solution not interchangeable—dosing varies with dosage form. Use with caution in elderly.



https://kat.cr/user/Blink99/

# DILTIAZEM: Cardizem, Various

**Class:** Calcium Channel Blocker

**Dosage Forms.** **Oral Tablet:** 30 mg, 60 mg, 90 mg, 120 mg; **Oral Capsule, Extended Release, 12 h:** 60 mg, 90 mg, 120 mg; **Oral Capsule, Extended Release, 24 h:** 120 mg, 180 mg, 240 mg, 300 mg, 360 mg, 420 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Hypertension: Extended release, 12 h, 60-120 mg po bid, may titrate to 360 mg/d po; Extended release, 24 h, 120-240 mg po daily, may titrate to 540 mg po daily
2. Stable, chronic angina: Immediate release, 30 mg po qid, may titrate to 360 mg/d po; Extended release, 24 h, 120 mg po daily, may titrate to 540 mg/d po

**Off-Label Uses.**

1. Atrial arrhythmia: 180-360 mg daily po
2. Hypertension: Children, 1.5-2 mg/kg/d po in 3-4 divided doses, may titrate to 3.5 mg/kg/d po

**MOA.** Diltiazem is a calcium-channel-blocking drug that decreases heart rate, prolongs AV nodal conduction, and decreases arteriolar and coronary vascular tone. It also has negative inotropic properties.

Mylan generic
180 mg pictured

Mylan generic
240 mg pictured

Teva generic
300 mg pictured

D

**Drug Characteristics: Diltiazem**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Dosage reduction may be needed | **Absorption** | F = 35-40% immediate release, F = 93-95% extended release; food decreases absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 305-391 L; 77-93% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic; substrate of CYP3A4/5. P-glycoprotein; moderate inhibitor of CYP3A4/5 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 35% with a half-life of 3-6.6 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to diltiazem; hypotension; 2nd- or 3rd-degree AV block, sick sinus syndrome | **Black Box Warnings** | None |

### Medication Safety Issues: Diltiazem

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| Cardizem CR, Cardizem LA | No | Extended-release formulations | Yes | Cardene | No |

### Drug Interactions: Diltiazem

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5, P-glycoprotein inducers | Increased diltiazem metabolism reduces diltiazem effectiveness | Monitor and consider dose increases of diltiazem |
| CYP3A4/5, P-glycoprotein inhibitors | Decreased diltiazem metabolism increases risk of diltiazem toxicity | Monitor and consider dose decreases of diltiazem |
| CYP3A4/5 substrates | Decreased metabolism and increased toxicity of CYP3A4/5 substrates | Avoid sensitive CYP3A4/5 substrates |
| Beta-blockers | Increased risk of hypotension, bradycardia, AV conduction disturbances | Avoid concurrent use or monitor BP and heart rate |

### Adverse Reactions: Diltiazem

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Edema, headache | Bradycardia, constipation, dizziness, fatigue, headache, hypotension, rash, syncope | Heart failure, heart block, hepatotoxicity |

**Efficacy Monitoring Parameters.** Decreased BP, reduction in chest pain, decreased number of angina attacks, reduction in use of nitroglycerin for chest pain.

**Toxicity Monitoring Parameters.** Signs/symptoms of heart failure, decreased heart rate, signs/symptoms of liver toxicity; exacerbations of angina pectoris or acute coronary insufficiency while tapering chronic therapy, especially in patients with CAD.

**Key Patient Counseling Points.** Report symptomatic hypotension, bradyarrhythmia, peripheral edema, or syncope. This drug is available in multiple brand names with varying properties by brand. Instruct patient to follow administration instructions specific to the prescribed brand with regards to meals and timing. Do not drink alcohol while taking this drug.

**Clinical Pearls.** Patient should avoid concomitant use of beta-blockers during drug therapy, unless otherwise directed by health-care professional.



https://kat.cr/user/Blink99/

# DIPHENOXYLATE/ATROPINE: Lomotil, Various

**Class:** Antidiarrheal. C-V

**Dosage Forms. Oral Tablet:** Diphenoxylate 2.5 mg with atropine 0.025 mg; **Oral Solution:** Diphenoxylate 2.5 mg/5 mL with atropine 0.025 mg/5 mL

Mylan generic 2.5 mg/0.025 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Diarrhea: Children ≥ 2 y of age, 0.3 mg-0.4 mg/kg/d (diphenoxylate) po qid to *max* of 20 mg/d (diphenoxylate); Adults, 2 tablets po qid until diarrhea resolves, then reduce dose to maintain efficacy, to *max* of 20 mg/d (diphenoxylate)

**Off-Label Uses.** None

**MOA.** Diphenoxylate is a synthetic meperidine congener without analgesic activity that slows GI motility. Because high doses of diphenoxylate (40-60 mg) cause systemic opioid activity, atropine is added in subtherapeutic amounts to decrease abuse potential.

D

**Drug Characteristics: Diphenoxylate/Atropine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 90% |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 324 L |
| **Dialyzable** | Not dialyzable | **Metabolism** | Rapidly and extensively hepatically metabolized to an active metabolite |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 14% with half-life of 2.5 h for parent compound and 12-14 h for active metabolite |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to diphenoxylate or atropine products; diarrhea associated with enterotoxin-producing bacteria or pseudomembranous enterocolitis; obstructive jaundice | **Black Box Warnings** | None |

**Medication Safety Issues: Diphenoxylate/Atropine**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | LaMICtal, LamISIL, loperamide | No |

### Drug Interactions: Diphenoxylate/Atropine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Agents with anticholinergic effects | Additive anticholinergic adverse effects can result | Avoid concurrent use or monitor carefully for adverse effects |
| MAOI | Increased risk of serotonin syndrome | Avoid concurrent use |

### Adverse Reactions: Diphenoxylate/Atropine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Abdominal discomfort, nausea and vomiting | Dizziness, sedation, somnolence, malaise, dry mouth | Pancreatitis, toxic megacolon, anaphylaxis |

**Efficacy Monitoring Parameters.** Frequency and volume of bowel movements; body temperature; blood in stool.

**Toxicity Monitoring Parameters.** Monitor for signs of atropine toxicity and for abdominal distention.

**Key Patient Counseling Points.** This drug can cause dry mouth, blurred vision, drowsiness, or dizziness; use caution while driving or performing other tasks requiring alertness, coordination, or physical dexterity. Avoid alcohol and other CNS depressants. Seek medical attention if diarrhea persists or if fever, palpitations, or abdominal distention occurs. Ensure *max* daily dose is not exceeded to avoid toxicity.

**Clinical Pearls.** Signs of atropine toxicity often referred to as "dry as a bone, hot as a hare, red as a beet, blind as a bat, mad as a hatter." Higher than usual doses may be administered to patients receiving irinotecan.



https://kat.cr/user/Blink99/

# DIPHTHERIA TOXOID: Daptacel, Adacel, Boostrix

**Class:** Vaccine

**Dosage Forms.** **Suspension for Intramuscular Injection:** For adults, available in combination with tetanus and acellular pertussis (Tdap); for children, available in combination with tetanus and acellular pertussis (DTaP), and in combinattion with other pediatric vaccines

**Common FDA Label Indication, Dosing, and Titration.**

1. Prevention of diphtheria: Children, all infants at age 2, 4, 6, and 12-15 mo, and a 5th dose at age 4-6 y, as primary series of DTaP; Tdap at age 11-12 y; single dose of Tdap for all adults at next opportunity; Td every 10 y for adults

**Off-Label Uses.** None

**Drug Characteristics: Diphtheria Toxoid**

| | | | |
|---|---|---|---|
| **Pregnancy Category** | C | **ADME** | Not known |
| **Lactation** | Caution advised; weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to diphtheria toxoid or a component of the vaccine | **Black Box Warnings** | None |

**Medication Safety Issues: Diphtheria Toxoid**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Adacel, Daptacel | No |

Infanrix GlaxoSmithKline pictured

D

### Drug Interactions: Diphtheria Toxoid

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Moderate- to high-dose corticosteroids | Immunosuppression | Delay diphtheria toxoid administration until corticosteroid therapy has been discontinued if possible |
| Immunosuppressing agents | Immunosuppression | Delay diphtheria administration until immunosuppressive therapy has been discontinued if possible |

### Adverse Reactions: Diphtheria Toxoid

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Injection site reactions, including erythema and soreness. Fever, headache, fatigue, swelling of limb | GI symptoms | Anaphylaxis, swelling or severe arm pain, Guillain-Barré syndrome |

**Efficacy Monitoring Parameters.** Prevention of diphtheria, although antibody concentrations might be measured; routine measurement for vaccine response is not recommended.

**Toxicity Monitoring Parameters.** Monitor for syncope, fever after administration.

**Key Patient Counseling Points.** Return to provider for each dose in the series.

**Clinical Pearls.** Use the same brand of vaccine to complete the entire series, if possible.



https://kat.cr/user/Blink99/

# DIPYRIDAMOLE: Persantine, Various

**Class:** Platelet Aggregation Inhibitor

**Dosage Forms.** **Oral Tablet:** 25 mg, 50 mg, 75 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Thromboprophylaxis after heart valve replacement: 75-100 mg po qid as an adjunct to warfarin therapy

**Off-Label Uses.** None

**MOA.** Inhibits the uptake of adenosine into platelets, endothelial cells, and erythrocytes resulting in an increase in local concentrations of adenosine, which is a coronary vasodilator and a platelet aggregation inhibitor.

Barr Labs generic 75 mg pictured



## Drug Characteristics: Dipyridamole

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 27-66% |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 2.43-3.38 L/kg; 99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensively metabolized but not by CYP; inhibits P-glycoprotein |
| **Pregnancy Category** | B | **Elimination** | Eliminated in bile, with a half-life of 10 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to dipyridamole | **Black Box Warnings** | None |

## Medication Safety Issues: Dipyridamole

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Periactin, disopyramide | Avoid oral. May cause orthostatic hypotension. |

### Drug Interactions: Dipyridamole

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Anticoagulants, antiplatelet drugs, NSAIDs | Increased risk of bleeding | Avoid concurrent use |
| SSRIs, SNRIs | Increased risk of bleeding | Monitor for signs/symptoms of bleeding |
| P-glycoprotein substrates | Inhibits metabolism of substrates and may result in substrate toxicity | Monitor and consider substrate dose reduction |

### Adverse Reactions: Dipyridamole

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Dizziness | Abdominal pain, diarrhea, headache | Ventricular arrhythmia, bronchospasm |

**Efficacy Monitoring Parameters.** Prevention of AMI, stroke, other thrombotic complications.

**Toxicity Monitoring Parameters.** Signs/symptoms of dizziness, GI distress.

**Key Patient Counseling Points.** Rise slowly from a sitting/supine position. Avoid alcohol.

**Clinical Pearls.** Safety and effectiveness in pediatric patients have not been studied. Injectable product also available for radionuclide cardiac perfusion studies. Oral combination product with dipyridamole and aspirin also available. Use with caution in the elderly.



https://kat.cr/user/Blink99/

# DIVALPROEX: Depakote, Various

**Class:** Anticonvulsant

**Dosage Forms.** **Oral Capsule, Extended Release:** 125 mg; **Oral Tablet, Extended Release:** 125 mg, 250 mg, 500 mg; **Oral Capsule, Sprinkles:** 125 mg

Northstar Rx generic 500 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Absence seizure, simple and complex: 15 mg/kg/d po, may titrate to 60 mg/kg/d
2. Complex partial epileptic seizure: 10-15 mg/kg/d po, may titrate to 60 mg/kg/d
3. Manic bipolar disorder: 25 mg/kg/d po, may titrate to 60 mg/kg/d
4. Migraine prophylaxis: 500 mg po daily for 1 wk, then 1000 mg po daily

**Off-Label Uses.** None

**MOA.** Divalproex is composed of sodium valproate and valproic acid. Valproic acid is a carboxylic acid compound whose anticonvulsant activity might be mediated by an inhibitory neurotransmitter, GABA. Valproic acid might increase GABA levels by inhibiting GABA metabolism or enhancing post-synaptic GABA activity. Valproic acid also limits repetitive neuronal firing through voltage- and usage-dependent sodium channels.

**Drug Characteristics: Divalproex**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Avoid use in severe hepatic dysfunction | **Absorption** | F = 89%, food has no effect on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 11 L; 88-90% protein bound |
| **Dialyzable** | Yes, but no dosage supplementation required | **Metabolism** | Extensive hepatic metabolism; minor substrate of multiple CYP pathways |
| **Pregnancy Category** | X for migraine prophylaxis; D for all other indications | **Elimination** | Renal elimination is 30-50% with a half-life of 9-16 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to divalproex, hepatic disease, urea cycle disorders | **Black Box Warnings** | Hepatotoxicity, teratogenicity, pancreatitis |

**Medication Safety Issues: Divalproex**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| Depakote ER | No | Extended release | No | Depakene | No |

### Drug Interactions: Divalproex

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Aspirin, macrolides | Increased valproic acid concentrations and risk of side effects | Monitor valproic acid levels |
| Carbamazepine, lamotrigine, TCAs | Divalproex inhibits metabolism of these drugs, increasing the risk of toxicity | Monitor for side effects and serum levels if available |
| Acyclovir, carbapenems, protease inhibitors, rifampin, risperidone | Decreased valproic acid concentrations and loss of anticonvulsant effect | Avoid concomitant use, monitor valproic acid levels |
| Phenytoin, phenobarbital | Altered levels of these and valproic acid levels | Monitor valproic acid levels and levels of other agents |
| Olanzapine, oxcarbazepine | Decreased olanzapine or oxcarbazepine concentrations | Monitor for efficacy |
| Warfarin | Warfarin displaced from protein binding, increasing warfarin effect | Monitor INR |

### Adverse Reactions: Divalproex

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Abdominal pain, alopecia, asthenia, diarrhea, diplopia, dizziness, headache, nausea, somnolence, tremor, vomiting | Amblyopia, blurred vision, feeling nervous, hyperammonemia, indigestion, infection, insomnia, loss of appetite | Hepatitis, palpitation, pancreatitis, tachycardia, thrombocytopenia |

**Efficacy Monitoring Parameters.** Reduction in number of seizures or control of manic symptoms. Therapeutic range for epilepsy, 50-100 mcg/mL. Therapeutic range for acute mania, 50-125 mcg/mL.

**Toxicity Monitoring Parameters.** Signs/symptoms of peripheral edema, increased heart rate, pancreatitis (abdominal pain, nausea, vomiting), monitor LFTs, ammonia levels, and CBC; emergence or worsening of depression, suicidal behavior or ideation, or unusual changes in behavior.

**Key Patient Counseling Points.** Avoid activities requiring mental alertness until drug effects are realized; drug may cause somnolence or dizziness. Take with food to avoid GI irritation. Do not discontinue drug abruptly, as this may precipitate status epilepticus. Avoid alcohol.

**Clinical Pearls.** Safety and efficacy in children <10 y of age have not been established. To convert from valproic acid to divalproex, initiate divalproex at the same daily dose and schedule; once stabilized, give divalproex bid or tid. Divalproex can produce teratogenic effects, so use with caution in women of childbearing potential. Multiple other dosage forms available as valproic acid.



https://kat.cr/user/Blink99/

# DONEPEZIL: Aricept, Aricept ODT, Various

**Class:** Cholinesterase Inhibitor

**Dosage Forms.** **Oral Tablet:** 5 mg, 10 mg, 23 mg; **Oral Disintegrating Tablet:** 5 mg, 10 mg

Pfizer pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Alzheimer disease, dementia (mild-moderate): 5 mg po daily hs, may titrate to *max* of 10 mg/d
2. Alzheimer disease, dementia (moderate-severe): 5 mg po daily qhs, may titrate to 10 mg/d at 4-6 wk to *max* of 23 mg/d (immediate-release tablet) or 10 mg/d (disintegrating tablet)

**Off-Label Uses.**

1. Multi-infarct dementia: 5-10 mg po daily hs

**MOA.** Donepezil enhances the action of acetylcholine by reversibly inhibiting acetylcholinesterase (AChE), the enzyme responsible for its hydrolysis. It has a high degree of selectivity for AChE in the CNS, which might explain the relative lack of peripheral side effects.

**Drug Characteristics: Donepezil**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 100%; no effect of food on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 12 L/kg; 96% protein bound |
| **Dialyzable** | Unknown | **Metabolism** | Extensive hepatic; minor substrate of CYP3A4/5 and CYP2D6 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 57% with a half-life of 70 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to donepezil or piperidine derivatives | **Black Box Warnings** | None |

**Medication Safety Issues: Donepezil**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| ODT | No | Disintegrating tablet, 23-mg tablet | No | AcipHex | No |

**Drug Interactions: Donepezil**

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Tolterodine, oxybutynin | Decreased efficacy of donepezil via cholinergic receptor antagonism by anticholinergic drugs | Avoid concurrent use |
| Ramelteon | Increased ramelteon exposure | Monitor for ramelteon toxicity and consider dose reduction |

**Adverse Reactions: Donepezil**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Asthenia, muscle cramps, depression, diarrhea, dizziness, dream disorder, ecchymosis, fatigue, headache, hypertension, insomnia, loss of appetite, nausea, syncope, urinary incontinence, vomiting, weight loss, peripheral edema | Atrioventricular block, GI bleeding, torsades de pointes |

**Efficacy Monitoring Parameters.** Improvement in symptoms of Alzheimer-type dementia.

**Toxicity Monitoring Parameters.** Symptoms of active or occult GI bleeding, particularly if patient has history of ulcer disease or is receiving concomitant NSAIDs.

**Key Patient Counseling Points.** Take at bedtime, with or without food. Allow disintegrating tablet to dissolve on tongue and follow with a glass of water. Adverse effects may be more frequent at dose escalation and tend to resolve with continued use. Report signs/symptoms of GI bleeding.

**Clinical Pearls.** Safety and effectiveness not established in children. No evidence suggests that donepezil alters the course of Alzheimer disease.



https://kat.cr/user/Blink99/

# DOXAZOSIN: Cardura, Cardura XL, Various

Teva generic pictured

D

**Class:** $\alpha_1$-Adrenergic Blocker

**Dosage Forms. Oral Tablet:** 1 mg, 2 mg, 4 mg, 8 mg; **Oral Tablet, Extended Release:** 4 mg, 8 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Benign prostatic hyperplasia: Immediate release, 1 mg po daily, may titrate to 1-8 mg po daily; Extended release, 4 mg po daily, may titrate to 8 mg po daily
2. Hypertension: Immediate release, 1 mg po daily, *max* 16 mg po daily

**Off-Label Uses.**

1. Expulsion of distal ureteral stone: Immediate release, 4 mg po daily in evening

**MOA.** Doxazosin selectively blocks postsynaptic $\alpha_1$-adrenergic receptors, reducing peripheral resistance through arterial and venous dilations. Reflex tachycardia that occurs with other vasodilators is infrequent because there is no presynaptic $\alpha_2$-receptor blockade. Increase urine flow by relaxing smooth muscle tone in the bladder neck and prostate.

**Drug Characteristics: Doxazosin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 65%, food increases AUC and Cmax of extended-release product |
| **Dose Adjustment Renal** | Not required | **Distribution** | 98% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic; substrate of CYP3A4/5 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 9%, fecal 63%, with a half-life of 22 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to doxazosin or other quinazolines | **Black Box Warnings** | None |

### Medication Safety Issues: Doxazosin

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| XL | No | Extended-release tablet | No | Cardene, Cordarone, doxepin, DOXOrubicin | Avoid use as an antihypertensive. High risk of orthostatic hypotension. |

### Drug Interactions: Doxazosin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Beta-blockers, nifedipine, PDE inhibitors | Increased risk of hypotension, especially with 1st dose of doxazosin | Monitor blood pressure |
| CYP3A4/5 inducers | Increased doxazosin metabolism reduces doxazosin efficacy | Monitor and consider dose increases of doxazosin |
| CYP3A4/5 inhibitors | Decreased doxazosin metabolism increases risk of doxazosin toxicity | Monitor and consider dose decreases of doxazosin |

### Adverse Reactions: Doxazosin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Asthenia, dizziness, edema, fatigue, headache, hypotension, nausea, somnolence, vertigo | Hepatotoxicity, priapism |

**Efficacy Monitoring Parameters.** Decreased BP, improvement in urinary symptoms.

**Toxicity Monitoring Parameters.** Signs of hypotension, increased HR.

**Key Patient Counseling Points.** Initial dose should be taken with breakfast. Avoid activities requiring coordination until drug effects are realized, as drug may cause vertigo or dizziness. Rise slowly from a sitting/lying position, as this drug may cause orthostatic hypotension. Syncope or loss of consciousness is possible with 1st dose or dose increases, especially if patient is in an upright position.

**Clinical Pearls.** Safety and effectiveness not established in children.



https://kat.cr/user/Blink99/

# DOXEPIN: Sinequan, Various

**Class:** Tricyclic Antidepressant

**Dosage Forms. Oral Capsule:** 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg; **Oral Tablet:** 3 mg, 6 mg; **Oral Solution:** 10 mg/mL

25 mg

50 mg

100 mg

Mylan generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Depression, anxiety, alcoholism: Very mild, 25-50 mg po daily, may titrate to 300 mg po daily; Mild-moderate, 75 mg po daily, may titrate to 300 mg po daily
2. Insomnia: Adults <65 y of age, 6 mg po daily hs; Adults ≥65 y of age, 3 mg po daily hs, may titrate to 6 mg po daily hs

**Off-Label Uses.** None

**MOA.** Doxepin is a tricyclic antidepressant, which influences the adrenergic activity at the synapses where it prevents norepinephrine deactivation through reuptake into the nerve terminals. By binding to histamine receptor sites, it competitively inhibits the biological activation of histamine receptors. Antagonism of the $H_1$ receptor is the most likely mechanism by which doxepin exerts its sleep maintenance effect.

**Drug Characteristics: Doxepin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Food increases AUC and Cmax |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 20.2 L/kg; 80% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic; major substrate of CYP2D6 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination with a half-life of 15 h |
| **Lactation** | Avoid | **Pharmacogenetics** | Caution with CYP2D6 poor metabolizers |
| **Contraindications** | Hypersensitivity to doxepin; MAOI use, glaucoma, severe urinary retention | **Black Box Warnings** | Suicidality |

**Medication Safety Issues: Doxepin**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | SINEquan | No | No | SEROquel, doxazosin, digoxin | Avoid >6 mg/d. Highly anticholinergic, sedating, and cause orthostatic hypotension. |

### Drug Interactions: Doxepin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| MAOIs | Increased risk of serotonin syndrome | Concurrent use contraindicated |
| Anticholinergics | Increased risk of additive anticholinergic side effects | Monitor for adverse effects |
| Agents that prolong QT interval | Increased risk of cardiotoxicity | Avoid concurrent use |
| SSRIs | Increased doxepin concentration and risk of serotonin syndrome | Use caution with concomitant therapy |
| CYP2D6 inhibitors | Decreased doxepin metabolism increases risk of doxepin toxicity | Monitor and consider dose decreases of doxepin |

### Adverse Reactions: Doxepin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Xerostomia | Blurred vision, confusion, constipation, dizziness, edema, fatigue, headache, nausea, sexual dysfunction, somnolence, rash, urinary retention, weight gain | Cardiac dysrhythmia, hepatotoxicity, suicidal thoughts |

**Efficacy Monitoring Parameters.** Improvement in depression (depressed mood, suicidal thoughts or intent, change in appetite, lack of energy, change in sleep patterns, etc).

**Toxicity Monitoring Parameters.** Worsening of depression, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases. Change in ECG, monitor LFTs.

**Key Patient Counseling Points.** Avoid activities requiring mental alertness until drug effects are realized. Symptomatic improvement in depression may not be seen for a few weeks. Avoid abrupt discontinuation of drug. Do not drink alcohol.

**Clinical Pearls.** Safety and effectiveness not established in children. Also available in topical formulation for pruritus due to atopic dermatitis.



https://kat.cr/user/Blink99/

# DOXYCYCLINE: Vibramycin, Various

**Class:** Tetracycline Antibiotic

**Dosage Forms.** **Powder for Oral Suspension:** 25 mg/5 mL; **Oral Tablet:** 20 mg, 50 mg, 75 mg, 100 mg, 150 mg; **Oral Tablet, Delayed Release:** 75 mg, 100 mg, 150 mg; **Oral Capsule:** 50 mg, 75 mg, 100 mg, 150 mg

West-ward generic 100 mg pictured

Mutual Pharmaceutical generic 50 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Acinetobacter infection: Children <8 y of age and <45 kg, 2.2-4.4 mg/kg po in 1-2 divided doses; Children >8 y of age and >45 kg and Adults, 100 mg po q12h on day 1, then 100 mg po daily
2. Acne vulgaris: Children <8 y of age and <45 kg, 2.2-4.4 mg/kg po in 1-2 divided doses; Children >8 y of age and >45 kg and Adults, 100 mg po q12h on day 1, then 100 mg po daily or bid
3. Gonorrhea, uncomplicated: 100 mg po bid × 7 d or 300-mg po single dose followed in 1 h by another 300-mg dose
4. Staphylococcal infection of skin: Children <8 y of age and <45 kg, 2.2-4.4 mg/kg po in 1-2 divided doses; Children >8 y of age and >45 kg and Adults, 100 mg po q12h on day 1, then 100 mg po daily

**Off-Label Uses.**

1. Lyme disease, prophylaxis: 200 mg po as a single dose

**MOA.** Doxycycline is a broad-spectrum bacteriostatic compound that inhibits protein synthesis at the 30S ribosomal subunit. Activity includes gram-positive, gram-negative, aerobic, and anaerobic bacteria, as well as spirochetes, mycoplasmas, rickettsiae, chlamydiae, and some protozoa. Many bacteria have developed plasmid-mediated resistance.

**Drug Characteristics: Doxycycline**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 100%, food has no effect on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 0.75 L/kg, 80% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, 50% |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 35-45% with a half-life of 15-24 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to doxycycline or concurrent acitretin | **Black Box Warnings** | None |

### Medication Safety Issues: Doxycycline

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Delayed release formulation | No | Doxepin, dicyclomine | No |

### Drug Interactions: Doxycycline

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Acitretin | Risk of increased intracranial pressure. Mechanism unknown. | Concurrent use contraindicated |
| Antacids | Decreased absorption via binding | Separate use by 1-2 h |
| Digoxin | Tetracyclines alter bacterial flora resulting in decreased metabolism of digoxin | Monitor and consider dose adjustments of digoxin |
| Penicillin | Tetracyclines may interfere with the bactericidal effect of penicillin | Avoid concurrent use |

### Adverse Reactions: Doxycycline

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Photosensitivity, tooth discoloration in children <8 y of age | Nausea, vomiting, diarrhea | Esophageal ulceration, hypersensitivity, hepatotoxicity, renal toxicity, *C. diff cile* colitis, increased intracranial pressure, decreased growth in children |

**Monitoring Parameters Efficacy.** Resolution of symptoms of infection.

**Monitoring Parameters Toxicity.** Burning or pain in the stomach, extreme headache, bloody diarrhea, tooth darkening.

**Key Patient Counseling Points.** May take with food that does not contain calcium. Complete full course of therapy. Symptoms should improve within 2-3 d. Wear sunscreen. Administer with 240 mL of water.

**Clinical Pearls.** May resume normal activities after 24 h of antibiotics if afebrile. Not for use in children <8 y of age (bone and tooth discoloration).



https://kat.cr/user/Blink99/

# DULOXETINE: Cymbalta, Various

**Class:** Serotonin/Norepinephrine Reuptake Inhibitor

**Dosage Forms. Oral Capsule, Delayed Release:** 20 mg, 30 mg, 60 mg

Lilly pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Anxiety: 60 mg po daily, may titrate to 120 mg po daily
2. Depression: 20-30 mg po bid, may titrate to 120 mg po daily
3. Diabetic peripheral neuropathy pain, fibromyalgia, musculoskeletal pain: 60 mg po daily, may titrate to 120 mg po daily

**Off-Label Uses.**

1. Urinary incontinence: 40 mg po bid

**MOA.** Duloxetine is a selective serotonin and norepinephrine reuptake inhibitor that exerts its antidepressant and pain inhibitory actions by potentiating the serotonergic and noradrenergic activity in the CNS. It has no significant affinity for adrenergic, dopaminergic, cholinergic, opioid, glutamate, or histaminergic receptors in vitro and does not inhibit monoamine oxidase.

**Drug Characteristics: Duloxetine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Avoid | **Absorption** | F = 30-80%; food slows absorption |
| **Dose Adjustment Renal** | Initiate at low dose and titrate slowly; avoid if CrCl <30 mL/min | **Distribution** | Vd = 1640 L; 90% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic; substrate of CYP1A2 and CYP2D6; inhibits CYP2D6 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 70% with a half-life of 8-17 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to duloxetine; MAOI, TCA, linezolid use, uncontrolled glaucoma | **Black Box Warnings** | Suicidality; not approved for children |

**Medication Safety Issues: Duloxetine**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | DULoxetine | No | No | FLUoxetine | No |

### Drug Interactions: Duloxetine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Anticoagulants, antiplatelet drugs, NSAIDs | Increased risk of bleeding | Monitor for bleeding |
| Triptans, SSRIs, tramadol | Additive serotonergic activity | Monitor closely for symptoms of serotonin syndrome (restlessness, hyperthermia, hyperref exia, incoordination) |
| Linezolid, TCAs, MAOIs | Increased risk of serotonin syndrome | Concomitant use contraindicated |
| CYP2D6 substrates | Duloxetine inhibits CYP2D6, increasing substrate concentrations and toxicity | Avoid concurrent use or monitor for adverse effects |
| CYP1A2 inducers | Increased duloxetine metabolism and decreased efficacy | Avoid concurrent use or consider duloxetine dose increase |
| CYP1A2 and 2D6 inhibitors | Decreased duloxetine metabolism and increased toxicity | Avoid concurrent use or consider duloxetine dose decrease |

### Adverse Reactions: Duloxetine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Headache, nausea | Agitation, anxiety, asthenia, bleeding, constipation, diarrhea, dizziness, diaphoresis, disorder of ejaculation, fatigue, hyponatremia, increased blood pressure, insomnia, loss of appetite, muscle cramps, mydriasis, rash, sexual dysfunction, somnolence, tremor, vomiting, xerostomia | Hepatotoxicity, serotonin syndrome, suicidal thoughts |

**Efficacy Monitoring Parameters.** Improvement in symptoms of depression, pain, or anxiety.

**Toxicity Monitoring Parameters.** Worsening of depression, suicidality, or unusual changes in behavior; monitor BP, CBC, electrolytes, and LFTs at baseline and periodically during therapy; ocular pressure and mydriasis.

**Key Patient Counseling Points.** Report withdrawal symptoms (eg, dysphoric mood, irritability, agitation, sensory disturbances), especially during abrupt discontinuation of therapy. Drug may cause hepatotoxicity and increased risk of bleeding (GI, ecchymoses, epistaxis, petechiae). May require 1-4 wk for improvement of depression symptoms. Report worsening depression, suicidal ideation, or unusual changes in behavior, especially at initiation of therapy or with dose changes. Children at higher risk for these effects during the first few months of therapy. Patient should watch for signs/symptoms of bleeding events and hepatotoxicity. Avoid alcohol. Monitor carefully if on concurrent meds that alter coagulation.

**Clinical Pearls.** Duloxetine not approved for use in children. Doses >60 mg/d have not been shown to provide increased effectiveness and were less well tolerated than the 60 mg/d dose.



https://kat.cr/user/Blink99/

# DUTASTERIDE: Avodart

**Class:** 5α-Reductase Inhibitor

**Dosage Forms. Oral Capsule:** 0.5 mg

GlaxoSmithKline 0.5 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Benign prostatic hyperplasia: 0.5 mg po daily

**Off-Label Uses.**

1. Male pattern alopecia: 0.5 mg po daily

**MOA.** Dutasteride inhibits the conversion of testosterone to 5α-dihydrotestosterone (DHT) by 5α-reductase, isoform 1 and 2.



**Drug Characteristics: Dutasteride**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 60%, minimal food effect |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 300-500 L |
| **Dialyzable** | Not known | **Metabolism** | Extensive hepatic; substrate of CYP3A4/5 |
| **Pregnancy Category** | X | **Elimination** | Renal elimination is <1% with a half-life of 5 wks |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to dutasteride, pregnancy, children | **Black Box Warnings** | None |

**Medication Safety Issues: Dutasteride**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Do not crush | No | No | No |

**Drug Interactions: Dutasteride**

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inducers | Increased dutasteride metabolism reduces dutasteride effectiveness | Consider dose increases of dutasteride |
| CYP3A4/5 inhibitors | Decreased dutasteride metabolism increases risk of dutasteride toxicity | Consider dose decreases of dutasteride |

**Adverse Reactions: Dutasteride**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Gynecomastia, impotence, reduced libido, dizziness | Heart failure, angioedema, allergic skin reactions |

**Efficacy Monitoring Parameters.** American Urologic Association (AUA) Symptom Score, decrease in residual urine volume, increased urinary flow, increased hair growth.

**Toxicity Monitoring Parameters.** Shortness of breath, skin rash, swelling.

**Key Patient Counseling Points.** Symptoms may not improve for up to 6 mo after starting treatment. Do not donate blood while taking or for 6 mo after stopping dutasteride, as it may be transfused to a pregnant woman. Women who are pregnant or may become pregnant should avoid touching or handling this medicine. This medicine can get into the body through the skin and may prevent development of genitalia in an unborn male baby.

**Clinical Pearls.** May be combined with the alpha-blocker tamsulosin for the treatment of BPH. Draw baseline PSA before initiating therapy. Note that PSA will decrease by 50% with treatment; double PSA values when assessing for prostate cancer.



https://kat.cr/user/Blink99/

# EFAVIRENZ: Sustiva

**Class:** Antiretroviral Agent, Reverse Transcriptase Inhibitor

**Dosage Forms. Oral Capsule:** 50 mg, 200 mg; **Oral Tablet:** 600 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Treatment of HIV-1 infections in combination with at least 2 other antiretroviral agents: Adults and Children ≥40 kg, 600 mg po daily; Children <40 kg, weight based and used in combination with ritonavir

**Off Label Uses.** None

**MOA.** Binds to HIV reverse transcriptase, blocking the RNA-dependent and DNA-dependent DNA polymerase activities including HIV-1 replication.

Bristol-Myers Squibb pictured

E

## Drug Characteristics: Efavirenz

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Avoid if moderate or severe hepatic impairment | **Absorption** | F = 42%, food increases absorption by 20-30% |
| **Dose Adjustment Renal** | Not required | **Distribution** | CSF concentration exceeds serum concentration |
| **Dialyzable** | No | **Metabolism** | Hepatic; substrate of via CYP3A/5, 2B6; inhibits CY2C9, and 2C19; induces CYP3A4/5 |
| **Pregnancy Category** | D | **Elimination** | 16-60% unchanged in feces, 14-34% renal as metabolites, with half-life of 52-76 h |
| **Lactation** | Avoid | **Pharmacogenetics** | Resistance is associated with HIV mutations |
| **Contraindications** | Hypersensitivity or concurrent use of bepridil, cisapride, midazolam, pimozide, triazolam, St. John's wort, or ergot alkaloids | **Black Box Warnings** | None |

## Medication Safety Issues: Efavirenz

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Do not open, crush, or chew capsule | Yes | No | No |

### Drug Interactions: Efavirenz

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Boceprivir | Decreased absorption concentration and loss of boceprivir activity | Avoid |
| CYP3A4/5, 2B6 inducers | Increased efavirenz metabolism reduces efavirenz effectiveness | Monitor and consider dose increases of efavirenz |
| CYP3A4/5, 2B6 inhibitors | Decreased efavirenz metabolism increases risk of efavirenz toxicity | Monitor and consider dose decreases of efavirenz |
| CYP2C9, 2C19 substrates | Decreased metabolism and increased toxicity substrates | Avoid sensitive substrates or increase monitoring and consider dose adjustments |
| CYP3A4/5, 2B6 substrates | Increased metabolism and decreased efficacy of substrates | Avoid sensitive substrates or increase monitoring and consider dose adjustments |
| Cisapride | Additive risk of arrhythmias | Contraindicated |
| Oral contraceptives | Reduced efficacy of oral contraceptives, unknown mechanism | Use an alternative form of contraception |

### Adverse Reactions: Efavirenz

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Anxiety, insomnia, headaches, rash, nausea, vomiting, diarrhea, hyperlipidemia | Fatigue, pruritus, hyperglycemia, elevated LFTs, neutropenia | Psychosis, seizures, hepatic failure, hypersensitivity, pancreatitis, suicidal ideation, fat redistribution, immune reconstitution syndrome |

**Efficacy Monitoring Parameters.** HIV viral load, CD4 count, HIV resistance testing prior to starting therapy.

**Toxicity Monitoring Parameters.** LFTs, bilirubin, CBCs, lipid panel.

**Key Patient Counseling Points.** Multiple, potentially serious drug interactions, do not take new medications, OTCs, or herbals without consulting health-care provider. Take on an empty stomach at bedtime. Do not open, chew, or crush capsule. Does not prevent transmission of HIV, practice safe sex. May cause drowsiness, avoid driving and concurrent CNS depressants.

**Clinical Pearls.** Not recommended for children <3 y of age. Efavirenz is the non-nucleoside reverse transcriptase inhibitor of choice for initial combination therapy for HIV.



https://kat.cr/user/Blink99/

# ELETRIPTAN: Relpax

**Class:** Antimigraine Serotonin Receptor Agonist

**Dosage Forms. Oral Tablet:** 20 mg, 40 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Migraine: 20-40 mg po at onset of migraine, may repeat after 2 h prn; *max* single dose 40 mg, *max* daily dose 80 mg/d

**Off-Label Uses.** None

**MOA.** Eletriptan binds with high affinity to serotonin (5-HT) subtypes 1B, 1D, and 1F receptors. It has no significant affinity or pharmacological activity at adrenergic $\alpha_1$, $\alpha_2$, or $\beta$; dopaminergic $D_1$ or $D_2$; muscarinic; or opioid receptors. Serotonin receptor agonists are believed to be effective in migraine, either through vasoconstriction (via activation of 5-$HT_1$ receptors located on intracranial blood vessels) or through activation of 5-$HT_1$ receptors on sensory nerve endings in the trigeminal system, resulting in the inhibition of pro-inflammatory neuropeptide release.

Pfizer 40 mg pictured

E

**Drug Characteristics: Eletriptan**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Avoid in severe hepatic dysfunction | **Absorption** | F = 50%, high-fat food increases bioavailability 20-30% |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 138 L |
| **Dialyzable** | Unknown | **Metabolism** | Hepatic; substrate of CYP3A4/5 |
| **Pregnancy Category** | C | **Elimination** | Nonrenal elimination 90% with a half-life of 4 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to eletriptan, cerebrovascular syndromes, hemiplegic or basilar migraine, ischemic bowel disease, ischemic heart disease, peripheral vascular disease, severe hepatic impairment, uncontrolled hypertension | **Black Box Warnings** | None |

**Medication Safety Issues: Eletriptan**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Sumatriptan | No |

### Drug Interactions: Eletriptan

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| SSRIs | Additive serotonergic effects | Avoid concurrent use; if not possible, monitor carefully for signs of serotonin syndrome |
| CYP3A4/5 inducers | Increased eletriptan metabolism reduces eletriptan effectiveness | Monitor and consider dose increases of eletriptan |
| CYP3A4/5 inhibitors | Decreased eletriptan metabolism increases risk of eletriptan toxicity | Monitor and consider dose decreases of eletriptan |
| Other 5HT agonists | Additive pharmacologic effect leading to additive toxicity | Administration within 24 h of other serotonin agonists is contraindicated |

### Adverse Reactions: Eletriptan

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Weakness | Nausea, asthenia, dizziness, somnolence | Angina, cardiac dysrhythmia, coronary arteriosclerosis, heart block, hypertension, acute myocardial infarction, aphasia, cerebral ischemia, stroke, dystonia, hemiplegia, neuropathy, transient ischemic attack, oculogyric crisis |

**Efficacy Monitoring Parameters.** Resolution of signs of migraine headache.

**Toxicity Monitoring Parameters.** Seek medical attention for signs of ischemic bowel disease (eg, sudden severe abdominal pain, bloody diarrhea) or peripheral vascular disease (eg, Raynaud syndrome), serotonin syndrome (eg, agitation, hallucinations, tachycardia, hyperreflexia, incoordination, diarrhea, nausea), ischemic cardiac syndrome, or hypertensive crisis.

**Key Patient Counseling Points.** Should avoid activities requiring mental alertness or coordination until drug effects are realized, as this drug may cause dizziness or somnolence.

**Clinical Pearls.** These agents are not for prophylaxis—these are used for the treatment of acute migraine headache. Several serotonin agonists ("triptans") exist for migraine, administered via a variety of routes (oral, inhaled, and injected). Each differs in onset and duration of action. If 1 agent is ineffective at *max* dose, recommend changing agents or route. Instruct patient to take a second dose 2 or more h after the first, if needed, and no more than 80 mg/d.



https://kat.cr/user/Blink99/

# EMTRICITABINE/TENOFOVIR: Truvada

**Class:** Antiretroviral Agent, Reverse Transcriptase Inhibitor; Antiretroviral Agent, Reverse Transcriptase Inhibitor

**Dosage Forms. Oral Tablet:** Emtricitabine/Tenofovir 200 mg/300 mg

Gilead 200 mg/300 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Treatment of HIV-1 infection in combination with other antiretroviral agents: Adults and Children ≥12 y of age, 1 tablet po daily
2. Preexposure prophylaxis (PrEP) for prevention of HIV-1 infection in adults who are at high risk for acquiring HIV: 1 tablet po daily (high risk is defined as inconsistent condom use, incarcerated, drug, and alcohol dependence)

**Off-Label Uses.**

1. Treatment of hepatitis B in patients with antiviral-resistant HBV or coinfection with HIV: 1 tablet po daily

**MOA.** Emtricitabine is a cytidine analogue while tenofovir is an analogue of adenosine 5′-monophosphate. Each drug interferes with HIV viral RNA-dependent DNA polymerase resulting in inhibition of viral replication.

**Drug Characteristics: Emtricitabine/Tenofovir**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Emtricitabine F = 92%; tenofovir F = 25%, no food effect |
| **Dose Adjustment Renal** | CrCl = 30-49 mL/min, increase dose interval to 48 h; CrCl <30 mL/min, avoid | **Distribution** | Emtricitabine, saliva, semen; tenofovir, lymphocytes |
| **Dialyzable** | No | **Metabolism** | Minimal; tenofovir induces P-glycoprotein |
| **Pregnancy Category** | B | **Elimination** | Emtricitabine, half-life of 10 h; tenofovir, half-life of 17 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | Resistance is associated with HIV mutations |
| **Contraindications** | Do not use for preexposure prophylaxis in patients with unknown or HIV-1 positive status. Only for use in combination with other antiretrovirals. | **Black Box Warnings** | Hepatitis B, lactic acidosis, preexposure prophylaxis |

### Medication Safety Issues: Emtricitabine/Tenofovir

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | Yes | No | No |

### Drug Interactions: Eletriptan/Tenofovir

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Atazanavir | Decreased atazanavir, unknown mechanism | Concurrent administration requires ritonavir boost |
| Didanosine | Increased bioavailability and toxicity of didanosine, unknown mechanism | Avoid |
| Lopinavir, ritonavir, tipranavir | Increased tenofovir bioavailability, unknown mechanism | Monitor for tenofovir toxicity; consider dose reductions |
| P-glycoprotein substrates | Induction of substrate metabolism decreases effectiveness of substrate | Monitor and consider substrate dose increase |

### Adverse Reactions: Emtricitabine/Tenofovir

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Hyperpigmentation, rash, hypophosphatemia, nausea, diarrhea, dizziness, insomnia, fatigue | Hyperglycemia, hyperlipidemia, anemia, neutropenia, elevated LFTs, neuropathy, hematuria | Lactic acidosis, HBV exacerbations, renal failure |

**Efficacy Monitoring Parameters.** Prior to therapy, HIV resistance testing, HBV testing as acute, and severe exacerbations of HBV have been reported following discontinuation of antiretroviral therapy. HIV viral load, CD4 count, for assessment of efficacy. If using for preexposure prophylaxis, patients must be HIV negative. Patients receiving preexposure prophylaxis who get HIV may be drug resistant at diagnosis. Also test for sexually transmitted diseases and treat as necessary.

**Toxicity Monitoring Parameters.** LFTs, bilirubin, CBC, glucose, renal function, phosphorus, assessment of osteoporosis. Lactic acidosis and severe hepatomegaly and sometimes fatal steatosis have been reported with nucleoside and nucleotide analogues.

**Key Patient Counseling Points.** Take with or without food.

**Clinical Pearls.** Not recommended for children <12 y of age. Recommended as a component of preferred regimens (in combination with atazanavir/ritonavir or darunavir/ritonavir or efavirenz or raltegravir) in antiretroviral-naive patients.



https://kat.cr/user/Blink99/

# ENALAPRIL: Vasotec, Various

**Class:** ACE-I, Antihypertensive

**Dosage Forms. Oral Tablet:** 2.5 mg, 5 mg, 10 mg, 20 mg; **Oral Solution:** 1 mg/mL

Wockhardt generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Heart failure: Infants ≥4 d of age, 0.1-0.5 mg/kg po daily, *max* 0.94 mg/kg po daily; Adults, 2.5 mg po daily or bid, *max* 40 mg po daily in divided doses
2. Hypertension: Infants ≥1 mo of age and Adolescents, 0.08 mg/kg up to 5 mg po daily, *max* 0.58 mg/kg or 40 mg po daily; Adults, 5 mg po daily, *max* 40 mg po daily in divided doses
3. Kidney disease, nondiabetic: Children 7-18 y of age, 0.1-0.5 mg/kg po daily, *max* 20 mg po daily; Adults, 5 mg po daily, *max* 20 mg po daily

**Off-Label Uses.**

1. Diabetic nephropathy: 5-20 mg po daily
2. MI: 2.5 mg po daily, may titrate to 20 mg po daily

**MOA.** Enalapril is a prodrug that is rapidly converted to its active metabolite, enalaprilat, a competitive ACE-I. It reduces serum aldosterone, leading to decreased sodium retention, potentiates the vasodilator kallikrein–kinin system, inhibits the sympathetic nervous system, and inhibits the tissue renin–angiotensin system. The net effect is reduction in total peripheral resistance and blood pressure in hypertensive patients, and reduction of elevated afterload in patients with heart failure.

**Drug Characteristics: Enalapril**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 60%, no effect of food on absorption |
| **Dose Adjustment Renal** | CrCl <30 mL/min, initial dose 2.5 mg po daily, *max* 40 mg po daily | **Distribution** | 50-60% protein bound |
| **Dialyzable** | Yes | **Metabolism** | Extensive hepatic to 1 active metabolite |
| **Pregnancy Category** | D | **Elimination** | Renal elimination is 61% with a half-life of 1.3 h (parent drug) and 11 h (metabolite) |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to enalapril, history of angioedema, pregnancy | **Black Box Warnings** | Pregnancy |

### Medication Safety Issues: Enalapril

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Elavil | No |

### Drug Interactions: Enalapril

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Potassium-sparing diuretics, ARBs, potassium supplements | Increased risk of hypotension and nephrotoxicity (diuretics and ARBs), hyperkalemia | Avoid concurrent use or monitor BP, SCr, and serum potassium levels |
| NSAIDs, aspirin | Decreased antihypertensive effect of enalapril, increased risk of nephrotoxicity | Avoid concurrent use or monitor BP and SCr |
| Aliskiren | Increased risk of hyperkalemia | Concurrent use contraindicated |
| Azathioprine | Increased risk of myelosuppression | Avoid concurrent use; monitor for anemia or leucopenia |
| Cyclosporine | Increased risk of nephrotoxicity | Avoid concurrent use or monitor SCr |

### Adverse Reactions: Enalapril

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Increased SCr | Diarrhea, dizziness, dry cough, fatigue, headache, hypotension, hyperkalemia, nausea, nephrotoxicity, rash, tachycardia | Angioedema, birth defects, liver failure |

**Efficacy Monitoring Parameters.** Decreased BP, signs of heart failure.

**Toxicity Monitoring Parameters.** Signs of angioedema (swelling of the face, eyes, lips, tongue, or throat), severe persistent cough, hypotension; monitor baseline and periodic electrolytes, SCr, BUN, and urine protein.

**Key Patient Counseling Points.** Use potassium supplements or salt substitutes only under medical supervision.

**Clinical Pearls.** Progressive renal impairment including acute renal failure may occur on enalapril therapy. Injectable formulation, enalaprilat, also available. Injectable and oral dosing not interchangeable.



https://kat.cr/user/Blink99/

# ENOXAPARIN: Lovenox, Various

**Class:** Anticoagulant

**Dosage Forms.** **Prefilled Syringes**: 30 mg/0.3 mL, 40 mg/0.4 mL, 60 mg/0.6 mL, 80 mg/0.8 mL, 100 mg/1 mL, 120 mg/0.8 mL, 150 mg/1 mL; **Multiple-Dose Vial:** 300 mg/3 mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Deep vein thrombosis prophylaxis, abdominal surgery: 40 mg sq once 2 h prior to surgery, then daily × 7-10 d
2. Deep vein thrombosis prophylaxis, hip or knee replacement surgery: 30 mg sq q12h starting 12-24 h postoperatively × 7-14 d
3. Deep vein thrombosis prophylaxis, acute medical illness: 40 mg sq daily × 6-11 d
4. Deep vein thrombosis treatment: 1 mg/kg sq q12h; initiate warfarin therapy as soon as possible and continue enoxaparin for at least 5 d and until target INR is reached
5. Acute ST segment elevation myocardial infarction: Age <75 y, 30 mg IV together with 1 mg/kg sq once, then 1 mg/kg sq q12h (*max* of 100 mg for the first 2 doses only); age ≥75 y, 0.75 mg/kg sq q12h (no initial bolus)
6. Unstable angina and non–Q-wave myocardial infarction: 1 mg/kg sq q12h × 2-8 d with aspirin 100-325 mg po daily

**Off-Label Uses.** None

**MOA.** Enoxaparin is a low-molecular-weight heparin which has antifactor Xa and IIa properties.

**Drug Characteristics: Enoxaparin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 100% following sq dose |
| **Dose Adjustment Renal** | CrCl <30 mL/min: avoid use or reduce dose by 50% | **Distribution** | Vd = 4.3 L |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 40% with a half-life of 7 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to enoxaparin, heparin, or pork products; active major bleeding; concurrent neuraxial analgesia | **Black Box Warnings** | Neuraxial anesthesia may cause hematomas |

Sanofi-Aventis 100 mg/mL pictured

### Medication Safety Issues: Enoxaparin

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | Yes | Lasix, Lotronex | No |

### Drug Interactions: Enoxaparin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| NSAIDs, antiplatelet agents, thrombolytics | Increased risk of bleeding by combined effects on platelet function | Avoid or discontinue concurrent use if possible; monitor carefully for bleeding complications |

### Adverse Reactions: Enoxaparin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Anemia, hemorrhage | Diarrhea, nausea, thrombocytopenia, increased LFTs, fever | Atrial fibrillation, heart failure, eczematous drug eruption, intracranial hemorrhage |

**Efficacy Monitoring Parameters.** Prevention or resolution of thrombosis, depending on indication.

**Toxicity Monitoring Parameters.** Signs and symptoms of bleeding, CBC, LFTs. Patients with renal failure, obese patients, pregnant patients, and others at risk of bleeding complications should be monitored using antifactor Xa testing.

**Key Patient Counseling Points.** If self-administered (outside health-care facility), instruct patient on appropriate administration technique. Monitor for signs of thrombosis and bleeding complications.

**Clinical Pearls.** Unlike unfractionated heparin, low-molecular-weight heparins cannot be monitored using standard activated partial thromboplastin time (aPTT). Antifactor Xa levels are needed for monitoring. Epidural or spinal hematomas may occur in patients who receive low-molecular-weight heparins for neuraxial anesthesia, who undergo spinal puncture, or who have an indwelling epidural catheter.



https://kat.cr/user/Blink99/

# ENTECAVIR: Baraclude, Various

**Class:** Antiretroviral Agent, Reverse Transcriptase Inhibitor

**Dosage Forms. Oral Tablet:** 0.5 mg, 1 mg; **Oral Solution:** 0.05 mg/1 mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Treatment of chronic HBV infection: Adults, 0.5-1 mg po daily

**Off-Label Uses.**

1. HBV reinfection prophylaxis: Adults, 0.5-1 mg po daily

**MOA.** Intracellularly phosphorylated to guanosine triphosphate which competes with natural substrates to effectively inhibit HBV polymerase; enzyme inhibition blocks reverse transcriptase activity thereby reducing viral DNA synthesis.

Bristol-Myers Squibb 1 mg pictured

E

**Drug Characteristics: Entecavir**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F approaches 100%, food decreases absorption by 50% |
| **Dose Adjustment Renal** | CrCl <50 mL/min, increase interval | **Distribution** | Extensive tissue |
| **Dialyzable** | Yes, administer after dialysis | **Metabolism** | Not metabolized |
| **Pregnancy Category** | C | **Elimination** | 60-70% renal, half-life 140 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | Resistance is associated with HBV mutations |
| **Contraindications** | None | **Black Box Warnings** | HIV resistance in chronic hepatitis B patients with unrecognized or untreated HIV infection; discontinuation of therapy may result in disease exacerbation; lactic acidosis |

**Medication Safety Issues: Entecavir**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | No |

**Drug Interactions: Entecavir**

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Ribavirin | Increased hepatotoxicity | Avoid concurrent use |
| Ganciclovir | Increased hematologic toxicity | Avoid concurrent use |

**Adverse Reactions: Entecavir**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Edema, elevated LFTs | Nausea, vomiting, diarrhea, headaches, hematuria, hyperglycemia, hepatic encephalopathy | Hypersensitivity, renal failure, hepatomegaly, and thrombocytopenia |

**Efficacy Monitoring Parameters.** HBV DNA, LFTs.

**Toxicity Monitoring Parameters.** HIV status (prior to initiation of therapy); LFTs, renal function. Call health-care provider for dark urine or yellow skin or eyes.

**Key Patient Counseling Points.** Complete full course of therapy; take on an empty stomach.

**Clinical Pearls.** Hepatitis may get worse if this drug is stopped; monitor HBV DNA after discontinuation. Consider genetic testing of HBV if suboptimal response to therapy.



https://kat.cr/user/Blink99/

# EPINEPHRINE: EpiPen, EpiPen Jr., Various

Dey 0.3 mg pictured

**Class:** Anaphylaxis Agent

**Dosage Forms. Auto-Injector Kit:** Delivers 0.3 mg epinephrine in 0.3 mL (1:1000 solution) or 0.15 mg epinephrine in 0.3 mL (1:2000 solution)

**Common FDA Label Indication, Dosing, and Titration.**

1. Emergency treatment of acute anaphylaxis due to allergic reactions: Children 15-30 kg, 0.15 mg (0.3 mL of a 1:2000 solution) IM or sq; Children >30 kg and Adults, 0.3 mg (0.3 mL of a 1:1000 solution) IM or sq; may be repeated if severe anaphylaxis persists

**Off-Label Uses.** None

**MOA.** Epinephrine treats severe allergic reactions to insect stings or bites, foods, drugs, and other allergens. It acts on both α- and β-adrenergic receptors. Through its action on α-adrenergic receptors, epinephrine lessens the vasodilation and increased vascular permeability that occurs during anaphylaxis, which can lead to loss of intravascular fluid volume and hypotension. Through its action on β-adrenergic receptors, epinephrine causes bronchial smooth muscle relaxation that helps alleviate bronchospasm, wheezing, and dyspnea that may occur during anaphylaxis. Epinephrine also alleviates pruritus, urticaria, and angioedema.

**Drug Characteristics: Epinephrine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | 20% of dose rapidly absorbed after sq dose; remaining 80% absorbed over 6-8 h |
| **Dose Adjustment Renal** | Not required | **Distribution** | N/A |
| **Dialyzable** | Not dialyzable | **Metabolism** | Rapid and complete hepatic |
| **Pregnancy Category** | C | **Elimination** | Inactivated metabolites renally |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | None in emergency situations | **Black Box Warnings** | None |

### Medication Safety Issues: Epinephrine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| Jr. | EPINEPHrine | No | Yes | Epifrin, ePHEDrine | No |

### Drug Interactions: Epinephrine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Cardiac glycosides | Combination may result in cardiac arrhythmias | Monitor closely for signs of arrhythmia |
| Beta-blockers, alpha-blockers | Effects of epinephrine are antagonized | Monitor closely for lack of response to epinephrine |
| TCAs, MAOIs, levothyroxine, linezolid | The effects of epinephrine may be potentiated due to inhibition of norepinephrine reuptake | Monitor closely for hypertension, cardiac arrhythmias |

### Adverse Reactions: Epinephrine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Palpitations, pale complexion, sweating, nausea, vomiting, asthenia, dizziness, headache, tremor, anxiety, apprehension, restlessness | | Angina, autonomic hyperreflexia, cardiac dysrhythmia, ventricular fibrillation, pulmonary edema |

**Efficacy Monitoring Parameters.** Resolution of symptoms of anaphylaxis (dyspnea, pruritus, urticaria, angioedema).

**Toxicity Monitoring Parameters.** Seek medical attention after emergency use and monitor for signs of cardiac toxicity and hypertension.

**Key Patient Counseling Points.** Instruct patient on proper administration technique. Immediately seek medical assistance, even if the patient feels better after epinephrine use.

**Clinical Pearls.** Epinephrine auto-injectors are intended for immediate self-administration as emergency supportive therapy only and are not a substitute for immediate medical care. Epinephrine is used for a wide variety of indications in the acute care setting, including in cardiac resuscitation attempts, and in combination with topical anesthetic as a vasodilator to reduce bleeding during suturing and other minor surgical procedures. Ophthalmic and inhaled dosage forms also available for other indications.



https://kat.cr/user/Blink99/

# EPOETIN: Epogen, Procrit

**Class:** Erythropoietic Stimulating Agent

**Dosage Forms.** **Injection Solution:** 2000 units/mL, 3000 units /mL, 4000 units/mL, 10,000 units/mL, 20,000 units/mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Anemia of cancer chemotherapy: Children, 600 units/kg (*max* 40,000 units) IV once weekly; Adults, 40,000 units sq weekly; dose adjusted based on changes in Hgb levels
2. Anemia of chronic renal failure: Children, 50 units/kg IV or sq 3 times per week; Adults not on dialysis, 10,000 units sq weekly, 20,000 units sq every other week, 30,000 units every 3rd wk, or 40,000 units sq every 4 wk; Adults on dialysis, 50-100 units/kg IV or sq 3 times per week; dose adjusted based on changes in Hgb levels
3. Perioperative collection of blood for allogeneic infusion: 300 units/kg/d sq for 10 d before surgery, on the day of surgery, and for 4 d postoperatively

**Off-Label Uses.**

1. Anemia due to myelodysplastic syndrome: 40,000-60,000 units sq 1-3 times/wk

**MOA.** Epoetin alfa is recombinant human erythropoietin. It binds to the erythropoietin receptor on erythroid progenitor cells, stimulating production/differentiation of mature red cells.

Amgen 4000 units/mL pictured

E

## Drug Characteristics: Epoetin

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Subcutaneously, F = 22-33% |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 52 mL/kg |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic via galactose receptors |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is minimal with a half-life of 4-13 h IV for CKD pts, and 16-67 h for anemic cancer pts |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to epoetin, albumin, uncontrolled hypertension | **Black Box Warnings** | Increased CV, stroke, mortality risk; cancer recurrence; REMS program |

## Medication Safety Issues: Epoetin

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Neupogen, darbepoetin | No |

### Drug Interactions: Epoetin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Thalidomide | Additive risk of thrombosis | Avoid concurrent use if possible; consider anticoagulation if agents must be combined |

### Adverse Reactions: Epoetin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Edema, hypertension, diarrhea, injection site thrombosis, myalgia, fatigue | Thromboembolism, myocardial infarction | Pure red cell aplasia, immune hypersensitivity, seizures, tumor progression |

**Efficacy Monitoring Parameters.** Monitor Hgb carefully and titrate dose to avoid transfusion and reduce or interrupt therapy if Hgb approaches 11 g/dL. Iron studies needed to ensure adequate iron stores, transferrin saturation >20% and ferritin >100 ng/mL.

**Toxicity Monitoring Parameters.** BP, weight to monitor edema, SCr in renal failure patients.

**Key Patient Counseling Points.** Do not shake, dilute, or expose to light. Store in box in refrigerator. Do not combine remainders from different vials; each vial is single use. May require several weeks for maximum effect.

**Clinical Pearls.** Typically administered in hospitals and clinics only. In cancer patients with certain tumor types (eg, breast, non–small cell lung, head and neck, lymphoid, cervical), epoetin and darbepoetin shortened overall survival and/or increased the risk of tumor progression or recurrence in some clinical studies. Discontinue after the completion of the chemotherapy course and if no response after 8 wk of therapy. Hospitals and health-care professionals who prescribe and/or dispense epoetin to patients with cancer must enroll and comply with the ESA APPRISE oncology program at www.esa-apprise.com. Renal failure patients experienced greater risks of death, stroke, and serious cardiovascular events when administered erythropoiesis-stimulating agent to target Hgb levels of 13 g/dL or higher in clinical studies. Clinical trials have shown that epoetin provides no improvement in quality of life, fatigue, or well-being.



https://kat.cr/user/Blink99/

# ESCITALOPRAM: Lexapro, Various

**Class:** SSRI Antidepressant

**Dosage Forms. Oral Tablet:** 5 mg, 10 mg, 20 mg; **Oral Solution:** 5 mg/5 mL

Forest Laboratories pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Depression: Children ≥ 12 y of age and Adults, 10 mg po daily, may titrate to 20 mg po daily
2. Generalized anxiety disorder: 10 mg po daily, may titrate to 20 mg po daily

**Off-Label Uses.**

1. OCD: 20-60 mg po daily
2. Panic disorder: 20-30 mg po daily, may titrate to 60 mg po daily
3. Hot flashes: 10 mg once po daily, may increase to 20 mg once daily after 4 wk

**MOA.** Escitalopram is the s-enantiomer of racemic citalopram and is an antidepressant that is a selective and potent inhibitor of presynaptic reuptake of serotonin (an SSRI). It does not affect reuptake of norepinephrine or dopamine and has a relative lack of affinity for muscarinic, histamine, $\alpha_1$- and $\alpha_2$-adrenergic, and serotonin receptors.

E

**Drug Characteristics: Escitalopram**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Dose at 10 mg po daily | **Absorption** | F = 80%, food has no effect on absorption |
| **Dose Adjustment Renal** | Use with caution in severe renal impairment | **Distribution** | Vd = 12 L/kg; 56% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic; substrate of CYP3A4/5, CYP2C19 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 10% with a half-life of 22-32 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to citalopram or escitalopram; concurrent MAOI use | **Black Box Warnings** | Suicidality; not approved for use in children |

**Medication Safety Issues: Escitalopram**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Loxitane | No |

### Drug Interactions: Escitalopram

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Anticoagulants, antiplatelet drugs, NSAIDs | Increased risk of bleeding | Monitor for bleeding |
| Triptans | Increased risk of serotonin syndrome | Monitor closely for symptoms of serotonin syndrome (restlessness, hyperthermia, hyperref exia, incoordination) |
| Linezolid, MAOIs | Increased risk of serotonin syndrome | Concomitant use contraindicated |
| Lithium | Increased lithium concentrations | Monitor for lithium side effects and consider dose decreases |
| CYP3A4/5, 2C19 inducers | Increased escitalopram metabolism reduces escitalopram effectiveness | Monitor and consider dose increases of escitalopram |
| CYP3A4/5, 2C19 inhibitors | Decreased escitalopram metabolism increases risk of escitalopram toxicity | Monitor and consider dose decreases of escitalopram |

### Adverse Reactions: Escitalopram

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Headache, nausea, sedation | Constipation, diaphoresis, diarrhea, disorder of ejaculation, dizziness, fatigue, impotence, indigestion, insomnia, rash, reduced libido, somnolence, vomiting, weight gain, xerostomia | Prolonged QT interval, serotonin syndrome, suicidal thoughts, torsades de pointes |

**Efficacy Monitoring Parameters.** Improvement in symptoms of depression, panic disorder (dyspnea, palpitations, trembling, experiencing an uncontrolled feeling, etc); OCD (recurrent and persistent impulses that are intrusive and senseless, or repetitive and intentional behaviors performed in response to obsessive thoughts); or generalized anxiety.

**Toxicity Monitoring Parameters.** Worsening of depression, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases; signs/symptoms of abnormal bleeding.

**Key Patient Counseling Points.** Avoid activities requiring mental alertness or coordination until drug effects are realized. Symptomatic improvement may not be seen for 4-6 wk. Report worsening depression, suicidal ideation, unusual changes in behavior, or unusual bleeding. Avoid abrupt discontinuation, may precipitate withdrawal symptoms. Do not drink alcohol or use NSAIDs or aspirin while taking this drug.

**Clinical Pearls.** If intolerable withdrawal symptoms occur following a decrease in dose or therapy discontinuation, may need to resume the previous dose and taper at a more gradual rate.



https://kat.cr/user/Blink99/

# ESOMEPRAZOLE: Nexium, Various

**Class:** Proton Pump Inhibitor

**Dosage Forms.** **Oral Capsule, Delayed Release:** 20 mg, 40 mg; **Oral Granules:** 2.5 mg, 5 mg, 10 mg, 20 mg, 40 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. *H. pylori* GI infection: 40 mg po daily × 10-14 d in combination with amoxicillin 1000 mg and clarithromycin 500 mg po bid
2. Erosive esophagitis, GERD treatment: Children 1-11 y of age and <20 kg, 10 mg po daily × 8 wk; Children ≥20 kg, 10-20 mg po daily × 8 wk; Adults, 20-40 mg po daily × 4-8 wk
3. Erosive esophagitis, heartburn: Children 1-11 y of age, 10 mg po daily × 8 wk; Children ≥12 y of age and Adults, 20-40 mg po daily × up to 8 wk
4. Prevention of NSAID-induced gastropathy: 20-40 mg po daily × up to 6 mo
5. Zollinger-Ellison syndrome: 40 mg po bid up to 240 mg/d

AstraZeneca pictured

**Off-Label Uses.** None

**MOA.** Esomeprazole is a proton pump inhibitor (PPI) that, when protonated in the secretory canaliculi of the parietal cells, covalently binds to $H^+/K^+$-ATPase (proton pump), which is the final pathway for acid secretion. Esomeprazole produces a profound and prolonged antisecretory effect, and inhibits basal, nocturnal, pentagastrin-stimulated, and food-stimulated gastric acid secretion.

**Drug Characteristics: Esomeprazole**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Severe, *max* dose of 20 mg daily | **Absorption** | F = 90%, food reduces F by 50% |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 16 L; 97% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic; substrate of CYP2C19; inducer of CYP2C19 |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 80% with a half-life of 60-90 min |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | 3% of Caucasians are poor CYP2C19 metabolizers; if known, consider 20 mg dose; moderate CYP2C19 inhibitor |
| **Contraindications** | Hypersensitivity to omeprazole or esomeprazole | **Black Box Warnings** | None |

### Medication Safety Issues: Esomeprazole

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | NexIUM | Capsules | No | NexAVAR | No |

### Drug Interactions: Esomeprazole

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Clopidogrel | Competitive inhibition of clopidogrel metabolism to active form, reducing clopidogrel effectiveness | Avoid concurrent use |
| CYP2C19 inhibitors | Decreased esomeprazole metabolism increases risk of esomeprazole toxicity | Consider dose decreases of esomeprazole |
| CYP2C19 inducers | Increased esomeprazole metabolism reduces esomeprazole effectiveness | Consider dose increases of esomeprazole |
| CYP2C19 substrates | Decreased metabolism and increased toxicity of substrates | Avoid concurrent use or decrease substrate dose |
| pH-dependent drugs | Lower gastric pH reduces absorption | Monitor for lack of effectiveness of interacting drug and adjust dose as necessary |
| Warfarin | Increased anticoagulant effect | Monitor INR and adjust warfarin dose accordingly |

### Adverse Reactions: Esomeprazole

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Headache | Abdominal pain, diarrhea, nausea, flatulence | Toxic epidermal necrolysis, pancreatitis, hepatotoxicity, bone fracture, rhabdomyolysis, acute interstitial nephritis |

**Efficacy Monitoring Parameters.** Resolution of GI discomfort, resolution of ulcers shown on endoscopy; for treatment of *H. pylori*, negative urea breath test.

**Toxicity Monitoring Parameters.** Severe headache or blistering skin rash.

**Key Patient Counseling Points.** Should be taken 1 h before meals.

**Clinical Pearls.** Multiple *H. pylori* regimens contain different combinations of PPIs and antibiotics; complete full regimen if prescribed for *H. pylori* treatment. Many PPI and $H_2$ antagonists available OTC; warn patients not to take multiple products concurrently. Also available in injectable formulation. Increased risk of fractures; use lowest effective dose in patients at risk for osteoporosis. Reassess for continuation after treatment duration is complete.



https://kat.cr/user/Blink99/

# ESTRADIOL ORAL: Estrace, Various

**Class:** Estrogen

**Dosage Forms. Oral Tablet:** 0.5 mg, 1 mg, 2 mg

Barr generic 1 mg pictured

Watson generic 0.5 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Abnormal vasomotor function (moderate to severe), menopause: 1-2 mg po daily for 21 d followed by 7 d off
2. Atrophic vulva or vagina (moderate-severe), menopause: Oral tablet, 1-2 mg po daily in a cyclical pattern (3 wk on, 1 wk off)
3. Breast cancer, metastatic, for palliation only: 10 mg po tid × 3 mo
4. Carcinoma of prostate, advanced, androgen-dependent, for palliation only: 1-2 mg po tid
5. Decreased estrogen level, secondary to hypogonadism, castration, or primary ovarian failure: 1-2 mg po daily
6. Postmenopausal osteoporosis, prophylaxis: 0.5 mg po daily for 23 d followed by 5 d off

**Off-Label Uses.** None

**MOA.** Estradiol (17β-estradiol; E2) is the most potent of the naturally occurring estrogens and the major estrogen secreted during the reproductive years. Estradiol and other estrogens produce characteristic effects on specific tissues (such as breast), cause proliferation of vaginal and uterine mucosa, increase calcium deposition in bone, and accelerate epiphyseal closure after initial growth stimulation.



**Drug Characteristics: Estradiol Oral**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 40%, food has no effect on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Widely distributed; 98% protein bound |
| **Dialyzable** | Yes | **Metabolism** | Extensive hepatic; substrate of many CYP pathways, major substrate of CYP3A4/5, 1A2, P-glycoprotein |
| **Pregnancy Category** | X | **Elimination** | Renal with a half-life of 21 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to estradiol; history of thromboembolic disorders, breast cancer, any estrogen-dependent neoplasm, known or suspected pregnancy | **Black Box Warnings** | Endometrial and breast cancer risk, dementia risk; should not be used to reduce CV risk |

### Medication Safety Issues: Estradiol Oral

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Aldara | Avoid oral and topical patch |

### Drug Interactions: Estradiol Oral

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5, 1A2, P-glycoprotein inducers | Increased estradiol metabolism reduces estradiol effectiveness | Consider dose increases of estradiol |
| CYP3A4/5, 1A2 , P-glycoprotein inhibitors | Decreased estradiol metabolism increases risk of estradiol toxicity | Consider dose decreases of estradiol |

### Adverse Reactions: Estradiol Oral

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Weight change, nausea, vomiting, disturbance in mood, swelling of breast, depression | Heart disease, MI, DM, venous thromboembolism, anaphylaxis, cerebrovascular accident, pulmonary embolism, breast, endometrial or ovarian cancer |

**Efficacy Monitoring Parameters.** Improvement in menopause symptoms; improved BMD for postmenopausal osteoporosis.

**Toxicity Monitoring Parameters.** Annual physical examination including cervical cytology (Pap smear) and breast exam.

**Key Patient Counseling Points.** Report abnormal vaginal bleeding or signs/symptoms of a thromboembolic disorder. Do not smoke during therapy, as this increases the risk of thromboembolic events.

**Clinical Pearls.** Estrogens increase the risk of endometrial cancer; monitor for abnormal vaginal bleeding. Increased risks of MI, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis in postmenopausal women have been reported. An increased risk of developing dementia in women ≥65 y of age has also been reported. Estrogens, with or without progestins, should be prescribed at the lowest effective doses and for the shortest duration possible. Also available in a variety of topical and vaginal formulations.



https://kat.cr/user/Blink99/

# ESTRADIOL TRANSDERMAL PATCH: Vivelle-DOT, Estraderm, Various

**Class:** Estrogen

**Dosage Forms.** **Transdermal Patch:** 0.025 mg/d, 0.0375 mg/d, 0.05 mg/d, 0.075 mg/d, 0.1 mg/d

**Common FDA Label Indication, Dosing, and Titration.**

1. Abnormal vasomotor function or atrophic vagina or vulva (moderate-severe), menopause: 0.0375 mg/d patch applied to the skin twice weekly
2. Postmenopausal osteoporosis, prophylaxis: 0.025 mg/d patch applied to the skin twice weekly

**Off-Label Uses.** None

**MOA.** Estradiol (17β-estradiol; E2) is the most potent of the naturally occurring estrogens and the major estrogen secreted during the reproductive years. Estradiol and other estrogens produce characteristic effects on specific tissues (such as breast), cause proliferation of vaginal and uterine mucosa, increase calcium deposition in bone, and accelerate epiphyseal closure after initial growth stimulation.

Novartis 0.05 mg/day pictured

E

**Drug Characteristics: Estradiol Transdermal Patch**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F improved by bypassing first-pass metabolism |
| **Dose Adjustment Renal** | Not required | **Distribution** | Widely distributed; 98% protein bound |
| **Dialyzable** | Yes | **Metabolism** | Extensive hepatic; substrate of many CYP pathways, major substrate of CYP3A4/5, 1A2, P-glycoprotein |
| **Pregnancy Category** | X | **Elimination** | Renal with a half-life of 21 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to estradiol; history of thromboembolic disorders, breast cancer, any estrogen-dependent neoplasm, pregnancy | **Black Box Warnings** | Endometrial and breast cancer risk, dementia risk; should not be used to reduce CV risk |

**Medication Safety Issues: Estradiol Transdermal Patch**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Aldara | Avoid oral and topical patch |

### Drug Interactions: Estradiol Transdermal Patch

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5, 1A2, P-glycoprotein inducers | Increased estradiol metabolism reduces estradiol effectiveness | Consider dose increases of estradiol |
| CYP3A4/5, 1A2 , P-glycoprotein inhibitors | Decreased estradiol metabolism increases risk of estradiol toxicity | Consider dose decreases of estradiol |

### Adverse Reactions: Estradiol Transdermal Patch

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Edema, application site irritation | Weight change, nausea, vomiting, disturbance in mood, swelling of breast, depression | Heart disease, MI, DM, venous thromboembolism, anaphylaxis, cerebrovascular accident, pulmonary embolism, breast, endometrial or ovarian cancer |

**Efficacy Monitoring Parameters.** Improvement in menopause symptoms; improved BMD evaluation for postmenopausal osteoporosis.

**Toxicity Monitoring Parameters.** Annual physical examination including cervical cytology (Pap smear) and breast exam.

**Key Patient Counseling Points.** Report abnormal vaginal bleeding or signs/symptoms of a thromboembolic disorder. Do not smoke during therapy, as this increases the risk of thromboembolic events. Place patch on clean, dry skin, preferably on the lower abdomen, upper quadrant of the buttock, or outer aspect of the hip; do not apply to the breasts or waistline; rotate sites of application with 1 wk allowed between applications to a particular site.

**Clinical Pearls.** Estrogens increase the risk of endometrial cancer; monitor for abnormal vaginal bleeding. Increased risks of MI, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis in postmenopausal women have been reported. An increased risk of developing dementia in women ≥65 y of age has also been reported. Estrogens, with or without progestins, should be prescribed at the lowest effective doses and for the shortest duration possible. Also available in oral and vaginal formulations. Patch contains metal, remove prior to MRI. Do not cut patch.



https://kat.cr/user/Blink99/

# ESZOPICLONE: Lunesta, Various

Sunovian Pharmaceutical pictured

**Class:** Nonbarbiturate Hypnotic. C-IV

**Dosage Forms. Oral Tablet:** 1 mg, 2 mg, 3 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Insomnia: 2 mg po immediately before bedtime; dosing may be initiated at or titrated to 3 mg

**Off-Label Uses.** None

**MOA.** The exact mechanism of action of eszopiclone, a non-benzodiazepine hypnotic, is unknown. It is believed that eszopiclone binds to or interacts allosterically at the GABA-receptor complex domain.

**Drug Characteristics: Eszopiclone**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Severe impairment, 1 mg po qhs, *max* 2 mg/d | **Absorption** | F = 75%, high-fat meal delays absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | 52-59% protein bound |
| **Dialyzable** | Unknown | **Metabolism** | Extensive hepatic; substrate of CYP3A4/5 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 75% with a half-life of 5-6 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to eszopiclone | **Black Box Warnings** | None |

**Medication Safety Issues: Eszopiclone**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Neulasta | Avoid chronic use (>90 d) |

**Drug Interactions: Eszopiclone**

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inducers | Increased eszopiclone metabolism reduces eszopiclone effectiveness | May require 3 mg dose |
| CYP3A4/5 inhibitors | Decreased eszopiclone metabolism increases risk of eszopiclone toxicity | Initial dose 1 mg, monitor for side effects |
| Opioids, benzodiazepines | Increased CNS or respiratory depression | Avoid concomitant use |

**Adverse Reactions: Eszopiclone**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Headache | Abnormal behavior or thinking, confusion, diarrhea, dizziness, nausea, rash, somnolence, taste disorder, vomiting, xerostomia | Anaphylaxis, angioedema |

**Efficacy Monitoring Parameters.** Improvement in sleep onset, duration, and quality.

**Toxicity Monitoring Parameters.** Excessive sedation, impaired coordination.

**Key Patient Counseling Points.** Instruct patient to take immediately before bedtime and to not take with heavy/high-fat meal. Severe anaphylactic/anaphylactoid reactions, some fatal, have been reported. Warn patient of the risk of "sleep-driving" and other complex behaviors (eg, preparing and eating food, making phone calls) when the patient is not fully awake. Risk is increased when drug is combined with alcohol or other CNS depressants. Patient should avoid activities requiring mental alertness or coordination until drug effects are realized. Patient should report insomnia that worsens or persists longer than 7-10 d. Advise patient to report abnormal thoughts or behavior (confusion, agitation, hallucinations, suicidal thoughts, new or worsening depression), memory loss, or anxiety. Instruct patient to take drug only when experiencing insomnia. This drug should not be taken on a regular schedule when insomnia is not present. Patient should not drink alcohol while taking this drug.

**Clinical Pearls.** Safety and efficacy not established in children. Elderly may be more susceptible; use a lower starting dose. Medication guide must be provided at dispensing.



https://kat.cr/user/Blink99/

# ETHINYL ESTRADIOL AND ETONOGESTREL RING: NuvaRing

**Class:** Contraceptive

**Dosage Forms.** **Vaginal Ring:** Releases ethinyl estradiol 15 mcg/d and etonogestrel 0.12 mg/d

**Common FDA Label Indication, Dosing, and Titration.**

1. Contraception: 1 ring inserted vaginally by patient and remaining continuously for 3 wk, then removed for 1 wk; a new ring is then inserted, regardless whether bleeding has or has not finished

**Off-Label Uses.**

1. Treatment of menorrhagia (dose same as for contraception)
2. Dysfunctional uterine bleeding (dose same as for contraception)

**MOA.** See Preface C Card: General Content Related to All Oral Contraceptives

**Drug Characteristics: Ethinyl Estradiol and Etonogestrel Ring**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 40% for ethinyl estradiol; F = 100% for etonogestrel |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 45 L/kg for ethinyl estradiol; Vd = 201-245 L for etonogestrel; highly protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic via CYP3A4/5 for both components |
| **Pregnancy Category** | X | **Elimination** | Renal elimination with a half-life of 24 h for ethinyl estradiol and 23-28 h for etonogestrel |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to ethinyl estradiol or progestin component; history of thromboembolic disorders, endometrial cancer, uncontrolled hypertension, pregnancy; smoking 15 or more cigarettes per day | **Black Box Warnings** | Smoking risk |

Schering-Plough pictured

E

**Drug Interactions and Adverse Reactions: Ethinyl Estradiol and Etonogestrel Ring.** See Preface C Card: **General Content Related to All Oral Contraceptives.**

**Efficacy Monitoring Parameters.** Lack of pregnancy.

**Toxicity Monitoring Parameters.** Annual physical examination including cervical cytology (Pap smear) and breast exam (in addition to monthly self-exam).

**Key Patient Counseling Points.** See Preface C Card: **General Content Related to All Oral Contraceptives** for drug-related counseling points. If the vaginal ring is inadvertently expelled or removed, it may be rinsed in cool to lukewarm water and reinserted as soon as possible, at the latest within 3 h. If the ring-free interval has been extended beyond 7 d or if the vaginal ring has been left in place for more than 4 wk, an additional form of contraception must be used until the vaginal ring has been used continuously for 7 d.

**Clinical Pearls.** Patients should not smoke during therapy, as this increases the risk of serious cardiovascular side effects.



https://kat.cr/user/Blink99/

# EXENATIDE: Byetta, Bydureon

**Class:** Glucagon-Like Peptide-1 Receptor Agonist

**Dosage Forms. Subcutaneous Solution for Injection:** 5 mcg/0.02 mL, 10 mcg/0.04 mL; **Subcutaneous Suspension for Injection:** 2 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Diabetes mellitus, Type 2: Immediate release, 5-10 mcg sq bid; Extended release, 2 mg sq weekly

**Off-Label Uses.** None

**MOA.** Exenatide is an incretin mimetic agent that mimics the enhancement of glucose-dependent insulin secretion and several other antihyperglycemic actions of incretins. Incretins enhance glucose-dependent insulin secretion and exhibit other antihyperglycemic actions following release into circulation from the gut.

Lilly pictured

E

## Drug Characteristics: Exenatide

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 65-76% after sq dose |
| **Dose Adjustment Renal** | CrCl 30-50 mL/min, dose 5 mcg and increase with caution; avoid if CrCl <30 mL/min | **Distribution** | Vd = 28.3 L after sq dose |
| **Dialyzable** | Unknown | **Metabolism** | Minimal |
| **Pregnancy Category** | C | **Elimination** | Renal elimination with a half-life of 2.4 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to exenatide | **Black Box Warnings** | Thyroid C-cell tumors (Bydureon) |

## Medication Safety Issues: Exenatide

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | No |

## Drug Interactions: Exenatide

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Warfarin | Increased risk of bleeding | Monitor INR and consider warfarin dose adjustments |

**Adverse Reactions: Exenatide**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Hypoglycemia, diarrhea, nausea | Diaphoresis, decreased appetite, GERD, antibody development, headache, asthenia | Pancreatitis, anaphylaxis, acute renal failure, worsening of preexisting renal disease |

**Efficacy Monitoring Parameters.** Preprandial blood glucose between 70 and 130 mg/dL; $HbA_{lc}$ <7%.

**Toxicity Monitoring Parameters.** Symptoms of hypoglycemia include nausea, sweating, and loss of consciousness; seek medical attention if severe GI upset, changes in urination, shortness of breath, or severe skin rash.

**Key Patient Counseling Points.** Immediate-release product is dispensed in a prefilled pen containing 60 doses. Use this medicine 1 h before eating. Store new, unused pens in the refrigerator in the original carton. After using the pen for the first time, store it in a closed container at room temperature. Remove the needle from the pen before storing the medicine. Throw the pen away after using it for 30 d, even if there is some medicine left in it. Monitor FPG in frequent intervals (2-4 times per day). Carry candy or some type of sugar with you at all times, especially if you are away from home, for episodes of hypoglycemia. Extended-release product is dispensed as powder with diluent in prefilled syringe. Patient instructions on weekly dose preparation and administration must be provided.

**Clinical Pearls.** Metformin is first-line therapy for type 2 diabetes. Exenatide may be added if $HbA_{lc}$ goals are not achieved with metformin alone. Many clinicians may try an oral sulfonylurea prior to exenatide. Dose- and duration-dependent thyroid C-cell tumors have developed in animal studies with Bydureon therapy; relevance in humans unknown. May increase risk of pancreatic duct metaplasia. Medication guide required with dispensing.



https://kat.cr/user/Blink99/

# EZETIMIBE: Zetia

**Class:** Antihyperlipidemic, Cholesterol Absorption Inhibitor

**Dosage Forms.** **Oral Tablet:** 10 mg

Merck 10 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Familial hypercholesterolemia-homozygous: with atorvastatin or simvastatin: Adults and Children >10 y of age, 10 mg po daily
2. Mixed hyperlipidemia: 10 mg po daily in combination with fenofibrate
3. Primary hypercholesterolemia: 10 mg po daily, alone or in combination with an HMG-CoA reductase inhibitor (statin)

**Off-Label Uses.** None

**MOA.** Ezetimibe localizes at the brush border of the small intestine and inhibits the absorption of cholesterol, leading to a decrease in the delivery of intestinal cholesterol to the liver. This causes a reduction of hepatic cholesterol stores and an increase in clearance of cholesterol from the blood; this distinct mechanism is complementary to that of statins and of fenofibrate.

E

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Avoid if moderate or severe hepatic dysfunction | **Absorption** | F variable, food has no effect on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 105 L; 90% protein bound |
| **Dialyzable** | Unknown | **Metabolism** | In intestine and liver, not via CYP450 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 11% with a half-life of 9-30 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to ezetimibe, gallbladder disease, severe hepatic dysfunction, concurrent use with a statin in a pregnant or nursing mother | **Black Box Warnings** | None |

**Medication Safety Issues: Ezetimibe**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Zestril | No |

### Drug Interactions: Ezetimibe

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Cholestyramine, colestipol | Decreased absorption of ezetimibe | Separate administration by 2-4 h |
| Fibrates | Increased risk of cholelithiasis | Avoid concurrent use or monitor for cholelithiasis |
| Warfarin | Increased risk of bleeding | Monitor INR and consider dose adjustments |

### Adverse Reactions: Ezetimibe

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Abdominal pain, constipation, diarrhea, headache, increased liver enzymes, myopathy, nausea | Rhabdomyolysis, cholelithiasis, hepatotoxicity, agranulocytosis, pancreatitis |

**Efficacy Monitoring Parameters.** Reduction in total cholesterol, LDL-cholesterol, and triglycerides levels; increase in HDL-cholesterol levels.

**Toxicity Monitoring Parameters.** Signs/symptoms of rhabdomyolysis (myalgias, dark urine, arthralgias, fatigue), yellowing of eyes or skin, severe abdominal pain, LFT and CBC, SCr.

**Key Patient Counseling Points.** Take with or without food and may be taken at the same time as a concurrent statin. In patients receiving a bile acid sequestrant concurrently, ezetimibe should be taken at least 2 h before or 4 h after the bile acid sequestrant is taken.

**Clinical Pearls.** Statins are the most effective lipid-altering agents for decreasing LDL cholesterol, and are considered drugs of choice. Ezetimibe has modest single agent activity and is used in combination with statin or in combination with fenofibrate. Ezetimibe is also available in fixed-dose combination with simvastatin.



https://kat.cr/user/Blink99/

# FAMOTIDINE: Pepcid, Various

**Class:** Histamine $H_2$ Antagonist

**Dosage Forms. Oral Tablet:** 10 mg, 20 mg, 40 mg; **Powder for Oral Suspension:** 40 mg/5 mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Duodenal ulcer, acute: Children >1 y, 0.5 mg/kg/d po hs, *max* of 40 mg/d; Adults, 20 mg po bid or 40 mg po daily hs
2. Duodenal ulcer, maintenance: Adults, 20 mg po daily hs
3. Gastroesophageal reflux disease: Children >1 y, 1 mg/kg/d po hs, *max* of 80 mg/d, duration based on response; Adults, 20-40 mg po bid × up to 12 wk
4. Gastric ulcer, acute: Children >1 y, 0.5 mg/kg/d po hs, *max* of 40 mg/d; Adults, 40 mg po daily hs
5. Indigestion (OTC): 10-20 mg po bid

Northstar Rx generic 20 mg pictured

**Off-Label Uses.** None

**MOA.** Famotidine is a competitive inhibitor of histamine $H_2$ receptors. The primary clinically important pharmacologic activity of famotidine is inhibition of gastric secretion. Both the acid concentration and the volume of gastric secretion are suppressed by famotidine, while changes in pepsin secretion are proportional to volume output.



**Drug Characteristics: Famotidine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 40-45%, no effect of food on absorption |
| **Dose Adjustment Renal** | Adults, CrCl <50 mL/min, reduce dose 50% or increase dosing interval to 36-48 h; children, CrCl 30-60 mL/min/1.73 $m^2$, administer 50% of dose; children, CrCl <30 mL/min/1.73 $m^2$, administer 25% of dose | **Distribution** | Vd = 1.3 L/kg; 10-20% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Minimal |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 60% with a half-life of 2.5-3.5 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to famotidine or other $H_2$ antagonists | **Black Box Warnings** | None |

### Medication Safety Issues: Famotidine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| Max Strength | No | No | No | FLUoxetine | No |

### Drug Interactions: Famotidine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Cefpodoxime | Decreased cefpodoxime absorption due to increase in gastric pH caused by $H_2$ antagonist | Choose alternative antibiotic |
| pH-dependent drugs | Lower gastric pH reduces absorption | Monitor pH-dependent drug and adjust dose as necessary |

### Adverse Reactions: Famotidine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Constipation, diarrhea, nausea, skin rash | | Stevens-Johnson syndrome, increased liver enzymes, seizure |

**Efficacy Monitoring Parameters.** Resolution of GI discomfort, resolution of ulcers shown on endoscopy.

**Toxicity Monitoring Parameters.** Severe blistering skin rash.

**Key Patient Counseling Points.** Take at bedtime. May take with food or antacids, if needed. Shake suspension well before use.

**Clinical Pearls.** Other PPI and $H_2$ antagonists available OTC; warn patients not to take multiple products concurrently to avoid additive risk of adverse effects. Injectable dosage form also available; when the intravenous route is used, treatment should be converted to oral route as soon as possible to avoid cost and risks associated with intravenous therapy.



https://kat.cr/user/Blink99/

# FEBUXOSTAT: Uloric

**Class:** Xanthine Oxidase Inhibitor

**Dosage Forms. Oral Tablet:** 40 mg, 80 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Hyperuricemia: 40 mg po daily, may titrate to 120 mg po daily

**Off-Label Uses.** None

**MOA.** Selectively inhibits xanthine oxidase, the enzyme responsible for converting xanthine to uric acid. Lowers uric acid and reduces gout

**Drug Characteristics: Febuxostat**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Use with caution if severe hepatic dysfunction | **Absorption** | F ≥49% |
| **Dose Adjustment Renal** | Use with caution if severe renal dysfunction | **Distribution** | 99% protein bound, Vd = 50L |
| **Dialyzable** | Unknown | **Metabolism** | Extensively metabolized by numerous enzymes, individual enzymes have little contribution to total metabolism |
| **Pregnancy Category** | C | **Elimination** | 50% renal elimination with a half-life of 5-8 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Concurrent azathioprine or mercaptopurine | **Black Box Warnings** | None |

**Medication Safety Issues: Febuxostat**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | No |

**Drug Interactions: Febuxostat**

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Substrates for xanthine oxidase (azathioprine, didanosine, mercaptopurine, theophylline) | Decreased metabolism of xanthine oxidase substrates and increased toxicity | Concurrent use of azathioprine and mercaptopurine is contraindicated; use other substrates with caution |

**Adverse Reactions: Febuxostat**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Rash, nausea, elevated LFTs, arthralgia | ECG abnormalities, hypersensitivity, stroke, mood changes |

**Efficacy Monitoring Parameters.** Reduction in uric acid levels to <6 mg/dL, decrease in gout attacks.

**Toxicity Monitoring Parameters.** Baseline and periodic LFTs.

**Key Patient Counseling Points.** Take without food. Weight loss and limiting alcohol consumption will reduce gout attacks and should be recommended to all patients. Seek medical attention for severe mood swings, rashes, or abnormal heartbeat.

**Clinical Pearls.** When compared to allopurinol 300 mg, febuxostat is more effective in lowering uric acid levels to <6 mg/dL; however, the drugs were equivalent in terms of preventing gout flares and patients receiving feboxostat were more likely to have elevated LFTs. Allopurinol remains the mainstay for prevention of gout flares and febuxostat is an alternative for patients unable to tolerate or without a satisfactory response to allopurinol. An increase in gout flares is typically seen when initiating agents such as febuxostat. Prophylactic therapy with NSAIDs at initiation of therapy for up to 6 mo may be beneficial to prevent gout flares.



https://kat.cr/user/Blink99/

# FELODIPINE: Plendil, Various

**Class:** Calcium Channel Blocker

**Dosage Forms. Oral Tablet, Extended Release:** 2.5 mg, 5 mg, 10 mg

**Common FDA Label Indication and Dosing.**

1. Hypertension: Children, 0.1-0.6 mg/kg/d po; Adults, 2.5-10 mg po daily

**Off-Label Uses.** None

**MOA.** Felodipine is a dihydropyridine calcium-channel-blocking drug with potent arterial and coronary vasodilating properties. A reflex increase in sympathetic tone (in response to vasodilation) counteracts the direct depressant effects on SA and AV nodal conduction. This renders felodipine ineffective in the treatment of supraventricular tachycardias.

Mutual Pharmaceutical generic pictured

## Drug Characteristics: Felodipine

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Liver failure, reduce dose to 2.5 mg po daily | **Absorption** | F = 13-20%, no food effect |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 10 L/kg, protein binding 99% |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic metabolism, CYP3A4/5 substrate; moderate CYP2C8 inhibitor |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 70% with a half-life of 26-33 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to felodipine | **Black Box Warnings** | None |

## Medication Safety Issues: Felodipine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Do not chew or crush SR tablet | No | Isordil, pindolol, Pletal, PriLOSEC, Prinivil | No |

### Drug Interactions: Felodipine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Amiodarone | Increased amiodarone concentrations and increased risk of bradycardia, heart block, sinus arrest | Avoid concurrent use in patients with sick sinus syndrome or AV block |
| Beta-blockers | Increased risk of hypotension, bradycardia | Avoid concurrent use or monitor BP and HR |
| Clopidogrel | Decreased antiplatelet activity of clopidogrel by felodipine | Avoid concurrent use |
| CYP3A4/5 inhibitors | Decreased felodipine metabolism and increased risk of felodipine toxicity | Avoid concurrent use |
| CYP3A4/5 inducers | Increased felodipine metabolism and decreased felodipine efficacy | Monitor BP and consider dose increases of felodipine |
| CYP2C8 substrates | Decreased metabolism and increased risk of substrate toxicity | Monitor and consider a decrease substrate dose |
| Fentanyl | Increased risk of hypotension | Avoid concurrent use with felodipine |

### Adverse Reactions: Felodipine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Peripheral edema | Abdominal pain, arthralgia, constipation, dizziness, fatigue, f ushing, headache, hypotension, hyperkalemia, impotence, myalgia, nausea, palpitations, pruritus, rash, tachycardia, urticaria | Hepatotoxicity, thrombocytopenia |

**Efficacy Monitoring Parameters.** Decreased BP, reduction in chest pain, decreased number of weekly angina attacks, reduction in use of prophylactic nitroglycerin to relieve chest pain, improvement in signs/symptoms of heart failure.

**Toxicity Monitoring Parameters.** Signs/symptoms of peripheral edema, increased heart rate, signs/symptoms of liver damage.

**Key Patient Counseling Points.** Report signs/symptoms of hypotension or exacerbation of angina with initial dosing and dose changes; report signs/symptoms of peripheral edema, fatigue, hypotension, or hepatic dysfunction. Do not drink alcohol while taking drug. Do not discontinue drug abruptly as this may cause rebound hypertension. This medicine may cause dizziness. Avoid driving, using machinery, or doing anything else that could be dangerous if not alert. Dizziness may be worse if too much water is lost from the body due to excessive sweating, diarrhea, or vomiting.

**Clinical Pearls.** Dose can be reduced by one-half if taken consistently with grapefruit juice and monitoring for efficacy (BP, angina frequency) occurs.



https://kat.cr/user/Blink99/

# FENOFIBRATE: Lofibra, Various

Global Pharmaceutical generic pictured

**Class:** Antihyperlipidemic

**Dosage Forms.** **Oral Tablet:** 35 mg, 40 mg, 48 mg, 54 mg, 105 mg, 145 mg, 160 mg; **Oral Capsule:** 30 mg, 43 mg, 50 mg, 67 mg, 130 mg, 134 mg, 150 mg, 200 mg; **Oral Capsule, Delayed Release:** 45 mg, 135 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Hypercholesterolemia, primary hypercholesterolemia, or mixed dyslipidemia (Frederickson type 2a, 2b): 160 mg po daily
2. Hypertriglyceridemia, Frederickson types 4 and 5 hyperlipidemia: 54-160 mg po daily

**Off-Label Uses.** None

**MOA.** Fibric acid derivatives activate peroxisome proliferator-activated receptor α (PPARα), which increases lipolysis and elimination of triglyceride-rich particles from plasma by activating lipoprotein lipase and reducing production of apoprotein C-III (an inhibitor of lipoprotein lipase activity). The resulting fall in triglycerides produces an alteration in the size and composition of LDL from small, dense particles to large buoyant particles. These larger particles have a greater affinity for cholesterol receptors and are catabolized rapidly.

**Drug Characteristics: Fenofibrate**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Avoid use in severe hepatic impairment | **Absorption** | F = 60%, minimal food effect |
| **Dose Adjustment Renal** | Avoid use in severe renal impairment | **Distribution** | Vd = 60 L; >99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Prodrug that undergoes rapid hydrolysis at the ester bond to fenofibric acid. Fenofibric acid is glucuronidated in the liver |
| **Pregnancy Category** | C | **Elimination** | Renal elimination 60-93%, with a half-life of 24 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity, gallbladder disease, severe renal or hepatic dysfunction, nursing mothers | **Black Box Warnings** | None |

### Medication Safety Issues: Fenofibrate

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Capsules | No | Fibricor, Tracleer | No |

### Drug Interactions: Fenofibrate

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Atorvastatin, HMG-CoA reductase inhibitors, colchicine | Increased risk of myopathy or rhabdomyolysis | Avoid concurrent use, or monitor for myopathy and consider dose reductions |
| Cholestyramine, colestipol | Decreased absorption of fenofibrate | Separate administration by 2 h |
| Ezetimibe | Increased ezetimibe concentrations and an increased risk of cholelithiasis | Avoid concurrent use or monitor for cholelithiasis |
| Glimeperide | Increased risk of hypoglycemia | Avoid concurrent use |
| Warfarin | Increased risk of bleeding | Monitor INR and consider dose adjustments |

### Adverse Reactions: Fenofibrate

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Hyperhomocysteinemia | Abdominal pain, constipation, diarrhea, headache, increased liver enzymes, myopathy, nausea, rash, thrombophlebitis | Rhabdomyolysis, cholelithiasis, hepatotoxicity, mood disorder, impotence, agranulocytosis, nephrotoxicity, pancreatitis |

**Efficacy Monitoring Parameters.** Reduction in total cholesterol, LDL-cholesterol, and triglycerides levels; increase in HDL-cholesterol levels.

**Toxicity Monitoring Parameters.** Signs/symptoms of rhabdomyolysis (myalgias, dark urine, arthralgias, fatigue), yellowing of eyes or skin, severe abdominal pain; monitor LFT, CBC at baseline, 12 wk after initiation of therapy, or dose increases; serum creatine kinase should be measured in patients experiencing muscle pain and in those receiving other drugs associated with myopathy.

**Key Patient Counseling Points.** Fenoglide tablets and Lipofen R capsules should be given with food; others can be taken without food. Take 1 h before or 4-6 h after a bile acid binding resin. Products are not interchangeable.

**Clinical Pearls.** The fibric acid derivatives (gemfibrozil, clofibrate, and fenofibrate) are recommended as alternatives to niacin in the treatment of types IIb, III, IV, and V hyperlipidemia. Gemfibrozil has less nephrotoxicity than other fibric acid derivatives. Clofibrate appears to have excess cardiovascular toxicity.



https://kat.cr/user/Blink99/

# FENTANYL TRANSDERMAL: Duragesic, Various

**Class:** Opioid Analgesic. C-II

**Dosage Forms. Transdermal Patch:** 12 mcg/h, 25 mcg/h, 50 mcg/h, 75 mcg/h, 100 mcg/h

**Common FDA Label Indication, Dosing, and Titration.**

1. Pain, chronic (moderate to severe), Adults and Children >2 y of age: opioid tolerant, which cannot be managed by other means in opioid-tolerant patients, transdermal fentanyl dosage based on the patient's current 24-h oral morphine requirement; replace patch q72h; may replace patch q48h in patients not achieving adequate analgesia

**Off-Label Uses.** None

**MOA.** Fentanyl is a phenylpiperidine opioid agonist with predominant effects on the mu opioid receptor and is about 50-100 times more potent as an analgesic than morphine.

Duragesic by Pricara 50 mcg/h pictured

**Drug Characteristics: Fentanyl Transdermal**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 92% with transdermal |
| **Dose Adjustment Renal** | CrCl <10 mL/min, reduce dose by 50% | **Distribution** | Vd = 6 L/kg; 80-85% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic metabolism, CYP3A4/5 substrate |
| **Pregnancy Category** | C | **Elimination** | 75% renal elimination, half-life of 20-24 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Acute or postoperative pain, bronchial asthma, hypersensitivity to fentanyl, mild or intermittent pain management, opioid nontolerant patients, paralytic ileus | **Black Box Warnings** | CYP3A4/5 inhibitors; respiratory depression; transdermal not for use post-op; fatalities in children; formulations not interchangeable; fever; care with disposal; REMS program |

**Medication Safety Issues: Fentanyl Transdermal**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| Suffix describes mcg/h of fentanyl delivered. Transdermal fentanyl patches should always be prescribed in mcg/h, not size | FentaNYL | No | Yes | Alfentanil, SUFentanil | No |

### Drug Interactions: Fentanyl Transdermal

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Barbiturates, benzodiazepines, centrally acting muscle relaxants, opioids, phenothiazines | Additive CNS depression | Monitor and consider dose adjustments |
| Beta-blockers and calcium channel blockers | Additive hypotension when combined with fentanyl anesthesia | Avoid concurrent use |
| Buprenorphine, opioid agonists/antagonists, opioid antagonists | Precipitation of withdrawal symptoms | Avoid concurrent use of opioid antagonists and opioid agonists |
| CYP3A4/5 inducers | Increased fentanyl metabolism decreases fentanyl efficacy | Consider dose increases of fentanyl |
| CYP3A4/5 strong/moderate inhibitors | Decreased fentanyl metabolism increases risk of fentanyl toxicity | Avoid concurrent use |
| MAOIs | Additive respiratory depression | Avoid concurrent use |

### Adverse Reactions: Fentanyl Transdermal

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Application site reactions, sweating, constipation, GI distress, confusion, headache, anxiety, urinary retention, upper respiratory tract infection, fatigue | Arrhythmias, chest pain, dyspnea, respiratory depression | Stevens-Johnson syndrome, physical dependence, tolerance |

**Efficacy Monitoring Parameters.** Relief of pain.

**Toxicity Monitoring Parameters.** Severe skin rash, excessive drowsiness, decreased breathing, severe constipation, chest pain, inability to urinate, constipation.

**Key Patient Counseling Points.** Use a stool softener and/or laxative for preventing constipation. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol and other CNS depressants. Apply to clean, dry skin. Skin breaks may increase absorption. Remove old patch when new patch applied. Febrile patients may have increased absorption. Monitor carefully.

**Clinical Pearls.** Use caution in elderly, appear more sensitive to the effects. Tolerance and physical dependence may occur with chronic use, avoid abrupt discontinuation. Significant addiction potential, care with storage and disposal. In an REMS program, provide medication guide. Substantial differences exist in the pharmacokinetic profile of fentanyl products. Do not convert patients on a mcg-per-mcg basis from one fentanyl product to another fentanyl product; the substitution of one fentanyl product for another fentanyl product may result in a fatal overdose. Do not cut patch. Contraindicated in opioid-naïve patients; use limited to opioid tolerant patients.



https://kat.cr/user/Blink99/

# FEXOFENADINE: Allegra, Various

**Class:** Antihistamine

**Dosage Forms.** **Oral Tablet**: 30 mg, 60 mg, 180 mg; **Oral Disintegrating Tablet:** 30 mg; **Oral Suspension:** 30 mg/5 mL

Teva generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Seasonal allergic rhinitis (OTC): Children 2-11 y of age, 30 mg po bid; Children ≥12 y of age and Adults, 60 mg po bid or 180 mg po daily
2. Idiopathic urticaria: Children 6 mo-2 y of age, 15 mg po bid; Children 2-11 y of age, 30 mg po bid; Children ≥12 y of age and Adults, 60 mg po bid or 180 mg po daily

**Off-Label Uses.**

1. Perennial allergic rhinitis: Children 2-11 y of age, 30 mg po bid; Children ≥12 y of age and Adults, 60 mg po bid or 180 mg po daily

**MOA.** Fexofenadine, the major active metabolite of terfenadine, is an antihistamine with selective peripheral $H_1$-receptor antagonist activity. Both enantiomers of fexofenadine displayed approximately equipotent antihistaminic effects.

F

**Drug Characteristics: Fexofenadine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Rapidly absorbed, bioavailability not established |
| **Dose Adjustment Renal** | Use with caution | **Distribution** | Vd = 5.4-5.8 L/kg |
| **Dialyzable** | Not dialyzable | **Metabolism** | Little hepatic or extrahepatic metabolism |
| **Pregnancy Category** | C | **Elimination** | Fecal elimination is 80% with a half-life of 14-18 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to fexofenadine | **Black Box Warnings** | None |

**Medication Safety Issues: Fexofenadine**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Do not split or chew disintegrating tablet | No | Viagra | No |

**Drug Interactions: Fexofenadine**

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CNS depressants (opioids, benzodiazepines, alcohol) | Possible increase in sedation effects | Use with caution, monitor for sedation |
| Antacids | Aluminum or magnesium containing products reduce the bioavailability of fexofenadine | Separate administration by 2 h |

**Adverse Reactions: Fexofenadine**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Headache | Sedation, dry mouth, fatigue, and nausea | Hypersensitivity, insomnia |

**Efficacy Monitoring Parameters.** Improvement in rhinitis or urticaria symptoms.

**Toxicity Monitoring Parameters.** Seek medical attention for signs of severe CNS toxicity.

**Key Patient Counseling Points.** Patients should avoid activities requiring mental alertness or coordination until drug effects are known, as drug may cause dizziness or sedative effects. Take the suspension with water only, shake well before use. The oral disintegrating tablet should be taken on an empty stomach and stored in the blister pack until used. Place on tongue and allow to dissolve, do not crush or chew. Can be swallowed with water but not with fruit juices.

**Clinical Pearls.** Product is available OTC in several additional dosage forms.



https://kat.cr/user/Blink99/

# FIDAXOMICIN: Dificid

**Class:** Macrolide Antibiotic

**Dosage Forms. Oral Tablet:** 200 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. *C. difficile* infection: 200 mg po bid × 10 d

**Off-Label Uses.** None

**MOA.** Fidaxomicin is an antibacterial agent that acts locally in the GI tract on *C. difficile* via inhibition of RNA polymerases.

Optimer 200 mg pictured

**Drug Characteristics: Fidaxomicin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Minimal oral bioavailability, no effect of food on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Not absorbed systemically |
| **Dialyzable** | Unknown | **Metabolism** | Not absorbed |
| **Pregnancy Category** | B | **Elimination** | Fecal >92% unchanged with half-life of 11.7 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | None | **Black Box Warnings** | None |

**Medication Safety Issues: Fidaxomicin**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | No |

**Drug Interactions: Fidaxomicin.** None known

**Adverse Reactions: Fidaxomicin**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Nausea | Abdominal pain, vomiting, anemia, neutropenia | Bowel obstruction, GI hemorrhage |

**Efficacy Monitoring Parameters.** Resolution of symptoms of *C. difficile* infection, including resolution of diarrhea, vomiting.

**Toxicity Monitoring Parameters.** Monitor for signs of bowel obstruction and blood in the stool.

**Key Patient Counseling Points.** May be given with or without food.

**Clinical Pearls.** Expensive alternative to oral vancomycin for management of *C. difficile*–associated diarrhea. Minimally absorbed; can not be used for systemic infections.



https://kat.cr/user/Blink99/

# FINASTERIDE: Proscar, Propecia, Various

**Class:** 5α-Reductase Inhibitor

**Dosage Forms. Oral Tablet:** 1 mg, 5 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Benign prostatic hyperplasia: 5 mg po daily
2. Male pattern alopecia: 1 mg po daily

**Off-Label Uses.**

1. Prostate cancer prevention: 5 mg po daily

**MOA.** Finasteride inhibits the conversion of testosterone to 5α-dihydrotestosterone (DHT) by 5α-reductase, isoform 2.

Northstar Rx generic 5 mg pictured

**Drug Characteristics: Finasteride**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 63%, minimal food effect |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 76 L; 90% protein bound |
| **Dialyzable** | Unknown | **Metabolism** | <20% hepatic, CYP3A4/5 substrate |
| **Pregnancy Category** | X | **Elimination** | Renal clearance is 40% with a half-life of 6 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to finasteride, pregnancy, children | **Black Box Warnings** | None |

**Medication Safety Issues: Finasteride**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | ProSom, Provera, PROzac | No |

**Drug Interactions: Finasteride.** None known

**Adverse Reactions: Finasteride**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Impotence, reduced libido | Gynecomastia, dizziness | Heart failure, angioedema, allergic skin reactions, male breast cancer |

**Efficacy Monitoring Parameters.** American Urologic Association (AUA) Symptom Score, decrease in residual urine volume, increased urine flow if using for BPH; increased hair growth if using for male pattern alopecia.

**Toxicity Monitoring Parameters.** Shortness of breath, swelling, breast pain, or mass.

**Key Patient Counseling Points.** For hair loss, you may need to take this medicine for 3 mo or longer before you see an effect. For an enlarged prostate, you may need to take this medicine for up to 6 mo to see the full effect. Women who are pregnant or may become pregnant should avoid touching or handling this medicine. This medicine can get into the body through the skin and may prevent development of genitalia in an unborn male baby. They should also avoid semen of a man taking finasteride.

**Clinical Pearls.** Not effective for the treatment of prostate cancer. Is effective in reducing the overall incidence of prostate cancer, although an increase in the incidence of high-grade prostate cancers has been observed. Draw baseline PSA before initiating therapy. Note that PSA will decrease by 50% with treatment, double PSA values when assessing for prostate cancer. Does not affect free PSA level. Hazardous agent: Use appropriate precautions for handling and disposal.



https://kat.cr/user/Blink99/

# FLUCONAZOLE: Diflucan, Various

**Class:** Imidazole Antifungal

**Dosage Forms.** **Powder for Oral Suspension:** 10 mg/mL, 40 mg/mL; **Oral Tablet:** 50 mg, 100 mg, 150 mg, 200 mg

Teva generic 100 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Candidal vulvovaginitis, uncomplicated: 150 mg po × 1
2. Candidal vulvovaginitis, complicated: 150 mg po q72h × 3 doses
3. Candidiasis: systemic: Adults, 400 mg po daily; Children ≥6 mo of age, 6-12 mg/kg/d po
4. Cryptococcal meningitis: Adults, 400-800 mg po daily × 8 wk, then 200 mg po daily × 6-12 mo; Children ≥6 mo of age, 12 mg/kg po on day 1, then 6 mg/kg/d (*max* 12 mg/kg/d) for 10-12 wk
5. Oropharyngeal candidiasis: Adults, 100-200 mg po daily × 7-14 d; Children ≥6 mo of age, 6 mg/kg po on day 1, then 3 mg/kg once daily for at least 2 wk

**Off-Label Uses.**

1. Onychomycosis due to dermatophyte: 200 mg po qwk × 3 mo (fingernails), × 6 mo (toenails)
2. Tinea: 200 mg po qwk × 3 doses

F

**MOA.** Fluconazole inhibits biosynthesis of ergosterol or other sterols, damaging the fungal cell wall membrane and altering its permeability.

**Drug Characteristics: Fluconazole**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 90% with no food effect |
| **Dose Adjustment Renal** | Not required for single-dose therapy; for repeated dose therapy, CrCl 21-50 mL/min, increase dosing interval to 48 h or decrease dose by 50%; CrCl <10 mL/min, extend dosing interval to 48 h and decrease dose by 50% | **Distribution** | Blister, CSF, nails, skin, saliva, sputum, vaginal tissue, urine |
| **Dialyzable** | 100% of dose is removed by hemodialysis | **Metabolism** | Minimal metabolism, but moderate inhibitor of CYP2C19, CYP3A4/5 and strong inhibitor of CYP2C9 |
| **Pregnancy Category** | C | **Elimination** | 80% of dose is eliminated renally unchanged, half-life of 30 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to f uconazole, concurrent ergot alkaloids, CYP3A4/5 substrates that prolong QT | **Black Box Warnings** | None |

### Medication Safety Issues: Fluconazole

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Flecainide, FLUoxetine, furosemide, itraconazole, voriconazole | No |

### Drug Interactions: Fluconazole

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Agents that prolong QT interval | Increased risk of QT prolongation | Avoid concurrent use; astemizole and cisapride are contraindicated |
| Atorvastatin, HMG-CoA reductase inhibitors | Increased risk of rhabdomyolysis | Monitor for signs and symptoms of myopathy or rhabdomyolysis |
| CYP2C19, CYP2C9, CYP3A4/5 substrates | Decreased metabolism of substrates and increased substrate toxicity | Avoid concurrent use if possible; monitor and consider dose reductions of substrates |
| Sulfonylureas | Increased risk of hypoglycemia | Avoid concurrent use; monitor and consider dose reductions |

### Adverse Reactions: Fluconazole

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Nausea | Stevens-Johnson syndrome, arrhythmias, adrenal suppression, agranulocytosis, seizures, elevated LFTs, hypokalemia |

**Efficacy Monitoring Parameters.** Resolution of signs and symptoms of infection.

**Toxicity Monitoring Parameters.** Severe skin irritation or rash, unusual bruising or bleeding, rapid heart beat, yellowing of the eyes or skin; monitor serum potassium.

**Key Patient Counseling Points.** Many medications, including OTC medications, interact with fluconazole. Do not take any new medications without consulting your doctor or pharmacist. If taking a weekly dose, take on same day and time each week.

**Clinical Pearls.** Oral and IV doses are interchangeable. Amphotericin is more effective than fluconazole in treating serious fungal infections; fluconazole is typically used as adjunctive therapy or maintenance therapy. In vaginal candidiasis, single-dose fluconazole is at least as effective as a 5-d course of oral ketoconazole or a 3-d course of intravaginal clotrimazole.



https://kat.cr/user/Blink99/

# FLUOCINONIDE TOPICAL: Lidex, Various

**Class:** Topical Corticosteroid

**Dosage Forms.** **Topical Cream:** 0.05%, 0.1%; **Topical Ointment:** 0.05%; **Topical Solution:** 0.05%; **Topical Gel:** 0.05%

**Common FDA Label Indication and Dosing.**

1. Skin disorders, corticosteroid responsive: Children ≥12 y of age and Adults, apply thin layer topically to affected area daily to qid for a *max* of 2 wk
2. Plaque psoriasis: Children ≥12 y of age and Adults, apply thin layer topically to affected area daily to qid for a *max* of 2-4 wk
3. Atopic dermatitis: Children ≥12 y of age and Adults, apply thin layer topically to affected area daily to qid for a *max* of 2 wk

**Off-Label Uses.**

1. Oral lichen planus: Apply thin layer topically bid with antimycotics

**MOA.** Fluocinonide is an anti-inflammatory, antipruritic, and vasoconstrictive corticosteroid. Corticosteroids are thought to act by the induction of phospholipase A2-inhibitory proteins, lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor, arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A2.

Teva generic 0.05% ointment pictured

F

**Drug Characteristics: Fluocinonide**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Minimal absorption unless covering large surface area or covering areas lacking skin integrity |
| **Dose Adjustment Renal** | Not required | **Distribution** | Not absorbed |
| **Dialyzable** | Unknown | **Metabolism** | Not absorbed |
| **Pregnancy Category** | C | **Elimination** | Not absorbed |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to f uocinonide or other corticosteroids | **Black Box Warnings** | None |

**Medication Safety Issues: Fluocinonide**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Lasix, Videx | No |

**Drug Interactions: Fluocinonide.** None known

**Adverse Reactions: Fluocinonide**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Dry skin, burning sensation, stinging, pruritus at site of administration; headache | HPA suppression has been reported when used with occlusive dressings over larger surface areas |

**Efficacy Monitoring Parameters.** Improvement in clinical signs of skin disorder (reduced inflammation, pruritus).

**Toxicity Monitoring Parameters.** Severe skin irritation or symptoms worsen after administration.

**Key Patient Counseling Points.** Apply thin layer to affected area of skin. Skin should be clean and intact at site of application. Avoid contact with eyes and do not ingest by mouth. Avoid occlusive dressings or tight-fitting clothes over site of administration.

**Clinical Pearls.** High-potency corticosteroid. Application to large surface areas, prolonged use, and use of occlusive dressings increases risk of systemic absorption and toxicity; pediatric patients are more susceptible to systemic absorption. Other corticosteroid-containing products are available OTC; warn patients not to take multiple products concurrently to avoid additive risk of adverse effects.



https://kat.cr/user/Blink99/

# FLUOXETINE: Prozac, Various

**Class:** SSRI Antidepressant

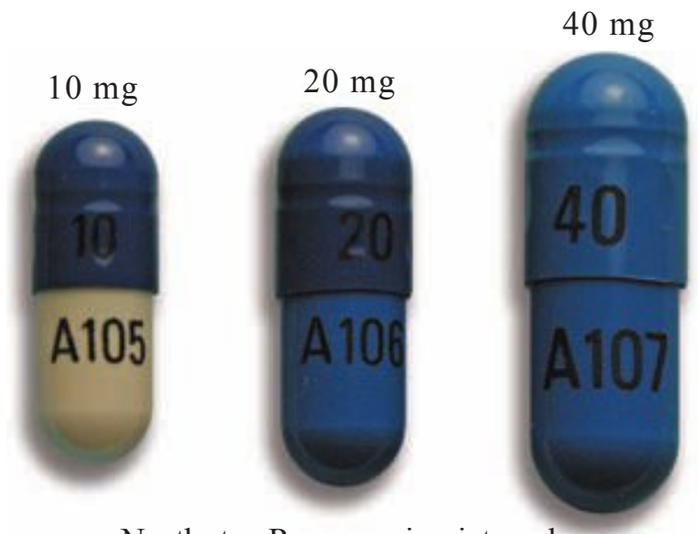
**Dosage Forms.** **Oral Capsule:** 10 mg, 20 mg, 40 mg; **Oral Capsule, Delayed Release, Weekly:** 90 mg; **Oral Tablet:** 10 mg, 20 mg, 60 mg; **Oral Solution, Oral Syrup:** 20 mg/5 mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Depression: Adults and Children ≥8 y of age, 20 mg po daily; may titrate to 80 mg po daily
2. OCD: Adults, 20 mg po daily, may titrate to 80 mg po daily; Children ≥7 y of age, 10 mg po daily, may titrate to 30 mg po daily
3. Panic disorder: 10 mg po daily, may increase to 60 mg po daily
4. Premenstrual dysphoric disorder: 20 mg po daily or for 14 d prior to expected start of menses; may titrate to 80 mg po daily

**Off-Label Uses.**

1. Posttraumatic stress disorder: 20-80 mg po daily
2. Fibromyalgia: 20-80 mg po daily



Northstar Rx generic pictured

**MOA.** Fluoxetine is a bicyclic antidepressant that is a selective and potent inhibitor of presynaptic reuptake of serotonin (an SSRI).

## Drug Characteristics: Fluoxetine

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Use lower dose | **Absorption** | F = 100%; no effect of food on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 12-43 L/kg; 95% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | >90% hepatic, CYP2C9 and CYP2D6 substrate; strong CYP2D6 inhibitor, moderate 2C19 inhibitor |
| **Pregnancy Category** | C | **Elimination** | Renal elimination 60% with half-life of 4-6 d |
| **Lactation** | Avoid | **Pharmacogenetics** | Use caution in CYP2D6 poor metabolizers |
| **Contraindications** | Hypersensitivity; concomitant pimozide, thioridazine, or MAOIs | **Black Box Warnings** | Suicidality; approved in children >7 y |

## Medication Safety Issues: Fluoxetine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| PROzac Weekly | FLUoxetine, PROzac | ER capsule | No | Paxil, Prelone, PriLOSEC, Prograf, Proscar, ProSom | No |

### Drug Interactions: Fluoxetine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Antiplatelet drugs, NSAIDs | Increased risk of bleeding | Monitor for bleeding |
| Agents that prolong the QT interval | Increased risk of QT prolongation, torsades de pointes, cardiac arrest | Avoid concurrent use |
| CYP2C9 and CYP2D6 substrates | Decreased metabolism of substrates, increased substrate toxicity | Monitor for adverse effects; consider dose reductions. Avoid concurrent use if narrow therapeutic index medication |
| CYP2C9 inducers | Increased metabolism of fluoxetine and decreased fluoxetine efficacy | Monitor for efficacy and consider dose increases of fluoxetine |
| CYP2C9 and CYP2D6 inhibitors | Decreased metabolism of fluoxetine and increased risk of fluoxetine toxicity | Avoid concurrent use if strong inhibitor; for moderate inhibitors, monitor for fluoxetine toxicity and consider dose decreases of fluoxetine |
| Triptans, dextroamphetamine, tramadol, linezolid, MAOIs | Increased risk of serotonin syndrome | Monitor closely for symptoms of serotonin syndrome; linezolid, MAOIs contraindicated |

### Adverse Reactions: Fluoxetine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Diarrhea, headache, nausea, somnolence, tremor, xerostomia | Anxiety, asthenia, bleeding, diaphoresis, disorder of ejaculation, fatigue, insomnia, loss of appetite, rash, sexual dysfunction, weight gain | Prolonged QT interval, serotonin syndrome, suicidal thoughts, torsade de pointes |

**Efficacy Monitoring Parameters.** Improvement in symptoms of depression, panic disorder, OCD, premenstrual syndrome.

**Toxicity Monitoring Parameters.** Worsening of depression, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases; signs/symptoms of abnormal bleeding.

**Key Patient Counseling Points.** Take without meals and in the morning. Avoid activities requiring mental alertness or coordination until drug effects are realized. Symptomatic improvement may not be seen for several weeks. Report worsening depression, suicidal ideation, unusual changes in behavior, or unusual bleeding. Do not drink alcohol or use NSAIDs or aspirin while taking this drug.

**Clinical Pearls.** If intolerable withdrawal symptoms occur following a decrease in dose or therapy discontinuation, may need to resume the previous dose and taper at a more gradual rate. Must be dispensed with medication guide. Weekly dosage form with more pharmacokinetic variability than daily dosing. If stable on 20 mg daily, can be converted to 90 mg weekly dose, starting 7 d after the last 20 mg dose.



https://kat.cr/user/Blink99/

# FLUTICASONE NASAL INHALER: Flonase, Various

**Class:** Intranasal Adrenal Glucocorticosteroid

**Dosage Forms. Nasal Spray:** 27.5 mcg/actuation, 50 mcg/actuation

**Common FDA Label Indication, Dosing, and Titration.**

1. Allergic rhinitis: Children ≥4 y of age and Adults, 2 sprays/nostril daily or 1 spray/nostril bid; *max* of 2 sprays/nostril/d (200 mcg/d)
2. Nonallergic rhinitis: Children ≥4 y of age and Adults, 2 sprays/nostril daily or 1 spray/nostril bid; *max* of 2 sprays/nostril/d (200 mcg/d)

**Off-Label Uses.**

1. Adjunct to antibiotics in empiric treatment of acute bacterial rhinosinusitis: 1 spray/nostril bid

**MOA.** Fluticasone has anti-inflammatory, antipruritic, and vasoconstrictive properties. Corticosteroids are thought to act by the induction of phospholipase A2-inhibitory proteins, lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor, arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A2.

Apotex Corp generic 50 mcg pictured

F

**Drug Characteristics: Fluticasone Nasal Inhaler**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | <2% of dose absorbed systemically after nasal administration |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd approximately 4 L/kg after nasal administration |
| **Dialyzable** | Not dialyzable | **Metabolism** | Complete first-pass metabolism |
| **Pregnancy Category** | C | **Elimination** | Primarily fecal elimination with half-life (calculated from IV dose) of 5-7 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

**Medication Safety Issues: Fluticasone Nasal Inhaler**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Flovent | No |

### Drug Interactions: Fluticasone Nasal Inhaler

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inhibitors | Decreased f uticasone metabolism and increased risk of f uticasone toxicity | Monitor for toxicity; reduce dose of f uticasone if necessary |

### Adverse Reactions: Fluticasone Nasal Inhaler

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Nasal irritation and burning | Epistaxis | Severe hypersensitivity, glaucoma, pneumonia, secondary hypocortisolism; osteoporosis |

**Efficacy Monitoring Parameters.** Control of rhinitis signs and symptoms.

**Toxicity Monitoring Parameters.** While only small amounts of fluticasone reach systemic circulation, bone mineral density and growth and development in children should be monitored. Routine ophthalmologic examinations should be performed. Monitor for signs and symptoms of adrenal suppression or infection.

**Key Patient Counseling Points.** Advise patients on the proper administration technique for this product. Instruct patients to monitor for signs of toxicity, especially adrenal insufficiency.

**Clinical Pearls.** Oral inhalation and topical dosage forms of fluticasone also available for treatment of other allergic disorders. While oral antihistamines (either OTC or prescription) remain the mainstay for treatment of rhinitis, nasal steroids are a recommended option if symptoms are severe, unresolved with oral antihistamines, or if oral antihistamines cause undesirable adverse effects.



https://kat.cr/user/Blink99/

# FLUTICASONE ORAL INHALER: Flovent HFA

**Class:** Inhaled Adrenal Corticosteroid

**Dosage Forms.** **Metered Dose Inhaler**: 44 mcg/actuation, 110 mcg/actuation, 220 mcg/actuation

**Common FDA Label Indication, Dosing, and Titration.**

1. Asthma: Children 4-11 y of age, regardless of previous treatment, starting dose 88 mcg bid with *max* dose of 88 mcg bid; Children ≥12 y of age and Adults: Patients previously treated with inhaled bronchodilators alone, 88 mcg bid, titrate dose to response with maximum of 440 mcg bid; Patients previously treated with inhaled corticosteroids, starting dose 88-220 mcg bid; titrate dose to response with *max* of 440 mcg bid; Patients previously treated with oral corticosteroids, starting dose 440 mcg bid; titrate dose to response with *max* of 880 mcg bid

GlaxoSmithKline pictured

**Off-Label Uses.** None

**MOA.** Fluticasone is a synthetic trifluorinated corticosteroid with anti-inflammatory effects. It is a human glucocorticoid receptor agonist that inhibits multiple cell types and mediator production or secretion involved in asthma. Glucocorticosteroids are naturally occurring and synthetic adrenocortical steroids, cause varied metabolic effects, modify the body's immune responses to diverse stimuli, and are used primarily for their anti-inflammatory effects in disorders of many organ systems.



**Drug Characteristics: Fluticasone Oral Inhaler**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 18-30% after MDI administration |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd ~4 L/kg after oral inhalation |
| **Dialyzable** | Not dialyzable | **Metabolism** | Complete first-pass metabolism via CYP3A4/5 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is <5% with a half-life of 11-12 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity or severe allergy to milk proteins (included in the inhalation powder); should not be used for primary treatment of status asthmaticus or other acute episodes of asthma requiring intensive intervention | **Black Box Warnings** | None |

### Medication Safety Issues: Fluticasone Oral Inhaler

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| HFA | No | No | No | Flonase | No |

### Drug Interactions: Fluticasone Oral Inhaler

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inhibitors | Decreased fluticasone metabolism and increase risk of fluticasone toxicity | Monitor for toxicity; reduce dose of fluticasone if necessary |

### Adverse Reactions: Fluticasone Oral Inhaler

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Pharyngeal candidiasis | Epistaxis | Severe hypersensitivity, glaucoma, cataracts, pneumonia, secondary hypocortisolism; osteoporosis |

**Efficacy Monitoring Parameters.** Control of asthma symptoms, as measured by PFTs.

**Toxicity Monitoring Parameters.** While only small amounts of fluticasone reach systemic circulation, BMD and growth and development in children should be monitored. Routine ophthalmologic examinations should be performed. Monitor for signs and symptoms of adrenal suppression or infection (including oral candidiasis).

**Key Patient Counseling Points.** Proper administration technique for these inhaled products. Instruct on rinsing mouth with water after each use to prevent oral infections. Monitor for signs of toxicity, especially adrenal insufficiency, oral candidiasis, and worsening pulmonary function.

**Clinical Pearls.** Flovent Diskus product also available for the treatment of asthma; delivers fluticasone in powder form with dosing similar to the metered dose inhaler formulation. Intranasal and topical dosage forms of fluticasone also available for treatment of other allergic disorders.



https://kat.cr/user/Blink99/

# FLUTICASONE/SALMETEROL: Advair Diskus, Advair HFA

GlaxoSmithKline 250 mcg/50 mcg pictured

**Class:** Inhaled Corticosteroid and Long-Acting $\beta_2$-Adrenergic Agonist Combination

**Dosage Forms. Inhalation Disk:** 100/50 (fluticasone 0.1 mg plus salmeterol 0.05 mg/actuation), 250/50 (fluticasone 0.25 mg plus salmeterol 0.05 mg/actuation), 500/50 (fluticasone 0.5 mg plus salmeterol 0.05 mg/actuation); **Metered Dose Inhaler (MDI):** 45/21 (fluticasone 45 mcg plus salmeterol 21 mcg/actuation), 115/30.45 (fluticasone 115 mcg plus salmeterol 21 mcg/actuation), 230/21 (fluticasone 230 mcg plus salmeterol 21 mcg/actuation)

**Common FDA Label Indication, Dosing, and Titration.**

1. Asthma: 1 disk or 2 MDI puffs q12h, adjust dose to patient response
2. Chronic obstructive pulmonary disease (COPD): 1 disk q12h, adjust dose to patient response

**Off-Label Uses.** None

**MOA.** Fluticasone is a synthetic trifluorinated corticosteroid with anti-inflammatory effects. It is a human glucocorticoid receptor agonist that inhibits multiple cell types and mediator production or secretion involved in asthma and COPD. Salmeterol is a long-acting $\beta_2$-adrenergic agonist, stimulates intracellular adenyl cyclase in catalyzing the conversion of adenosine triphosphate (ATP) to cyclic-3′,5′-adenosine monophosphate (cyclic AMP). The increased cyclic AMP levels result in the relaxation of bronchial smooth muscle and inhibition of the release of mediators of instantaneous hypersensitivity from mast cells.

F

**Drug Characteristics: Fluticasone/Salmeterol**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | After inhalation, f uticasone F = 18% and salmeterol is undetectable |
| **Dose Adjustment Renal** | Not required | **Distribution** | Both f uticasone and salmeterol are largely (>90%) protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Fluticasone undergoes complete first-pass metabolism; salmeterol is extensively metabolized in the liver by CYP3A4/5 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is <5% for both components; f uticasone half-life after inhalation of 5-7 h, salmeterol half-life after oral administration of 5.5 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to any component of the product, including milk proteins (included in the inhalation powder); should not be used as primary treatment of status asthmaticus or acute episodes of asthma or COPD, posaconazole coadministration | **Black Box Warnings** | Increased asthma related deaths |

### Medication Safety Issues: Fluticasone/Salmeterol

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| HFA | No | No | No | Adcirca, Advicor | No |

### Drug Interactions: Fluticasone/Salmeterol

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inhibitors | Decreased fluticasone metabolism and increase risk of fluticasone toxicity | Monitor for toxicity; reduce dose of fluticasone if necessary |

### Adverse Reactions: Fluticasone/Salmeterol

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Headache, pharyngitis, upper respiratory infection, difficulty speaking | Nausea, oral candidiasis, musculoskeletal pain, throat irritation, bronchitis, dizziness | Atrial fibrillation, myocardial infarction, anaphylaxis, osteoporosis, bronchospasm, exacerbation of asthma, paradoxical bronchospasm |

**Efficacy Monitoring Parameters.** Control of asthma or COPD symptoms, as measured by PFTs.

**Toxicity Monitoring Parameters.** While only small amounts of fluticasone and almost no salmeterol reach systemic circulation, bone mineral density and growth and development in children should be monitored. Routine ophthalmologic examinations should be performed. Monitor for signs and symptoms of adrenal suppression or infection (including oral candidiasis).

**Key Patient Counseling Points.** Proper administration technique for these inhaled products; rinse mouth with water after each use to prevent oral infections. Monitor for signs of toxicity, especially adrenal insufficiency, oral candidiasis, and worsening pulmonary function.

**Clinical Pearls.** Long-acting $\beta_2$-agonists (LABAs), such as salmeterol, increase the risk of asthma-related deaths; fluticasone and salmeterol should only be used in patients not adequately controlled on a long-term asthma control medication (ie, inhaled corticosteroid) or whose disease severity requires initiation of 2 maintenance therapies. Once asthma control is achieved and maintained, discontinue fluticasone/salmeterol if possible without loss of asthma control and maintain the patient on a long-term asthma control medication. Medication guide required at dispensing.



https://kat.cr/user/Blink99/

# FOLIC ACID: Folacin-800, Various

**Class:** Essential B Vitamin

**Dosage Forms.** **Oral Tablet:** 0.4 mg, 0.8 mg, 1 mg; **Oral Capsule:** 0.8 mg, 5 mg, 20 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Folic acid deficiency: Adults, 0.4-1 mg po daily; Children, infants, 0.1 mg/d; Children age <4 y, up to 0.3 mg/d; Children ≥age 4 y of age, 0.4-1 mg/d
2. Pregnancy, prophylaxis: 0.4-1 mg po daily

Amneal generic 1 mg pictured

**Off-Label Uses.**

1. Prevention of neural tube defects: 4 mg po daily
2. Prevention of methotrexate toxicity: 5-27.5 mg po weekly

**MOA.** Folic acid is required for the conversion of deoxyuridylate to thymidylate, which is a rate-limiting step in DNA synthesis, which presents clinically as macrocytic anemia when red blood cells are unable to extrude their nucleus.

**Drug Characteristics: Folic Acid**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 76-93% |
| **Dose Adjustment Renal** | Not required | **Distribution** | Stored in the liver and most tissues |
| **Dialyzable** | Yes, hemodialysis | **Metabolism** | Metabolized in the liver to active metabolite, 5-methyltetrahydrofolate |
| **Pregnancy Category** | A | **Elimination** | Renal = 30% |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

**Medication Safety Issues: Folic Acid**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Folinic acid | No |

**Drug Interactions: Folic Acid**

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Barbiturates | Decreased folic-acid absorption; increased barbiturate metabolism and less efficacy | Monitor barbiturate efficacy |
| Phenytoin | Decreased folic-acid serum levels; decreased phenytoin effectiveness | Monitor for seizure control |

### Adverse Reactions: Folic Acid

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Loss of appetite | Confusion, irritation | Anaphylaxis |

**Efficacy Monitoring Parameters.** $B_{12}$ and folic acid levels, normalization of MCV, normalization of Hgb, resolution of symptoms of anemia (fatigue, shortness of breath). Absence of neural tube defects in newborns.

**Toxicity Monitoring Parameters.** Seek medical attention if severe shortness of breath, skin rash, or hives.

**Key Patient Counseling Points.** May require several weeks for maximum effect. Avoid alcohol as it inhibits the absorption of folic acid.

**Clinical Pearls.** Drugs that interfere with folate metabolism (methotrexate, hydroxyurea, pemetrexed) will cause an elevated MCV in the absence of vitamin B deficiency. Folic acid is given to women intending to become pregnant and in the early months of pregnancy to reduce the risk of neural tube defects and other birth defects (imperforate anus, cleft lip). Patients on pemetrexed receive folic acid to reduce pemetrexed toxicity. Enriched flour, bread, corn meal, pasta, rice, and other grain products have added folic acid to help decrease the risk of neural tube defects by increasing folic acid intake. Other foods that contain folic acid include dark green leafy vegetables, citrus fruits and juices, and lentils.

# FOSINOPRIL: Monopril, Various

**Class:** ACE-I, Antihypertensive

**Dosage Forms. Oral Tablet:** 10 mg, 20 mg, 40 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Heart failure: 5-10 mg po daily, may titrate to 40 mg po daily
2. Hypertension: Adults, 10 mg po daily, may titrate to 80 mg po daily; Children 6-16 y of age and weighing >50 kg, 5-10 mg po daily, may titrate to 40 mg po daily

**Off-Label Uses.** None

**MOA.** Fosinopril is a competitive ACE-I. It also reduces serum aldosterone, leading to decreased sodium retention, potentiates the vasodilator kallikrein–kinin system, and can alter prostanoid metabolism, inhibit the sympathetic nervous system, and inhibit the tissue renin–angiotensin system.

Sandoz generic 40 mg pictured

F

**Drug Characteristics: Fosinopril**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 36%, food decreases rate (not extent) of absorption |
| **Dose Adjustment Renal** | CrCl = 10-30 mL, 5 mg po daily; CrCl <10 mL/min, 2.5 mg daily | **Distribution** | 99% protein bound |
| **Dialyzable** | Removed by hemodialysis | **Metabolism** | Metabolized in liver to active metabolite (fosinoprilat) not via CYP450 |
| **Pregnancy Category** | C (1st trimester), D (2nd and 3rd trimesters) | **Elimination** | 50% renal elimination with a half-life of 12 h (fosinoprilat) |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity, history of ACEI-induced angioedema, and hereditary or idiopathic angioedema | **Black Box Warnings** | Pregnancy |

**Medication Safety Issues: Fosinopril**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | FLUoxetine, Fosamax, furosemide, lisinopril | No |

### Drug Interactions: Fosinopril

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Antacids | Binding and decreased absorption | Separate administration by 2 h |
| Potassium-sparing diuretics | Increased risk of hypotension, hyperkalemia | Avoid concurrent use or monitor BP and serum potassium levels |
| Angiotensin receptor blockers | Increased risk of hypotension, hyperkalemia, nephrotoxicity | Avoid concurrent use or monitor BP, SCr, and potassium levels |
| Potassium supplements | Increased risk of hyperkalemia and cardiac arrhythmias | Avoid concurrent use or monitor serum potassium levels |
| NSAIDs | Decreased antihypertensive effect of fosinopril, increased risk of nephrotoxicity | Avoid concurrent use or monitor BP and SCr levels |
| Aliskiren | Increased risk of hyperkalemia | Monitor serum potassium levels |
| Azathioprine | Increased risk of myelosuppression | Avoid concurrent use; monitor for anemia or leukopenia |
| Diuretics | Increased risk of postural hypotension due to hypovolemia | Monitor BP; rise from seated position slowly |

### Adverse Reactions: Fosinopril

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Dizziness | Diarrhea, dry cough, headache, hypotension, hyperkalemia, nausea, nephrotoxicity, rash, tachycardia, vomiting | Angioedema, birth defects, liver failure |

**Efficacy Monitoring Parameters.** Decreased BP, decrease in signs of heart failure.

**Toxicity Monitoring Parameters.** Signs/symptoms of angioedema (swelling of the face, eyes, lips, tongue, or throat), severe persistent cough, hypotension; monitor baseline and periodic electrolytes, SCr, BUN, urine protein.

**Key Patient Counseling Points.** Full effect may require 2-4 wk. Avoid pregnancy. Use potassium supplements or salt substitutes only under medical supervision. May cause dizziness that may worsen if dehydrated.

**Clinical Pearls.** Observe patients who are volume depleted for at least 2 h after taking the initial dose of fosinopril. Discontinue if renal deterioration occurs.

# FUROSEMIDE: Lasix, Various



**Class:** Loop Diuretic

**Dosage Forms. Oral Tablet:** 20 mg, 40 mg, 80 mg; **Oral Solution:** 8 mg/1 mL, 10 mg/1 mL

Ranbaxy generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Edema related to heart failure, renal failure: Adults, initial 20-80 mg po daily, may titrate to maintenance dose (*max* 600 mg/d); Premature neonates (<29 wk), 1-2 mg/kg/dose po daily, may titrate to 6 mg/kg/dose; Premature neonates (>29 wk), 1-2 mg/kg/dose po 1-2 times per day, may titrate to 6 mg/kg/dose; Neonates, 1-3 mg/kg po q8h as needed; Infants and Children, initial, 2 mg/kg/dose po, may titrate at intervals of 6-8 h to maintenance dose (*max* 6 mg/kg/dose)
2. Hypertension: Adults, 40 mg po BID, may titrate to patient response; Children, 0.5-2 mg/kg/dose po once or twice daily; Infants <6 mo of age, may require doses up to 3 mg/kg po daily in 2 divided doses; Infants <2 y of age, *max* dose 37.5 mg/d; Children 2-12 y of age, *max* dose 100 mg/d

**Off-Label Uses.** None

**MOA.** Furosemide is a loop diuretic that is actively secreted via the nonspecific organic acid transport system into the lumen of the thick ascending limb of Henle's loop, where it decreases sodium reabsorption by competing for the chloride site on the $Na^+$-$K^+$-$2Cl^-$ cotransporter.

**Drug Characteristics: Furosemide**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required, patients with hepatic failure may need higher doses to achieve diuresis | **Absorption** | F = 47-70%, food may lower Cmax and Tmax |
| **Dose Adjustment Renal** | Not required, patients with renal failure may need higher doses to achieve diuresis | **Distribution** | Protein binding 91-99% |
| **Dialyzable** | Not dialyzable | **Metabolism** | Minimal hepatic metabolism (10%) |
| **Pregnancy Category** | C | **Elimination** | Eliminated 60-90% unchanged in urine, 7-9% in feces, and 6-8% in bile, with a half-life of 30-120 min |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to furosemide; anuria | **Black Box Warnings** | Fluid and electrolyte loss |

**Medication Safety Issues: Furosemide**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Lanoxin, Lidex, Lomotil, Lovenox, Luvox | No |

### Drug Interactions: Furosemide

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| ACE-Is | Increased risk of postural hypotension (first dose) | Start with low dose of ACE-I and monitor BP |
| Aminoglycosides | Increased aminoglycoside serum concentrations, additive ototoxicity and/or nephrotoxicity | Avoid concomitant use; monitor SCr and hearing |
| Antidiabetic drugs | Decreased hypoglycemic effect | Monitor blood glucose levels |
| Antiarrhythmic agents, digoxin | Increased risk of ventricular arrhythmias (torsade de pointes) due to hypokalemia, hypomagnesemia | Monitor serum potassium and magnesium levels; supplement electrolytes |
| Bile acid resins | Decreased furosemide efficacy | Give cholestyramine 4 h after furosemide; monitor diuretic effect |
| Diuretics | Increased diuretic response to furosemide | Monitor serum electrolytes and SCr |
| Lithium | Increased lithium concentrations and risk of toxicity | Decrease lithium dose and monitor serum lithium levels |
| NSAIDs | Decreased antihypertensive and diuretic effect, increased risk of nephrotoxicity | Avoid concurrent use or monitor BP and SCr levels |

### Adverse Reactions: Furosemide

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Hyperuricemia | Asthenia, constipation, headache, hyperglycemia, hypocalcemia, hypokalemia, hypomagnesemia, muscle spasm, orthostatic hypotension, rash, vomiting | Nephrotoxicity, ototoxicity, thrombocytopenia, tinnitus |

**Efficacy Monitoring Parameters.** Decreased BP, increased urine output, reduction in edema, daily weights. For treating renal failure, increase in urine volume, CrCl, BUN, and electrolytes.

**Toxicity Monitoring Parameters.** Severe volume depletion can occur. Monitor serum and urine electrolytes, uric acid, and blood glucose at baseline and every 3-6 mo after therapy. Audiometric test (if ototoxicity suspected).

**Key Patient Counseling Points.** Avoid alcohol and NSAIDs. Increased risk of sun sensitivity; use sunscreen and avoid tanning. Avoid activities requiring coordination until drug effects are realized, as drug may cause dizziness, vertigo, or blurred vision. Report signs/symptoms of hypotension, decreased urine output, or ototoxicity; severe skin reactions. Eat high-potassium foods, as directed by health-care professional.

**Clinical Pearls.** Drug of first choice for edema.

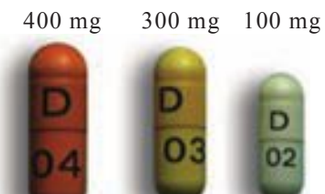
# GABAPENTIN: Neurontin, Gralise, Various

**Class:** Gamma Aminobutyric Acid, Anticonvulsant

**Dosage Forms.** **Oral Capsule:** 100 mg, 300 mg, 400 mg; **Oral Tablet:** 300 mg, 600 mg, 800 mg; **Oral Solution:** 250 mg/5 mL; **Oral Tablet, Extended Release:** 300 mg, 600 mg

Teva generic 800 mg pictured

Glenmark generic 600 mg pictured




Northstar Rx generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Partial seizure, adjunct: Immediate release, Adults and Children ≥12 y of age, initial, 300 mg po tid, may titrate to 1800 mg/d in 3 divided doses (*max* 2400-3600 mg/d); Children 3-11 y of age, initial, 10-15 mg/kg/d in 3 divided doses, maintenance (Children 3-4 y of age), may titrate over 3 d to 40 mg/kg/d in 3 divided doses, maintenance (Children 5-11 y of age), may titrate over 3 d to 25-35 mg/kg/d in 3 divided doses.
2. Postherpetic neuralgia: Immediate release, Adults, 300 mg po on day 1, 300 mg bid on day 2, 300 mg tid on day 3, may titrate dose to 1800 mg/d in 3 divided doses; extended release, 300 mg on day 1, 600 mg on day 2, 900 mg days 3-6, 1200 mg days 7-10, 1500 mg days 11-14, and 1800 mg po daily thereafter

**Off-Label Uses.**

1. Diabetic peripheral neuropathy: Adults, 900-3600 mg/d po
2. Restless leg syndrome: 300 mg po 2 h prior to bedtime
3. Neuropathic pain: Immediate release, 300 mg po daily, may titrate to 3600 mg po daily

**MOA.** Gabapentin is a cyclohexane compound that is structurally related to GABA; its mechanism of action is not known. Gabapentin does not interact with GABA receptors or alter the formation, release, degradation, or reuptake of GABA.



**Drug Characteristics: Gabapentin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 27-60%; food increases absorption |
| **Dose Adjustment Renal** | CrCl ≥60 mL/min, 900-3600 mg/d in 3 divided doses; CrCl 30-59 mL/min, 400-1400 mg/d in 2 divided doses; CrCl 15-29 mL/min, 200-700 mg/d given once daily | **Distribution** | Vd = 58 L; <3% protein bound |
| **Dialyzable** | Hemodialysis: 100-300 mg/d given once daily; give supplemental dose postdialysis | **Metabolism** | Not metabolized |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 76-81% (unchanged) and 10-23% in feces, with a half-life of 5-7 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

### Medication Safety Issues: Gabapentin

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Do not crush or chew ER tablet | No | Motrin, Neoral, Nitrofurantoin, Noroxin | No |

### Drug Interactions: Gabapentin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Antacids | Decreased gabapentin absorption | Separate administration by 2 h |

### Adverse Reactions: Gabapentin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Dizziness, somnolence | Ataxia, blurred vision, diarrhea, fatigue, hostile behavior, peripheral edema, nausea, nystagmus, vomiting, weight gain, xerostomia | Stevens-Johnson syndrome, suicidal thoughts |

**Efficacy Monitoring Parameters.** Reduction in seizure frequency or relief of pain associated with postherpetic neuralgia.

**Toxicity Monitoring Parameters.** Emergence or worsening of depression, suicidality, and/or any unusual behavioral or mood changes (anxiety, agitation, hostility, mania, and hypomania).

**Key Patient Counseling Points.** First dose on 1st day should be taken at bedtime. ER formulation should be taken with the evening meal. Patient should avoid activities requiring mental alertness or coordination until drug effects are realized, as drug may cause dizziness and somnolence. Report worsening depression, suicidal ideation, or unusual changes in behavior. Avoid sudden discontinuation of drug, as this may precipitate status epilepticus. Wait 2 h after antacid before taking gabapentin.

**Clinical Pearls.** Use in renally compromised patients <12 y of age has not been studied. Dosage interval should not exceed 12 h. Gabapentin dose reductions, discontinuation, or substitutions with alternative medications should be performed gradually over a min of 1 wk. Medication guide required at dispensing.

# GATIFLOXACIN OPHTHALMIC: Zymar, Zymaxid

**Class:** Fluoroquinolone Antibiotic

**Dosage Forms.** **Ophthalmic Solution:** 0.5%

**Common FDA Label Indication, Dosing, and Titration.**

1. Bacterial conjunctivitis: Adults and Children ≥1 y of age, 0.5% ophthalmic solution, 1 drop to affected eye(s) q2h while awake × 2 days, then qid while awake for 5 more d

**Off-Label Uses.** None

**MOA.** Gatifloxacin is a fluoroquinolone that inhibits bacterial topoisomerase II and IV. It is highly active against aerobic, gram-negative bacilli, especially Enterobacteriaceae. It has poor activity against streptococci and anaerobes.

**Drug Characteristics: Gatifloxacin Ophthalmic**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | After ocular instillation, serum concentrations are undetectable |
| **Dose Adjustment Renal** | Not required | **Distribution** | Not absorbed |
| **Dialyzable** | Not dialyzable | **Metabolism** | Not absorbed |
| **Pregnancy Category** | C | **Elimination** | Not absorbed |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to gatif oxacin or other quinolones | **Black Box Warnings** | None |

Allergan 0.3% solution pictured

**Medication Safety Issues: Gatifloxacin Ophthalmic**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | No |

**Drug Interactions: Gatifloxacin Ophthalmic.** None known

**Adverse Reactions: Gatifloxacin Ophthalmic**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Conjunctivitis, dry eyes, eye pain, subconjunctival hemorrhage, tearing and burning of the eyes, decreased visual acuity | Conjunctival hemorrhage |

**Efficacy Monitoring Parameters.** Resolution of signs and symptoms of eye infection.

**Toxicity Monitoring Parameters.** Severe eye pain, itching, redness, or burning.

**Key Patient Counseling Points.** Complete full course of therapy. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner. Wash hands with soap and water before and after use. Lie down or tilt your head back. With your index finger, pull down the lower lid of your eye to form a pocket. Hold the dropper close to your eye, but not touching, with the other hand. Drop the correct number of drops into the pocket made between your lower lid and eyeball. Gently close your eyes. Place your index finger over the inner corner of your eye for 1 min. Do not rinse or wipe the dropper or allow it to touch anything, including your eye.

**Clinical Pearls.** Bacterial conjunctivitis is very contagious and spread by direct contact.

# GEMFIBROZIL: Lopid, Various

**Class:** Antihyperlipidemic

**Dosage Forms. Oral Tablet:** 600 mg

Teva generic 600 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Coronary arteriosclerosis; prophylaxis-familial combined hyperlipidemia: 600 mg po bid
2. Familial type V hyperlipoproteinemia-Fredrickson type IV hyperlipoproteinemia: 600 mg po bid

**Off-Label Uses.** None

**MOA.** Fibric acid derivatives activate PPARα, which increases lipolysis and elimination of triglyceride-rich particles from plasma by activating lipoprotein lipase and reducing production of apoprotein C-III (an inhibitor of lipoprotein lipase activity). Activation of PPARα also induces an increase in the synthesis of apoproteins A-I and A-II and HDL-cholesterol.

## Drug Characteristics: Gemfibrozil

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Avoid in severe liver impairment | **Absorption** | Well absorbed, food reduces absorption, take on empty stomach |
| **Dose Adjustment Renal** | CrCl 10-50 mL/min, administer 75% of the dose; CrCl <10 mL/min, reduce dose by 50% | **Distribution** | Vd = 60 L; 99% protein bound |
| **Dialyzable** | Unknown | **Metabolism** | <20% hepatic, CYP3A4/5 substrate. Inhibitor of CYP1A2 (moderate), CYP2C19 (strong), CYP2C8 (strong), CYP2C9 (strong) |
| **Pregnancy Category** | C | **Elimination** | Renal elimination 70%, with a half-life of 2 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to gemfibrozil, concurrent repaglinide or simvastatin, gallbladder disease, severe renal or hepatic dysfunction | **Black Box Warnings** | None |

## Medication Safety Issues: Gemfibrozil

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Levbid, Lipitor, Lodine | No |

### Drug Interactions: Gemf brozil

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Atorvastatin, HMG-CoA reductase inhibitors, colchicine, fibrates, niacin | Increased risk of myopathy or rhabdomyolysis | Avoid concurrent use, or monitor for myopathy and consider dose reductions |
| Cholestyramine, colestipol | Decreased absorption of gemfibrozil | Separate administration by 2 h |
| CYP1A2, CY2C19, CYP2C8, CYP2C9 substrates | Increased plasma concentrations of substrates via inhibition of CYPs by gemfibrozil | Avoid concurrent use if narrow therapeutic index, or monitor and consider dose reductions of substrate |
| CYP3A4/5 inhibitors | Decreased metabolism of gemfibrozil increases risk of gemfibrozil toxicity | Monitor for toxicity and consider dose reductions of gemfibrozil |
| CYP3A4/5 inducers | Increased metabolism of gemfibrozil reduces gemfibrozil efficacy | Monitor for efficacy and consider dose increases of gemfibrozil |
| Glyburide | Increased risk of hypoglycemia via competition for renal tubular secretion | Avoid concurrent use |

### Adverse Reactions: Gemf brozil

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Indigestion | Abdominal pain, constipation, diarrhea, headache, increased liver enzymes, myopathy, nausea, rash | Rhabdomyolysis, cholelithiasis, hepatotoxicity, mood disorder, impotence, agranulocytosis |

**Efficacy Monitoring Parameters.** Primary, reduction in triglyceride levels. Secondary, reduction in total cholesterol, LDL-cholesterol, increase in HDL-cholesterol levels. Monitor baseline and every 6 mo.

**Toxicity Monitoring Parameters.** Seek medical attention if signs/symptoms of rhabdomyolysis (myalgias, dark urine, arthralgias, fatigue), yellowing of eyes or skin, and severe abdominal pain. LFTs and complete blood counts should be performed at baseline, 12 wk after initiation of therapy or dose increases. Serum creatine kinase should be measured in patients experiencing muscle pain and in those receiving other drugs associated with myopathy.

**Key Patient Counseling Points.** Take 30 min before breakfast and dinner. Instruct patient to report signs/symptoms of rhabdomyolysis, jaundice (yellowing of skin or eyes), or renal failure.

**Clinical Pearls.** The fibric acid derivatives (gemfibrozil, clofibrate, and fenofibrate) are recommended as alternatives to niacin in the treatment of types IIb, III, IV, and V hyperlipidemia.

# GLIMEPIRIDE: Amaryl, Various

**Class:** Second-Generation Sulfonylurea, Antidiabetic

**Dosage Forms. Oral Tablet:** 1 mg, 2 mg, 4 mg

**Common FDA Label Indication, Dosing, and Titration.**

Diabetes mellitus, type 2: 1-2 mg po daily, may titrate by 1-2 mg every 1-2 wk to effect, *max* dose 8 mg po daily

**Off-Label Uses.** None

**MOA.** Sulfonylureas enhance insulin secretion from pancreatic β-cells and potentiate insulin action on several extrahepatic tissues. Long-term sulfonylureas increase peripheral utilization of glucose, suppress hepatic gluconeogenesis, and possibly increase the sensitivity and/or number of peripheral insulin receptors.

2 mg 4 mg

Teva generic pictured

## Drug Characteristics: Glimepiride

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Avoid use in patients with severe liver dysfunction | **Absorption** | F = 100%, food decreases absorption |
| **Dose Adjustment Renal** | Start with 1 mg po daily | **Distribution** | Vd = 8.8 L; >99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | >90% hepatic, CYP2C9 substrate |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 60% with a half-life of 5-9 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | G6PD |
| **Contraindications** | Hypersensitivity to sulfonylureas, diabetic ketoacidosis | **Black Box Warnings** | None |

## Medication Safety Issues: Glimepiride

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | Yes | GlipiZIDE | No |

### Drug Interactions: Glimepiride

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Beta-blockers | Altered glucose metabolism and increased risk of hypoglycemia. Symptoms of hypoglycemia masked | Avoid propranol; use others with caution and increased monitoring |
| CYP2C9 inducers | Increased glimepiride metabolism and decreased glimepiride efficacy | Monitor blood glucose and consider dose increases of sulfonylureas |
| CYP2C9 inhibitors | Decreased glimepiride metabolism and increased risk of glimepiride toxicity | Monitor blood glucose and consider dose decreases of sulfonylureas |
| Fluoroquinolones, NSAIDs, fenofibrate, SSRIs, somatostatin analogues | Altered glucose metabolism and increased risk of hypoglycemia and hyperglycemia | Avoid concurrent use if possible; monitor and consider dose adjustments |
| MAOIs | Stimulation of insulin secretion, hypoglycemic effects | Avoid concurrent use if possible; monitor and consider dose adjustments |
| Psyllium | Psyllium may delay absorption of glucose from meals, hypoglycemic effects | Avoid concurrent use if possible; monitor and consider dose adjustments |
| Sulfonamides | Increased risk of hypoglycemia | Monitor blood glucose and consider dose adjustments of sulfonylureas |

### Adverse Reactions: Glimepiride

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Hypoglycemia, nausea, headache, dizziness, asthenia | Cutaneous hypersensitivity, hemolytic anemia, hepatotoxicity, disulfiram reaction |

**Efficacy Monitoring Parameters.** Preprandial blood glucose between 70 and 130 mg/dL, $HbA_{1c}$ <7%.

**Toxicity Monitoring Parameters.** Symptoms of hypoglycemia include nausea, sweating, and loss of consciousness. Seek medical attention if yellowing of skin or eyes, severe skin rash, unusual bruising, or bleeding.

**Key Patient Counseling Points.** Monitor blood glucose in frequent intervals (2-4 times per day); if <70 mg/dL, eat candy or sugar and contact prescriber. Take with food or milk in the morning. Use a sunscreen and avoid sunlamps and tanning beds. Do not drink alcohol; may cause a disulfiram reaction.

**Clinical Pearls.** Metformin is first-line therapy for type 2 diabetes. A sulfonylurea may be added if $HbA_{1c}$ goals are not achieved with metformin alone. Not for use in children. Hemolytic anemia is most likely to occur in patients with G6PD deficiency.

# GLIPIZIDE: Glucotrol, Various

**Class:** Second-Generation Sulfonylurea, Antidiabetic

**Dosage Forms. Oral Tablet:** 5 mg, 10 mg; **Oral Tablet, Extended Release:** 2.5 mg, 5 mg, 10 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Diabetes mellitus: Immediate release, 5-10 mg po daily, may titrate to *max* of 40 mg daily, divide bid if doses >15 mg; extended release, 5-10 mg po daily, may titrate to *max* of 20 mg daily

**Off-Label Uses.** None

**MOA.** Sulfonylureas enhance insulin secretion from pancreatic β-cells and potentiate insulin action on several extrahepatic tissues. Long-term sulfonylureas increase peripheral utilization of glucose, suppress hepatic gluconeogenesis, and possibly increase the sensitivity and/or number of peripheral insulin receptors.

Sandoz generic
5 mg pictured

Watson generic
5 mg ER pictured

Greenstone generic
2.5 mg ER pictured

Sandoz generic
10 mg pictured

Watson generic
10 mg ER pictured

Greenstone generic
5 mg ER pictured

## Drug Characteristics: Glipizide

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Start with 2.5 mg po daily | **Absorption** | Immediate release and extended release: F = 100%, food delays absorption by 40 min |
| **Dose Adjustment Renal** | Start with 2.5 mg po daily | **Distribution** | Vd = 11 L; 99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | 80% hepatic, CYP2C9 substrate |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 70% with a half-life of 2-5 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | G6PD |
| **Contraindications** | Hypersensitivity to sulfonylureas, diabetic ketoacidosis, type 1 diabetes | **Black Box Warnings** | None |

## Medication Safety Issues: Glipizide

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| XL | GlipiZIDE | Do not crush XL form | Yes | Glimepiride, glyBURIDE | No |

## Drug Interactions: Glipizide

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Beta-blockers | Altered glucose metabolism and increased risk of hypoglycemia. Symptoms of hypoglycemia masked | Avoid propranol; use others with caution and increased monitoring |
| CYP2C9 inducers | Increased glipizide metabolism and decreased glipizide efficacy | Monitor blood glucose and consider dose increases of sulfonylureas |
| CYP2C9 inhibitors | Decreased glipizide metabolism and increased risk of glipizide toxicity | Monitor blood glucose and consider dose decreases of sulfonylureas |
| Fluoroquinolones, NSAIDs, fenofibrate, SSRIs, somatostatin analogues | Altered glucose metabolism and increased risk of hypoglycemia and hyperglycemia | Avoid concurrent use if possible; monitor and consider dose adjustments |
| MAOIs | Stimulation of insulin secretion, hypoglycemic effects | Avoid concurrent use if possible; monitor and consider dose adjustments |
| Psyllium | Psyllium may delay absorption of glucose from meals, glycemic effects | Avoid concurrent use if possible; monitor and consider dose adjustments |
| Sulfonamides | Increased risk of hypoglycemia | Monitor blood glucose and consider dose adjustments of sulfonylureas |

## Adverse Reactions: Glipizide

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Asthenia | Hypoglycemia, nausea, headache, tremors, constipation, diarrhea, dizziness, nervousness, tremor | Cutaneous hypersensitivity, hemolytic anemia, hepatotoxicity, disulfiram reaction |

**Efficacy Monitoring Parameters.** Preprandial blood glucose between 70 and 130 mg/dL, $HbA_{1c}$ <7%.

**Toxicity Monitoring Parameters.** Symptoms of hypoglycemia include nausea, sweating, and loss of consciousness. Seek medical attention if yellowing of skin or eyes, severe skin rash, unusual bruising, or bleeding.

**Key Patient Counseling Points.** Monitor blood glucose in frequent intervals (2-4 times per day); if <70 mg/dL, eat candy or sugar and contact prescriber. Use a sunscreen and avoid sunlamps and tanning beds. Do not drink alcohol; may cause a disulfiram reaction. Take 30 min before morning meal. Do not chew or crush extended-release formulation.

**Clinical Pearls.** Metformin is first-line therapy for type 2 diabetes. A sulfonylurea may be added if $HbA_{1c}$ goals are not achieved with metformin alone. Not for use in children. Hemolytic anemia is most likely to occur in patients with G6PD deficiency. Patients on insulin: when starting glipizide, reduce insulin dose by 50%, or discontinue if <20 units/d.

# HAEMOPHILUS INFLUENZAE, TYPE B, CONJUGATE: Hiberix, PedvaxHIB, ActHIB

**Class:** Vaccine

**Dosage Forms.** **Lyophilized Powder for Intramuscular Injection:** 0.5 mL after reconstitution; also available in combination with other pediatric vaccines

**Common FDA Label Indication, Dosing, and Titration.**

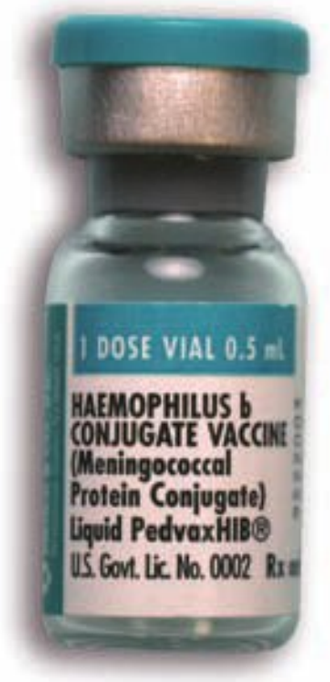
1. Prevention of invasive *H. influenzae* type B infection, Children: Dose schedule depends on product and timing of start of vaccination series. For ActHIB, dose at 2, 4, 6, and 12-15 mo of age as primary series. If PedvaxHIB used, doses at 2, 4, and 12-15 mo are used. If dosing begins later than 2 mo, adjusted dosing schedule used and number of doses changes. Hiberix can be used only for the last dose for children aged 12 mo to 4 y.

**Off-Label Uses.**

1. Prevention of invasive *H. influenzae* type B infection, Adults: 1 dose. May use any of the Hib conjugate vaccines for unvaccinated or partially vaccinated persons aged ≥5 y who have leukemia, malignant neoplasms, anatomic or functional asplenia (including sickle cell disease), HIV infection, or other immunocompromising conditions.

**Drug Characteristics:** H. influenzae **Type B, Conjugate**

| | | | |
|---|---|---|---|
| **Pregnancy Category** | C | **ADME** | None known |
| **Lactation** | Unlikely to be used in lactating woman; vaccines generally considered safe during lactation | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to Hib vaccine or a component of the vaccine | **Black Box Warnings** | None |




Merck pictured

**Medication Safety Issues:** H. influenzae **Type B, Conjugate**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | None | No |

**Drug Interactions:** H. influenzae **Type B, Conjugate**

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Moderate- to high-dose corticosteroids | Immunosuppression | Delay Hib vaccine administration until corticosteroid therapy has been discontinued if possible |
| Immunosuppressing agents | Immunosuppression | Delay Hib vaccine administration until immunosuppressive therapy has been discontinued if possible |

**Adverse Reactions:** H. influenzae **Type B, Conjugate**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Injection site reactions, including erythema and soreness. Headache, irritability, and somnolence | Fever, nausea, malaise | Thrombocytopenia, anaphylaxis, Guillain-Barré syndrome |

**Efficacy Monitoring Parameters.** Prevention of invasive *H. influenzae* type B infection.

**Toxicity Monitoring Parameters.** Monitor for syncope for 15 min after administration. Monitor for fever following administration.

**Key Patient Counseling Points.** Return to provider for each dose in the series.

**Clinical Pearls.** Clinicians can exchange among brands of vaccines for the primary series (with the exception of Hiberix). Seroconversion after 1 dose is 75-90%. Onset of action is 1-2 wk and immunity lasts 1.5 y.

# HEPATITIS A VACCINE, INACTIVATED: Havrix, Vaqta

**Class:** Vaccine

**Dosage Forms.** **Intramuscular Suspension:** Havrix, 720 ELISA units/0.5 mL, 1440 ELISA units/mL; Vaqta 25 units/0.5 mL, 50 units/1 mL; also available in combination with hepatitis B vaccine

**Common FDA Label Indication, Dosing, and Titration.**

1. Hepatitis A prophylaxis: Adults, Havrix 1440 ELISA units IM once, with a 2nd dose 6-12 mo later, or Vaqta 50 units IM once, with a 2nd dose 6-18 mo later; Children 12 mo to 18 y, Havrix 720 ELISA units IM once, with a 2nd dose 6-12 mo later, or Vaqta 25 units IM once, with a booster dose 6-18 mo later

**Off-Label Uses.**

1. Hepatitis A postexposure prophylaxis for individuals aged 1-40 y: Same regimen as for preexposure prophylaxis; vaccine series should be started within 2 wk of exposure

**Drug Characteristics: Hepatitis A Vaccine, Inactivated**

| | | | |
|---|---|---|---|
| **Pregnancy Category** | C | **ADME** | None known |
| **Lactation** | Infant risk is minimal | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to hepatitis A vaccine or a component of the vaccine | **Black Box Warnings** | None |

GlaxoSmithKline pictured

**Medication Safety Issues: Hepatitis A Vaccine, Inactivated**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | None | No |

**Drug Interactions: Hepatitis A Vaccine, Inactivated**

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Moderate- to high-dose corticosteroids | Immunosuppression | Delay hepatitis A vaccine administration until corticosteroid therapy has been discontinued if possible |
| Immunosuppressing agents | Immunosuppression | Delay hepatitis A vaccine administration until immunosuppressive therapy has been discontinued if possible |

### Adverse Reactions: Hepatitis A Vaccine, Inactivated

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Injection site reactions, including erythema and soreness. Headache, irritability, and somnolence | Fever, nausea, malaise | Thrombocytopenia, anaphylaxis, Guillain-Barré syndrome |

**Efficacy Monitoring Parameters.** Prevention of hepatitis A infection; although antibody concentrations might be measured, routine measurement for vaccine response is not recommended.

**Toxicity Monitoring Parameters.** Monitor for syncope, fever, or anaphylactic hypersensitivity reaction after administration. LFTs for adults at risk for liver failure.

**Key Patient Counseling Points.** Return to provider for booster dose in 6-12 mo or 6-18 mo after 1st dose (depending on product initially used).

**Clinical Pearls.** Not indicated for children <12 mo of age. The vaccines are interchangeable, so 2nd dose can be administered with the other brand of vaccine. Administer 2 wk prior to exposure (travel or international adoption of child). Vaccination recommended for all children ≥12 mo of age, and adults at risk for hepatitis A infection, including homosexual men, IV drug users, patients with chronic liver disease, international travelers, and those in close contact with those from endemic areas (Africa, India, etc). Hepatitis A transmits via oral/fecal route. After vaccination, 94-100% seroconversion within 1 mo.

# HEPATITIS B VACCINE, RECOMBINANT: Engerix-B, Recombivax HB

**Class:** Vaccine

**Dosage Forms.** **Suspension for Intramuscular Injection:** Engerix 10 mcg/0.5 mL, 20 mcg/1 mL; Recombivax 5 mcg/0.5 mL, 10 mcg/1 mL, 40 mcg/1 mL; also available in combination with hepatitis A vaccine and in combination products with other pediatric vaccines

**Common FDA Label Indication, Dosing, and Titration.**

1. Prevention of hepatitis B infection: Adults ≥20 y of age, Engerix 20 mcg IM or Recombivax 10 mcg IM given once, with 2 additional doses given 1 and 5 mo later; Children, Engerix 10 mcg IM or Recombivax 5 mcg IM given once, with 2 additional doses given 1 and 5 mo later; Patients undergoing hemodialysis, 40 mcg IM given once, with 2 additional doses given 1 and 5 mo later; several alternative regimens approved for adults and children of varying ages

**Off-Label Uses.** None

GlaxoSmithKline pictured

Merck pictured

**Drug Characteristics: Hepatitis B Vaccine, Recombinant**

| | | | |
|---|---|---|---|
| **Pregnancy Category** | C | **ADME** | None known |
| **Lactation** | Infant risk is minimal | **Pharmacogenetics** | Not clinically relevant |
| **Contraindications** | Hypersensitivity to hepatitis B vaccine or a component of the vaccine, including yeast | **Black Box Warnings** | None |

**Medication Safety Issues: Hepatitis B Vaccine, Recombinant**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| Engerix-B, Recombivax HB | No | No | No | Adult and pediatric formulations of Engerix-B | No |

**Drug Interactions:** **Hepatitis B Vaccine, Recombinant.** None

**Adverse Reactions: Hepatitis B Vaccine, Recombinant**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Injection site reactions, including erythema and soreness | Fever | Anaphylaxis, pancytopenia |

**Efficacy Monitoring Parameters.** Prevention of hepatitis B infection; measurement of antibody to the surface antigen (anti-HBs) 1-2 mo after dose 3 is recommended for individuals at risk for vaccine nonresponse and is required for those at occupational risk for hepatitis B exposure.

**Toxicity Monitoring Parameters.** Monitor for syncope, fever, seizure-like activity, or anaphylactic hypersensitivity reaction after administration.

**Key Patient Counseling Points.** Return to provider for all doses in the series.

**Clinical Pearls.** The brands of vaccines are considered interchangeable for the series. Use a needle of appropriate length to ensure intramuscular administration. Recommended for all infants, adolescents, health-care personnel, patients with renal failure, individuals with hepatitis C, residents and staff of psychiatric institutions, household and contacts of individuals with chronic hepatitis B, those with frequent exposure to blood products, international travelers, those at increased risk due to sexual practices, prisoners, and injection drug users. Lifetime immunity achieved in those with initial response.

# HUMAN PAPILLOMAVIRUS VACCINE: Cervarix, Gardasil

**Class:** Vaccine

**Dosage Forms.** **Intramuscular Suspension**: Cervarix HPV (bivalent) 16 L1 protein 20 mcg/0.5 mL and HPV 18 L1 protein 20 mcg/0.5 mL; Gardasil HPV (quadrivalent) 6 L1 protein 20 mcg/0.5 mL, HPV 11 L1 protein 40 mcg/0.5 mL, HPV 16 L1 protein 40 mcg/0.5 mL, and HPV 18 L1 protein 20 mcg/0.5 mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Human papillomavirus bivalent vaccine (HPV2, Cervarix, types 16 and 18): Prevention of cervical cancer and precancerous lesions in females aged 10-25 y, 3 dose series at 0, 1, and 6 mo
2. Human papillomavirus quadrivalent vaccine (HPV4, Gardasil, types 6, 11, 16, and 18): Prevention of cancer and precancerous lesions of the cervix, vulva, vagina, and anus and genital warts in individuals aged 9-26 y, 3 dose series at 0, 2, and 6 mo
3. Routine immunization of females is recommended at age 11-12 y with either vaccine preparation. Catch-up immunization is recommended for females aged 13-26 y
4. Routine immunization of males is recommended at age 11-12 y with HPV4 (Gardasil). Catch-up immunization is recommended for males aged 13-21 y. HPV4 (Gardasil) is recommended for men who have sex with men aged 22-26 y

**Off-Label Uses.** None

Merck pictured

**Drug Characteristics: Human Papillomavirus Vaccine**

| | | | |
|---|---|---|---|
| **Pregnancy Category** | B; recommend completing the series after pregnancy completion | **ADME** | None known |
| **Lactation** | Caution advised; weigh risk and benefit | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to HPV vaccine or a component of the vaccine; Cervarix, yeast allergy; Gardasil, latex allergy | **Black Box Warnings** | None |

**Medication Safety Issues: Human Papillomavirus Vaccine**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Bivalent and quadrivalent products often confused | No |

### Drug Interactions: Human Papillomavirus Vaccine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Moderate- to high-dose corticosteroids | Immunosuppression | Delay vaccine administration until corticosteroid therapy has been discontinued if possible |
| Immunosuppressing agents | Immunosuppression | Delay vaccine administration until immunosuppressive therapy has been discontinued if possible |

### Adverse Reactions: Human Papillomavirus Vaccine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Injection site reactions, including erythema and soreness. Arthralgia, myalgia, headache, fever | Rash, GI symptoms | Anaphylaxis, Guillain-Barré syndrome |

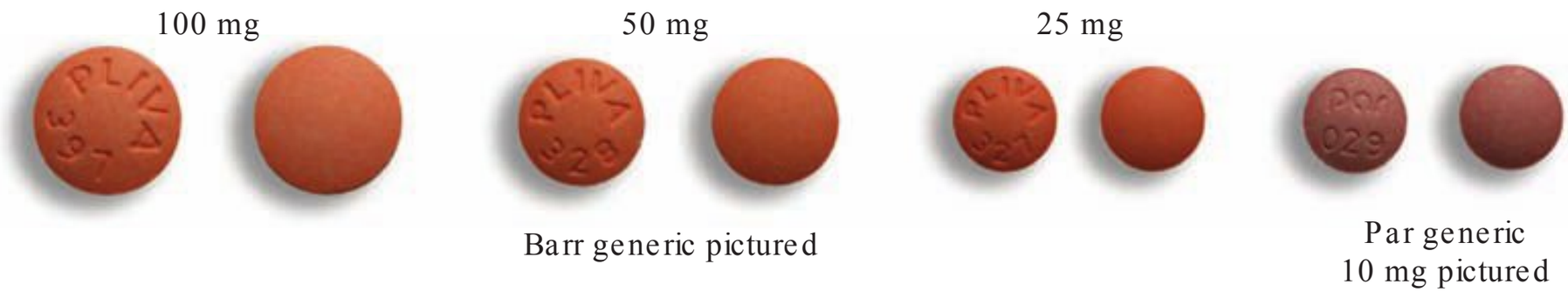
**Efficacy Monitoring Parameters.** Prevention of cervical cancer, other diseases caused by HPV.

**Toxicity Monitoring Parameters.** Syncope; continue routine cervical cancer screening; negative HPV test not required for vaccination.

**Key Patient Counseling Points.** Return to provider for all doses in the series.

**Clinical Pearls.** Complete the vaccine series with the same brand whenever possible. Syncope is common following vaccine administration. Observe immunized individual for 15 min following vaccine administration. Individuals already infected with HPV will not be protected by vaccine. Does not treat active HPV infection or other subtypes of HPV not included in vaccine. HPV types 16 and 18 cause 70% of cervical cancers; Cervarix only protects against cervical cancer. HPV types 6 and 11 cause 90% of genital warts; Gardasil protects against both cervical cancer and genital warts.

# HYDRALAZINE: Apresoline, Various




Barr generic pictured

Par generic
10 mg pictured

**Class:** Peripheral Vasodilator

**Dosage Forms.** **Oral Tablet:** 10 mg, 25 mg, 50 mg, 100 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Hypertension: Adults, initial, 10 mg po qid for 2-4 d, may titrate to 25 mg po qid for 3-5 d, then titrate to lowest effective dose at intervals of 1 wk (*max* 300 mg/d); Children, 0.75-1 mg/kg/d po in 2-4 divided doses; may titrate dose gradually over 3-4 wk (*max* dose 7.5 mg/kg or 200 mg/d)

**Off-Label Uses.**

1. Heart failure: Adults, 25-50 mg po daily in 3-4 divided doses in combination with isosorbide dinitrate (*max* hydralazine dose of 300 mg/d in divided doses)

**MOA.** Hydralazine is a vasodilator that reduces total peripheral resistance by direct action on vascular smooth muscle, with an effect greater on arterioles than on veins.



## Drug Characteristics: Hydralazine

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 38-50%, no effect of food on absorption |
| **Dose Adjustment Renal** | CrCl 10-50 mL/min, increase dosing interval to q8h; CrCl <10 mL/min, increase dosing interval to q8-16h | **Distribution** | 88-90% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic metabolism to 2 metabolites not via CYP |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 3-14% and 3-12% in feces, with a half-life of 3-5 h |
| **Lactation** | Compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to hydralazine; dissecting aortic aneurysm | **Black Box Warnings** | None |

### Medication Safety Issues: Hydralazine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | HydrALAZINE | No | No | HydrOXYzine | No |

### Drug Interactions: Hydralazine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| NSAIDs | Decreased antihypertensive effect of hydralazine | Avoid concurrent use or monitor BP |
| Furosemide | Increased diuretic response to furosemide | Monitor serum electrolytes, diuresis, CrCl |
| Metoprolol, propranolol | Increased beta-blocker toxicity (bradycardia, fatigue, shortness of breath) | If concurrent therapy required, take with food or switch to sustained-release beta-blocker; monitor BP |

### Adverse Reactions: Hydralazine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Anorexia, chest pain, diarrhea, dizziness, headache, hypotension, nasal congestion, palpitations, reflex tachycardia, vomiting | Agranulocytosis, hepatotoxicity, leucopenia, systemic lupus erythematosus |

**Efficacy Monitoring Parameters.** Decrease in systolic and diastolic BP, improvement in signs/symptoms of heart failure.

**Toxicity Monitoring Parameters.** Signs/symptoms of hypotension or liver damage. CBC and antinuclear antibody titers at baseline and periodically during prolonged treatment.

**Key Patient Counseling Points.** Patient should not drink alcohol while taking drug. Advise patient against sudden discontinuation of drug as this may cause rebound hypertension. This medicine may cause dizziness. Avoid driving, using machinery, or doing anything else that could be dangerous if not alert. Patient should report chest pain, palpitations, signs/symptoms of tachyarrhythmia, hypotension, agranulocytosis, systemic lupus erythematosus, or hepatotoxicity.

**Clinical Pearls.** Hydralazine is not a first-line therapy for hypertension. Hydralazine may cause drug-induced lupus erythematosus (DILE), and has a higher incidence compared to other drugs associated with DILE. Thiazide diuretics, calcium channel blockers, ACE-Is, and ARBs are preferred. Hydralazine may be beneficial in patients intolerant of ACE-Is or ARBs and when added ACE-Is or ARBs in African Americans.

# HYDROCHLOROTHIAZIDE: Esidrix, Various

**Class:** Thiazide Diuretic, Antihypertensive

**Dosage Forms.** **Oral Capsule:** 12.5 mg; **Oral Tablet:** 12.5 mg, 25 mg, 50 mg

Teva generic pictured

Watson generic 12.5 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Edema; adjunct: Adults, 25-100 mg po daily in single or divided doses; Children, 1-2 mg/kg po daily in single or divided doses; Infants <6 mo of age may require doses up to 3 mg/kg po daily in 2 divided doses; Infants <2 y of age, *max* dose 37.5 mg/d; Children 2-12 y of age, *max* dose 100 mg/d
2. Hypertension: Adult, initial, 12.5-25 mg po daily, may titrate to 50-100 mg po daily in single or divided doses; Children, 1-2 mg/kg po daily in single or divided doses; Infants <6 mo of age may require doses up to 3 mg/kg po daily in 2 divided doses, *max* dose 37.5 mg/d; Infants <2 y of age, *max* dose 37.5 mg/d; Children 2-12 y of age, *max* dose 100 mg/d

**Off-Label Uses.**

1. Hypercalciuria: Adults, 25 mg po bid; Children, 1-2 mg/kg/d po

**MOA.** Thiazides increase sodium and chloride excretion by interfering with their reabsorption in the cortical diluting segment of the nephron.

**Drug Characteristics: Hydrochlorothiazide**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 60-80%, reduced in patients with hepatic, renal, or cardiac (heart failure) disease |
| **Dose Adjustment Renal** | CrCl <25 mL/min, avoid | **Distribution** | Vd = 3.6-7.8 L/kg; 40% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Not metabolized |
| **Pregnancy Category** | B | **Elimination** | Eliminated 50-70% unchanged in urine, half-life 10-12 h (prolonged in patients with heart failure or renal disease) |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to hydrochlorothiazide or sulfonamide, concomitant dofetilide therapy, or anuric patients | **Black Box Warnings** | None |

**Medication Safety Issues: Hydrochlorothiazide**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | HCTZ is an error-prone abbreviation<br>Maxide, Micronase | No |

### Drug Interactions: Hydrochlorothiazide

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| ACE-Is | Increased risk of postural hypotension (1st dose) | Start with low dose of ACE-I and monitor BP |
| Antiarrhythmic agents, digoxin | Increased risk of ventricular arrhythmias (torsades de pointes) due to hypokalemia, hypomagnesemia | Monitor serum potassium and magnesium levels; supplement electrolyte if necessary |
| Antidiabetic medications | Decreased hypoglycemic effect | Monitor blood glucose levels |
| Calcium supplements | Increased risk of hypercalcemia | Avoid concurrent use or monitor serum calcium levels |
| Carbamazepine | Increased risk of hyponatremia | Avoid concurrent use or monitor serum sodium levels |
| NSAIDs | Decreased antihypertensive and diuretic effect, increased risk of nephrotoxicity | Avoid concurrent use or monitor BP and serum creatinine levels |
| Topiramate, lithium | Increased topiramate or lithium concentrations and increased risk of toxicity | Monitor levels and consider dose reduction |

### Adverse Reactions: Hydrochlorothiazide

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Hypotension, dizziness, headache | Constipation, hypercalcemia, hyperglycemia, hyperuricemia, hypokalemia, hypomagnesemia, hyponatremia, impotence, loss of appetite, nausea, photosensitivity, rash | Cardiac arrhythmias, hepatitis, pancreatitis, Stevens-Johnson syndrome |

**Efficacy Monitoring Parameters.** Decreased BP, reductions in edema.

**Toxicity Monitoring Parameters.** Decreased serum and urine electrolytes, decreased renal function, increased serum uric acid or blood glucose. Seek medical attention if skin rash, yellowing of eyes or skin, decreased urine output, or symptoms of gout occur.

**Key Patient Counseling Points.** May be taken with or without food. Take early in the day to avoid nocturia. May cause dizziness. Avoid driving, using machinery, or doing anything else that could be dangerous if not alert. Report signs/symptoms of hypotension. Eat high-potassium foods during therapy. Avoid alcohol and using NSAIDs.

**Clinical Pearls.** Full hypotensive effect may require 2-3 wk. Thiazides are first-line therapies for managing hypertension. Available as a component of many combination products with other antihypertensives.

# HYDROCODONE: Zohydro ER, Vicodin, Various

5 mg/325 mg | 7.5 mg/325 mg | 10 mg/325 mg | 10 mg/500 mg | 7.5 mg/500 mg

Mallinckrodt generic pictured

**Class:** Opioid Analgesic. C-II

**Dosage Forms.** **Oral Capsule, Extended Release (Hydrocodone Alone):** 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 50 mg; **Oral Tablet (With Acetaminophen):** Hydrocodone/Acetaminophen 2.5 mg/325 mg, Hydrocodone/Acetaminophen 5 mg/325 mg, Hydrocodone/Acetaminophen 7.5 mg/325 mg, Hydrocodone/Acetaminophen 10 mg/325 mg; **Oral Elixir, Oral Solution (With Acetaminophen):** Hydrocodone/Acetaminophen 7.5 mg/325 mg per 15 mL, Hydrocodone/Acetaminophen 10 mg/325 mg per 15 mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Pain, moderate to moderately severe: Adults: 10 mg q 12 h initially, may titrate to response

**Off-Label Uses.** None

**MOA.** Hydrocodone is an opioid analgesic and antitussive with unknown mechanism of action, but it is thought to be related to the presence of opiate receptors in the CNS.

## Drug Characteristics: Hydrocodone

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Severe: Start with 10mg dose | **Absorption** | Well absorbed, minimal food effect |
| **Dose Adjustment Renal** | Severe: Start with 10mg dose | **Distribution** | Unknown |
| **Dialyzable** | Not dialyzable | **Metabolism** | Pro-drug activated to hydromorphone by CYP2D6, deactivated by CYP3A4/5 |
| **Pregnancy Category** | C | **Elimination** | 26% renal, half-life of 8 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity, paralytic ileus, respiratory depression, severe asthma | **Black Box Warnings** | Addiction potential, respiratory depression, accidental exposure, neonatal opioid withdrawal, alcohol, CYP3A4/5 interactions |

## Medication Safety Issues: Hydrocodone

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| ER | HYDROcodone | Do not chew or crush ER formulation | Yes | HYDROmorphone, oxyCODONE | No |

### Drug Interactions: Hydrocodone

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Barbiturates, benzodiazepines, centrally acting muscle relaxants, opioids, phenothiazines | Additive CNS depression | Monitor and consider dose adjustments |
| Buprenorphine, opioid agonists/antagonists, opioid antagonists | Precipitation of withdrawal symptoms | Avoid concurrent use with opioids |
| CYP3A4/5 inducers | Increased hydrocodone metabolism decreases hydrocodone efficacy | Monitor and consider hydrocodone dose increase |
| CYP3A4/5 inhibitors | Decreased hydrocodone metabolism and increased hydrocodone toxicity | Avoid concurrent strong CYP3A4/5 inhibitors, uses moderate CYP3A4/5 inhibitors with caution and consider a hydrocodone dose decrease |
| CYP2D6 inhibitors | Decreased activation of hydrocodone to hydromorphone, decreased hydrocodone efficacy | Monitor and consider dose increases of hydrocodone |
| MAOIs | Additive respiratory depression | Avoid concurrent use |

### Adverse Reactions: Hydrocodone/Acetaminophen

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Constipation, GI distress, somnolence | Rash, respiratory depression, euphoria, pruritus | Stevens-Johnson syndrome, physical dependence, tolerance, respiratory depression |

**Efficacy Monitoring Parameters.** Relief of pain.

**Toxicity Monitoring Parameters.** Seek medical attention if severe skin rash, excessive drowsiness, decreased breathing, severe constipation, black tarry stools, or yellowing of eyes or skin.

**Key Patient Counseling Points.** Use a stool softener and/or laxative for preventing constipation with chronic use. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol and other CNS depressants.

**Clinical Pearls.** Use caution in elderly, appear more sensitive to the effect. Tolerance and physical dependence may occur with chronic use; avoid abrupt discontinuation. If using a combination product including acetaminophen, do not exceed *max* daily dose (4 g) of acetaminophen. The *max* dose of acetaminophen in combination products is 325 mg per dosage unit as of April 2014; higher strengths were common and are in the process of being withdrawn from the market. All hydrocodone-containing combination products are now schedule II, including Vicodin. Various other combinations available, including hydrocodone with chlorpheniramine cough liquid (Tussionex).

# HYDROCORTISONE TOPICAL: Various

2.5% cream

1% cream

Fougera generic pictured

**Class:** Topical Corticosteroid

**Dosage Forms.** **Rectal Cream:** 1%, 2.5%; **Topical Cream:** 0.5%, 1%, 2.5%; **Topical Lotion:** 1%, 2.5%; **Topical Ointment:** 0.5%, 1%, 2.5%

H

**Common FDA Label Indication, Dosing, and Titration.**

1. Skin disorders, corticosteroid responsive: Apply thin layer topically to affected area daily to bid

**Off-Label Uses.** None

**MOA.** Hydrocortisone has anti-inflammatory, antipruritic, and vasoconstrictive properties. Corticosteroids are thought to act by the induction of phospholipase A2-inhibitory proteins, lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor, arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A2.

**Drug Characteristics: Hydrocortisone Topical**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Minimal absorption unless covering large surface area or covering areas lacking skin integrity |
| **Dose Adjustment Renal** | Not required | **Distribution** | Not absorbed |

| | | | |
|---|---|---|---|
| **Dialyzable** | Not dialyzable | **Metabolism** | Not absorbed |
| **Pregnancy Category** | C | **Elimination** | Not absorbed |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to hydrocorti-sone or other corticosteroids | **Black Box Warnings** | None |

### Medication Safety Issues: Hydrocortisone Topical

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| HC, Maximum strength | No | No | No | HCT (occasional abbreviation for hydrocortisone) is an error-prone abbreviation, may be confused with HCTZ (hydrochlorothiazide) | No |

**Drug Interactions:** **Hydrocortisone Topical.** None known

### Adverse Reactions: Hydrocortisone Topical

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Dry skin, burning sensation, stinging, pruritus at site of administration; headache | HPA suppression has been reported when used with occlusive dressings, or when applied over larger surface areas |

**Efficacy Monitoring Parameters.** Improvement in clinical signs of skin disorder.

**Toxicity Monitoring Parameters.** Seek medical attention if severe skin irritation or symptoms worsen after administration.

**Key Patient Counseling Points.** Apply thin layer to affected area of skin. Skin should be clean and intact at site of application. Avoid contact with eyes and do not ingest by mouth. Avoid occlusive dressings or tight-fitting clothes over site of administration. Wash hands after application.

**Clinical Pearls.** Large number of dosage presentations (foams, gels, shampoos, etc), both by prescription and over the counter, are available. Oral and rectal formulations, administered for systemic action, also available and used for similar indications as other oral corticosteroids (eg, prednisone). Application to large surface areas, prolonged use, and occlusive dressings may increase risk of systemic absorption and toxicity; pediatric patients are more susceptible to systemic absorption.

# HYDROXYCHLOROQUINE: Plaquenil, Various

**Class:** Aminoquinoline

**Dosage Forms. Oral Tablet:** 200 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Lupus erythematosus: 400-800 mg po daily (may divide into 2 doses), then may reduce to maintenance dose of 200-400 mg po daily
2. Malaria, suppression: Adults, 400 mg po q week on the same day; Children, 5 mg base/kg (200 mg hydroxychloroquine sulfate = 155 mg hydroxychloroquine base); begin 2 wk prior to entering an endemic area and continue for 4 wk after leaving the endemic area
3. Rheumatoid arthritis: maintenance: 400-600 mg po daily, after 4-12 wk reduce dose to 200-400 mg for maintenance therapy

Goldline generic 200 mg pictured

**Off-Label Uses.** None

**MOA.** The mechanism of action of hydroxychloroquine is unknown. It is effective in treating *P. vivax, P. malariae*, and susceptible strains of *P. falciparum*.

**Drug Characteristics: Hydroxychloroquine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Severe hepatic dysfunction, avoid | **Absorption** | F = 74%, minimal food effect |
| **Dose Adjustment Renal** | Severe renal dysfunction, avoid | **Distribution** | Concentration in red blood cells is 5 times higher than plasma |
| **Dialyzable** | Not dialyzable | **Metabolism** | 40% and occurs by unknown enzymes |
| **Pregnancy Category** | D | **Elimination** | Renal elimination 16-25%, with a half-life of 40 d |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to hydroxychloroquine, retinal or visual field changes from prior hydroxychloroquine, long-term use in children | **Black Box Warnings** | Experienced physician |

### Medication Safety Issues: Hydroxychloroquine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Platinol | No |

### Drug Interactions: Hydroxychloroquine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Aurothioglucose | Increased risk of blood dyscrasias | Contraindicated |
| Digoxin | Increased digoxin levels | Avoid concurrent use or monitor digoxin levels |
| Fibrates | Increased risk of cholelithiasis | Avoid concurrent use or monitor for cholelithiasis |
| Metoprolol | Decreased metabolism and increased toxicity of metoprolol | Avoid concurrent use |

### Adverse Reactions: Hydroxychloroquine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Abdominal pain, constipation, diarrhea, headache, nausea, dizziness, visual disturbances, hyperpigmentation | Arrhythmias, cardiomyopathy, Stevens-Johnson syndrome, agranulocytosis, seizures, retinopathy, psychosis |

**Efficacy Monitoring Parameters.** Rheumatoid arthritis: decreased pain and improved range of motion. Lupus: decreased joint pain, decrease in butterfly rash, improved energy.

**Toxicity Monitoring Parameters.** Seek medical attention if heart palpitations, severe rash, unusual bruising or bleeding, or difficulty seeing or changes in visual fields. Baseline and periodic eye exams.

**Key Patient Counseling Points.** If taking weekly, take on same day each week. Take with food or milk.

**Clinical Pearls.** One tablet of 200 mg of hydroxychloroquine sulfate is equivalent to 155 mg base. If serious adverse effects or overdose occurs, ammonium chloride (8 g daily in divided doses for adults) may be administered 3-4 d a week for several months to increase the renal excretion of hydroxychloroquine.

# HYDROXYZINE: Atarax, Vistaril, Various

**Class:** Antihistamine

**Dosage Forms.** **Oral Tablet:** 10 mg, 25 mg, 50 mg; **Oral Capsule:** 25 mg, 50 mg, 100 mg; **Oral Syrup:** 10 mg/5 mL; **Oral Solution:** 10 mg/5 mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Anxiety: 50-100 mg po qid
2. Pruritus: 25 mg po tid-qid
3. Sedation: 50-100 mg po q4h prn

**Off-Label Uses.**

1. Seasonal allergic rhinitis: 10-25 mg po tid-qid

Northstar Rx generic pictured

**MOA.** Hydroxyzine hydrochloride is a rapid-acting agent with probable action of suppressing activity in key locations of the CNS's subcortical area. Primary skeletal muscle relaxation, bronchodilator activity, antiemetic effects, and antihistaminic and analgesic effects have been demonstrated experimentally and confirmed clinically.

**Drug Characteristics: Hydroxyzine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Patients with chronic liver failure receive a lower dose; administer lowest effective dose once daily only and increase carefully to avoid toxicity | **Absorption** | Rapidly absorbed after oral administration |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 16 L/kg |
| **Dialyzable** | Not dialyzable | **Metabolism** | Metabolized to cetirizine in the liver |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 70% with a half-life of 3-20 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to cetirizine or hydroxyzine | **Black Box Warnings** | None |

### Medication Safety Issues: Hydroxyzine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | HydrOXYzine | No | No | HydrALAZINE, hydroxyurea | Avoid. Highly anticholinergic. |

### Drug Interactions: Hydroxyzine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CNS depressants (opioids, benzodiazepines, alcohol) | Possible increase in sedation effects | Use concurrently with caution |

### Drug Interactions: Hydroxyzine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Sedation, headache, dry mouth, fatigue | |

**Efficacy Monitoring Parameters.** Improvement in symptoms for which administered (anxiety, pruritus, insomnia).

**Toxicity Monitoring Parameters.** Seek medical attention for signs of severe CNS toxicity.

**Key Patient Counseling Points.** Patients should avoid activities requiring mental alertness or coordination until drug effects are known, as drug may cause dizziness or sedative effects.

**Clinical Pearls.** Product is available OTC in several dosage forms. Injectable formulation available for use as an adjunct to pain medications and antiemetics for perioperative pain, nausea, and vomiting, and alone as a sedative.

# IBANDRONATE: Boniva, Various

**Class:** Bisphosphonate

**Dosage Forms. Oral Tablet:** 150 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Postmenopausal osteoporosis (Treatment): 150 mg po once monthly
2. Postmenopausal osteoporosis (Prophylaxis): 150 mg po once monthly

**Off-Label Uses.** None

**MOA.** Ibandronate binds to bone hydroxyapatite and, at the cellular level, inhibits osteoclast activity, thereby modulating bone metabolism.

**Drug Characteristics: Ibandronate**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F <1%, food impairs absorption; take 30-60 min prior to meal |
| **Dose Adjustment Renal** | CrCl <30 mL/min, avoid use | **Distribution** | Vd = 90 L; 85-99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Not metabolized |
| **Pregnancy Category** | C | **Elimination** | 50% renal elimination with a half-life of 37-157 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Esophageal abnormalities, which delay esophageal emptying, hypocalcemia, inability to sit or stand upright for at least 60 min | **Black Box Warnings** | None |

GlaxoSmithKline 150 mg pictured

### Medication Safety Issues: Ibandronate

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Do not chew, crush, or suck tablet | No | No | No |

### Drug Interactions: Ibandronate

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Aluminum, calcium-containing products | Decreased bisphosphonate absorption | Separate administration by 1-2 h |
| $H_2$-blockers and PPIs | Decreased bisphosphonate absorption | Separate administration by 1-2 h |

### Adverse Reactions: Ibandronate

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Indigestion, backache, respiratory tract infections | Hypertension, diarrhea, abdominal pain, headache, myalgia | Osteonecrosis of the jaw, esophageal cancer, esophageal ulcers, immune hypersensitivity, arrhythmia, bone fractures, severe muscle pain |

**Efficacy Monitoring Parameters.** Increased BMD. Decreased incidence of bone fractures.

**Toxicity Monitoring Parameters.** Baseline serum creatinine, calcium, phosphorous. Seek medical attention if severe skin rash, difficulty swallowing, swelling, tooth problems, or severe pain.

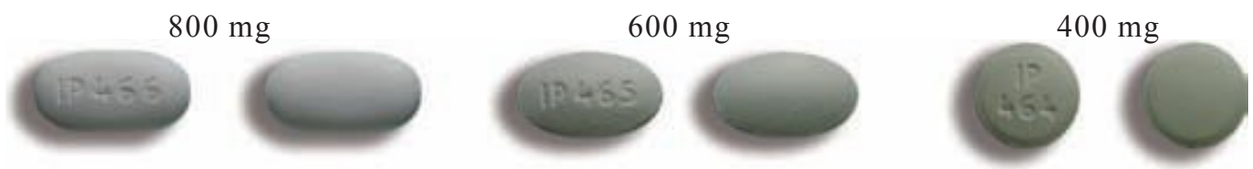
**Key Patient Counseling Points.** Take this medicine as soon as you get out of bed in the morning, before you eat or have anything to drink. Swallow the tablet whole with a large glass (240 mL) of plain water only (not mineral water, coffee, juice, or any other liquid). Do not take the medicine while you are still in bed, and do not take it at bedtime. Wait for at least 60 min after you swallow the tablet before you eat or drink anything or take any other medicines. This will help your body absorb the medicine. Do not lie down for at least 60 min after taking this medicine, and do not lie down until after you have eaten some food.

**Clinical Pearls.** Concurrent chemotherapy and poor oral hygiene increase the risk for osteonecrosis of the jaw. Atypical fractures of the thigh (subtrochanteric and diaphyseal femur fractures) have been reported in patients taking bisphosphonates for osteoporosis; discontinue therapy in patients who develop evidence of a femoral shaft fracture. Given the toxicities, FDA recommends consideration of discontinuation of ibandronate in patients at lower risk of osteoporosis after 3-5 y of therapy. Medication guide required at dispensing. Recommend adjunct calcium and vitamin D if dietary intake is inadequate.

# IBUPROFEN: Motrin, Various

**Class:** NSAID

**Dosage Forms. Oral Tablet:** 100 mg, 200 mg, 400 mg, 600 mg, 800 mg; **Oral Suspension:** 100 mg/5 mL, 50 mg/1.25 mL, 40 mg/mL; **Oral Capsule:** 200 mg; **Oral Tablet, Chewable**: 50 mg, 100 mg



Amneal generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Fever: Children, 6 mo-12 y of age, 5-10 mg/kg po q6-8h prn; Children ≥12 y of age and Adults, 200-400 mg po q4-6h prn, *max* 1200 mg/d for OTC use
2. Pain, headache: Children, 6 mo-12 y of age, 5-10 mg/kg po q6-8h prn; Children ≥12 y of age and Adults, 200-400 mg po q4-6h prn, *max* 1200 mg/d for OTC use
3. Osteoarthritis or rheumatoid arthritis: 1200-3200 mg/d po in 3-4 divided doses
4. Juvenile rheumatoid arthritis: 30-50 mg/kg/d divided qid, *max* 2400 mg/d

**Off-Label Uses.** None

**MOA.** Nonselective inhibitor of cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2), and reversibly alters platelet function and prolongs bleeding time.

**Drug Characteristics: Ibuprofen**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 90%, minimal food effect |
| **Dose Adjustment Renal** | Severe renal dysfunction, avoid | **Distribution** | Vd = 0.1 L/kg; 99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | 20% hepatic metabolism, CYP2C19 substrate |
| **Pregnancy Category** | C (1st and 2nd trimesters); D (3rd trimester) | **Elimination** | 45-80% renal elimination with a half-life of 1.8-2.2 h |
| **Lactation** | Compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to ibuprofen; concurrent use with ketorolac or pentoxifylline; asthma, urticaria, or allergic-type reaction following aspirin or other NSAID administration; CABG surgery, treatment of perioperative pain | **Black Box Warnings** | Cardiovascular events, GI toxicity, CABG |

**Medication Safety Issues: Ibuprofen**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| Junior, Migraine, 200, Prin | No | No | No | Halfprin, Neurontin | Avoid chronic use unless other alternatives are not effective and patient can take gastroprotective agent. |

### Drug Interactions: Ibuprofen

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Aspirin, low-molecular-weight heparins, SSRIs | Additive GI toxicity and increased risk of bleeding | Monitor for GI toxicity |
| ACE-Is, angiotensin II receptor blockers, beta-blockers, loop diuretics, thiazide diuretics | Decreased diuretic and antihypertensive efficacy via decreased renal prostaglandin production | Monitor and consider alternative therapy |
| Cyclosporine, tacrolimus, lithium | Increased risk of cyclosporine, lithium toxicity, unknown mechanism | Monitor cyclosporine, tacrolimus, or lithium levels and consider dose adjustments |
| Ketorolac, pentoxifylline | Additive GI toxicity and increased risk of bleeding | Contraindicated |
| Pemetrexed | Decreased renal clearance and increased toxicity of pemetrexed | Avoid NSAIDs in combination with pemetrexed in patients with renal dysfunction |
| Sulfonylurea antidiabetic agents | Increased risk of hypoglycemia via inhibition of sulfonylurea metabolism | Monitor blood glucose and adjust as necessary |
| Warfarin | Competitive metabolism | Monitor INR and adjust warfarin dose |

### Adverse Reactions: Ibuprofen

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Edema, itching, rash, GI distress, dizziness, tinnitus, ototoxicity | Stevens-Johnson syndrome, GI bleeding, thrombosis, elevated liver functions, acute renal failure, congestive heart failure, aplastic anemia |

**Efficacy Monitoring Parameters.** Osteoarthritis and rheumatoid arthritis: decreased pain and improved range of motion.

**Toxicity Monitoring Parameters.** CBC, LFTs, SCr, fecal occult blood tests if chronic use. Seek medical attention if severe skin rash, black tarry stools, chest pains, yellowing of eyes or skin, or change in urination.

**Key Patient Counseling Points.** Take with food or milk to decrease GI upset.

**Clinical Pearls.** Elderly patients are at increased risk of GI ulceration. NSAIDs are associated with an increased risk of adverse cardiovascular thrombotic events, including fatal MI and stroke. Use lowest effective dose for shortest possible duration; after observing initial response, adjust dose and frequency to meet individual patient's needs. Various OTC ibuprofen products are available; caution patients not to duplicate dosing with multiple ibuprofen products. Medication guide required at dispensing.

# IMIQUIMOD: Zyclara, Various

**Class:** Immune Response Modifier

**Dosage Forms. Topical Cream:** 2.5%, 3.75%, 5%

**Common FDA Label Indication, Dosing, and Titration.**

1. Actinic keratosis: Apply topically to affected treatment area 2 times per week at bedtime for 16 wk
2. Condyloma acuminatum, external: Apply topically to affected area 3 times per week until total clearance or up to a *max* duration of 16 wk
3. Superficial basal cell carcinoma, on trunk, neck, or extremities; when surgical methods are less appropriate and follow-up is assured: Apply topically once daily 5 times per week for 6 wk

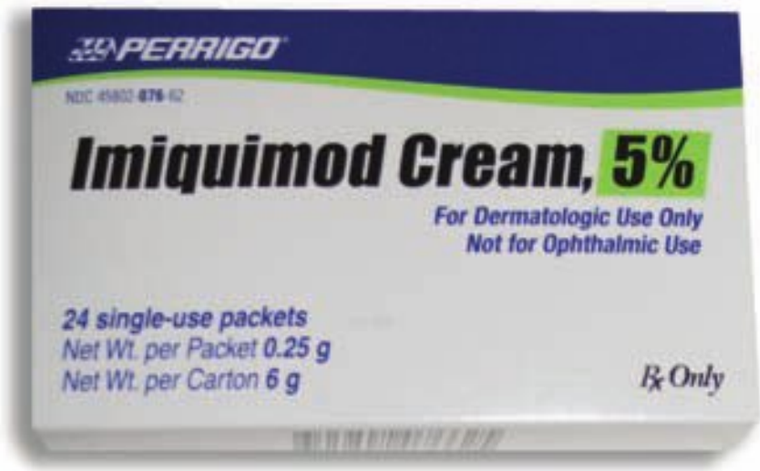
**Off-Label Uses.**

1. Condyloma acuminatum, external-HIV infection: Apply topically to lesion at bedtime 3 times per week on nonconsecutive nights for up to 16 wk; wash with soap and water 6-10 h after each application.

**MOA.** Toll-like receptor 7 agonist that induces cytokines, including interferon-α and others.

**Drug Characteristics: Imiquimod**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Absorption is dose dependent; 75 mg of cream yielded a Cmax = 3.5 ng/mL |
| **Dose Adjustment Renal** | Not required | **Distribution** | Unknown |
| **Dialyzable** | Not dialyzable | **Metabolism** | Unknown |
| **Pregnancy Category** | C | **Elimination** | Minimal, <1% with a half-life of 20 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | None | **Black Box Warnings** | None |



Perrigo generic 5% cream pictured

**Medication Safety Issues: Imiquimod**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| Zyclara Pump | No | No | No | Alora | No |

**Drug Interactions: Imiquimod.** None known

**Adverse Reactions: Imiquimod**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Local itching, burning, and pain | Headache, myalgia | Exfoliative dermatitis |

**Efficacy Monitoring Parameters.** Resolution of skin lesions.

**Toxicity Monitoring Parameters.** Seek medical attention if signs/symptoms of severe rash, burning, or itching.

**Key Patient Counseling Points.** Apply at bedtime and leave on skin for 8 h; when you get up, wash the treated skin area with mild soap and water. Do not cover treated skin areas with bandages. Do not use cosmetics or other skin care products on the treated skin areas. Apply on same days of each week. May increase sensitivity to sun.

**Clinical Pearls.** Condyloma acuminata are also known as genital warts and are sexually transmitted. Patients should be advised to abstain from sex while being treated. Imiquimod is not a cure for genital or anal warts; patients may develop new warts or spread warts while using the cream.

# INDOMETHACIN: Indocin, Various

**Class:** NSAID

**Dosage Forms.** **Oral Capsule, Immediate Release:** 25 mg, 50 mg; **Oral Capsule, Extended Release:** 75 mg; **Oral Suspension:** 25 mg/5 mL; **Rectal Suppository:** 50 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Ankylosing spondylitis, osteoarthritis, rheumatoid arthritis: Immediate Release, 25-50 mg po bid-tid, *max* 200 mg/d; Extended Release, 75 mg po daily bid
2. Pain: Immediate Release, 75-150 mg/d in 3-4 divided doses for 7-14 d

Sandoz generic pictured

**Off-Label Uses.**

1. Preterm labor, prevention: 25 mg po q6-12h

**MOA.** Nonselective inhibitor of COX-1 and COX-2, and reversibly alters platelet function and prolongs bleeding time.

**Drug Characteristics: Indomethacin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Severe hepatic failure, use with caution | **Absorption** | F = 90%, no food effect |
| **Dose Adjustment Renal** | CrCl <15 mL/min, use with caution | **Distribution** | Vd = 0.34-1.57 L/kg; 99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | 40% hepatic |
| **Pregnancy Category** | C | **Elimination** | 60% renal elimination with a half-life of 4.5 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity, concurrent use with ketorolac or pentoxifylline; asthma, urticaria, or allergic-type reaction following aspirin or other NSAID administration; CABG surgery, treatment of perioperative pain | **Black Box Warnings** | Cardiovascular events, GI toxicity, CABG |

**Medication Safety Issues: Indomethacin**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | ER capsule | No | Imodium, Lincocin, Minocin, Vicodin | Avoid |

### Drug Interactions: Indomethacin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Aspirin, low-molecular-weight heparins, SSRIs | Additive GI toxicity and increased risk of bleeding | Monitor for GI toxicity |
| ACE-Is, angiotensin II receptor blockers, beta-blockers, loop diuretics, thiazide diuretics | Decreased diuretic and antihypertensive efficacy via decreased renal prostaglandin production | Monitor and consider alternative therapy |
| Cyclosporine, tacrolimus, lithium | Increased risk of cyclosporine, lithium toxicity, unknown mechanism | Monitor cyclosporine, tacrolimus, or lithium levels and consider dose adjustments |
| Ketorolac, pentoxifylline | Additive GI toxicity and increased risk of bleeding | Contraindicated |
| Pemetrexed | Decreased renal clearance and increased toxicity of pemetrexed | Avoid NSAIDs in combination with pemetrexed in patients with renal dysfunction |
| Sulfonylurea antidiabetic agents | Increased risk of hypoglycemia via inhibition of sulfonylurea metabolism | Monitor blood glucose and adjust as necessary |
| Warfarin | Competitive metabolism | Monitor INR and adjust warfarin dose |

### Adverse Reactions: Indomethacin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Headache | Edema, itching, rash, GI distress, dizziness, tinnitus, ototoxicity | Stevens-Johnson syndrome, GI bleeding, thrombosis, elevated LFTs, acute renal failure, heart failure, aplastic anemia |

**Efficacy Monitoring Parameters.** Osteoarthritis and rheumatoid arthritis: decreased pain and improved range of motion.

**Toxicity Monitoring Parameters.** CBC, LFTs, SCr, fecal occult blood tests if chronic use. Seek medical attention if severe skin rash, black tarry stools, chest pains, yellowing of eyes or skin, or change in urination.

**Key Patient Counseling Points.** Take with food or milk to decrease GI upset.

**Clinical Pearls.** Elderly patients are at increased risk of GI ulceration. NSAIDs are associated with an increased risk of adverse cardiovascular thrombotic events, including fatal MI and stroke. Use lowest effective dose for shortest possible duration; after observing initial response, adjust dose and frequency to meet individual patient's needs. Various OTC NSAID products are available; caution patients not to duplicate dosing with multiple NSAID products. Indomethacin is effective for stopping premature labor and delaying delivery for several weeks, but should be used with caution as it may cause harm to the infant. Medication guide required at dispensing.

# INFLUENZA VIRUS VACCINE, INACTIVATED: Afluria, Flublok, Fluzone, Fluzone High-Dose; Fluzone Intradermal, FluLaval, Fluarix, Fluvirin, Flucelvax, Various

**Class:** Vaccine

**Dosage Forms.** **Suspension for Intramuscular Injection:** 0.5 mL vial (available as trivalent product containing 2 strains of influenza A virus and 1 influenza B virus strain and as a quadrivalent product containing 2 strains of influenza A virus and 2 influenza B virus strains); **Suspension for Intradermal Injection:** 0.1 mL in prefilled intradermal injection system

**Common FDA Label Indication, Dosing, and Titration.**

1. Prevention of influenza infection: Adults, 1 dose annual prior to or during influenza season; Children aged 6 mo to 8 y who have not been vaccinated in the past, 2 doses separated by at least 4 wk during the 1st season they receive influenza vaccine

**Off-Label Uses.** None

**Drug Characteristics: Inf uenza Virus Vaccine, Inactivated**

| | | | |
|---|---|---|---|
| **Pregnancy Category** | C | **ADME** | None known |
| **Lactation** | Infant risk is minimal | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to inf uenza vaccine, egg protein or a component of the vaccine; asthma, chronic medical conditions, immunosuppression | **Black Box Warnings** | None |

**Medication Safety Issues: Inf uenza Virus Vaccine, Inactivated**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Flumazenil; vials and syringes often mistaken for tetanus toxoid or tuberculin skin test | No |

Sanofi Pasteur pictured

I

### Drug Interactions: Inf uenza Virus Vaccine, Inactivated

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Moderate- to high-dose corticosteroids | Immunosuppression and increased risk of infection by vaccine | Delay vaccine administration until corticosteroid therapy has been discontinued if possible |
| Immunosuppressing agents, including cyclosporine, cancer chemotherapy | Immunosuppression and increased risk of infection by vaccine | Delay vaccine administration until corticosteroid therapy has been discontinued if possible |

### Adverse Reactions: Inf uenza Virus Vaccine, Inactivated

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Injection site reactions, including erythema and soreness. Itching, fatigue, headache, nasal congestion | Fever, myalgia, arthralgia | Anaphylaxis, Guillain-Barré syndrome, febrile seizures |

**Efficacy Monitoring Parameters.** Prevention of influenza infection.

**Toxicity Monitoring Parameters.** Syncope.

**Key Patient Counseling Points.** Annual seasonal immunization is recommended.

**Clinical Pearls.** Choose the vaccine preparation for appropriate age group. Use current year vaccine only (virus strains and vaccine vary year to year). Not all influenza vaccines are licensed for young children. Intradermal influenza vaccine licensed for adults aged 18-64 y. High-dose influenza vaccine licensed for individuals aged ≥65 y. Flublok is a recombinant influenza vaccine for ages 18-49 y and can be used in egg-allergic individuals. Flucelvax vaccine virus is grown in cell culture, but the seed virus is grown in eggs. Afluria is not recommended for children <9 y of age due to risk of febrile seizures. Recommended for pregnant females.

# INFLUENZA VIRUS VACCINE, LIVE: FluMist, Quadrivalent

**Class:** Vaccine

**Dosage Forms.** **Intranasal Spray:** 0.2 mL (quadrivalent product containing 2 strains of influenza A virus and 2 influenza B virus strains)

**Common FDA Label Indication, Dosing, and Titration.**

1. Prevention of influenza infection: Adults, healthy, aged 18-49 y, 1 spray each nostril annually; Children, healthy, aged 2-18 y, 1 spray in each nostril annually
2. Preferred influenza vaccine preparation for healthy children aged 2-8 y

**Off-Label Uses.** None

MedImmune pictured

**Drug Characteristics: Inf uenza Virus Vaccine, Live**

| | | | |
|---|---|---|---|
| **Pregnancy Category** | B | **ADME** | None known |
| **Lactation** | Infant risk is minimal | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to inf uenza vaccine, egg protein or a component of the vaccine; asthma, chronic medical conditions, immunosuppression; pregnancy | **Black Box Warnings** | None |

**Medication Safety Issues: Inf uenza Virus Vaccine, Live**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Flumazenil | No |

## Drug Interactions: Inf uenza Virus Vaccine, Live

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Aspirin, salicylates | Increased risk of Reye syndrome | Avoid giving salicylates to children for the 6 wk following live inf uenza virus vaccine administration |
| Moderate- to high-dose corticosteroids | Immunosuppression and increased risk of infection by vaccine | Delay live inf uenza virus vaccine administration until corticosteroid therapy has been discontinued |
| Immunosuppressing agents, including cyclosporine, cancer chemotherapy | Immunosuppression and increased risk of infection by vaccine | Delay live inf uenza virus vaccine administration until immunosuppressive therapy has been discontinued |
| Inf uenza antiviral medications: adamantanes, neuraminidase inhibitors | Interference with immune response to inf uenza virus vaccine | Hold antiviral agent for at least 2 wk |

## Adverse Reactions: Inf uenza Virus Vaccine, Live

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Headache, nasal congestion | Fever | Anaphylaxis, Guillain-Barré syndrome, Bells palsy |

**Efficacy Monitoring Parameters.** Prevention of influenza infection.

**Toxicity Monitoring Parameters.** Nasal discharge.

**Key Patient Counseling Points.** Annual seasonal immunization is recommended.

**Clinical Pearls.** Use current year vaccine only (virus strains and vaccine vary year to year). LAIV has an 18-wk expiration date so it can expire before the end of the season. Transmission of the vaccine virus to susceptible individuals without clinical consequences has been documented. Avoid administering to contacts of individuals so severely immunocompromised that they require protective isolation. The dose is sprayed into each nostril with no cooperation (active inhalation) required by the individual being vaccinated. Vaccine dosing does not need to be repeated if the individual sneezes following administration.

# INSULIN: Humulin R, Humulin N, Humulin 70/30, Various

**Class:** Insulin, Short-Acting (R); Intermediate-Acting (NPH)

**Dosage Forms.** **Injection Solution:** Humulin R (Regular): 100 units/mL, 500 units/mL; Humulin N (NPH): 100 units/mL; Humulin 70/30 (NPH/Regular): 70 units NPH/30 units Regular/mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Diabetes mellitus, type 1 and 2: Subcutaneous dosing is individualized to patient needs

**Off-Label Uses.** None

**MOA.** Insulin promotes cellular uptake of glucose, fatty acids, and amino acids, and their conversion to glycogen, triglycerides, and proteins.

**Drug Characteristics: Insulin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Regular: onset: 30 min, peak effect: 2 h, duration: 4-6 h; NPH: onset: 2 h, peak effect: 4-8 h, duration: 8-12 h |
| **Dose Adjustment Renal** | Not required | **Distribution** | Protein binding 5% |
| **Dialyzable** | Not dialyzable | **Metabolism** | 50% hepatic, 30% renal, 20% adipose tissue |
| **Pregnancy Category** | Not categorized, but used in pregnancy | **Elimination** | Renal elimination is 30% with a half-life of 1-5 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

Lilly NPH 100 units/mL pictured

**Medication Safety Issues: Insulin**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| R = Regular, N = NPH, 70/30 = 70% NPH/30% R, U-500 (high concentration) | HumuLIN, NovoLIN | No | Yes | HumaLOG, HumuLIN, NovoLIN, NovoLOG | Avoid sliding scale |

### Drug Interactions: Insulin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Beta-blockers | Altered glucose metabolism and increased risk of hypoglycemia | Avoid propranol; use others with caution and increased monitoring |
| Fluoroquinolones | Altered glucose metabolism and increased risk of hypoglycemia and hyperglycemia | Avoid concurrent use if possible; monitor and consider dose adjustments |
| MAOIs | Stimulation of insulin secretion, hypoglycemic effects | Avoid concurrent use if possible; monitor and consider dose adjustments |
| Somatostatin analogues | Altered glucose metabolism and increased risk of hypoglycemia | Avoid concurrent use if possible; monitor and consider dose adjustments |
| Psyllium | Psyllium may delay absorption of glucose from meals, leading to less postprandial hyperglycemia and potentially allowing a reduced dosage of the antidiabetic agent | Avoid concurrent use if possible; monitor and consider dose adjustments |

### Adverse Reactions: Insulin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Injection site reactions, weight gain | Hypoglycemia, lipodystrophy | Severe hypersensitivity, insulin resistance, severe hypoglycemia |

**Efficacy Monitoring Parameters.** Preprandial blood glucose between 70 and 130 mg/dL, $HbA_{1c}$ <7%.

**Toxicity Monitoring Parameters.** Symptoms of hypoglycemia include nausea, sweating, and loss of consciousness, tremor.

**Key Patient Counseling Points.** Monitor blood glucose in frequent intervals (2-4 times per day); if <70 mg/dL, eat candy or sugar and contact prescriber. Store in refrigerator. Dispose needles in sharps container. Do not share needles; this increases the risk of transmission of infectious diseases. Rotate injection sites.

**Clinical Pearls.** Beef and pork insulins are extracted and purified from the animal's pancreas. Human insulin is produced by recombinant DNA technology or enzymatic conversion of pork insulin. No differences in side effects or long-term control of diabetes have been observed between human insulin and highly purified pork insulin. Use caution when dispensing 500 units/mL insulin solution, can result in accidental overdose of insulin and hypoglycemia. Regular is short acting; NPH is intermediate acting. Rapid acting inhaled insulin was approved by FDA in June 2014, but is not yet available.

# INSULIN ASPART: NovoLog, NovoLog FlexPen

**Class:** Insulin, Rapid-Acting

**Dosage Forms. Injection Solution:** 100 units/mL; **Pen and Refills (Administration Device)**: 100 units/mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Diabetes mellitus, type 1 and 2: Dosing is individualized to patient needs

**Off-Label Uses.** None

**MOA.** Insulin promotes cellular uptake of glucose, fatty acids, and amino acids, and their conversion to glycogen, triglycerides, and proteins.

Novo Nordisk pictured

## Drug Characteristics: Insulin Aspart

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Onset: 15-30 min, peak: 1-2 h, duration: 3-5 h |
| **Dose Adjustment Renal** | Not required | **Distribution** | Protein binding 5% |
| **Dialyzable** | Not dialyzable | **Metabolism** | 50% hepatically metabolized |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 30% with a half-life of 1.5 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

## Medication Safety Issues: Insulin Aspart

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| FlexPen, FlexFill | NovoLOG | No | Yes | HumaLOG, HumuLIN, Nimbex, NovoLIN, NovoLOG Mix 70/30 | Avoid sliding scale |

### Drug Interactions: Insulin Aspart

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Beta-blockers | Altered glucose metabolism and increased risk of hypoglycemia | Avoid propranol; use others with caution and increased monitoring |
| Fluoroquinolones | Altered glucose metabolism and increased risk of hypoglycemia and hyperglycemia | Avoid concurrent use if possible; monitor and consider dose adjustments |
| MAOIs | Stimulation of insulin secretion, hypoglycemic effects | Avoid concurrent use if possible; monitor and consider dose adjustments |
| Somatostatin analogues | Altered glucose metabolism and increased risk of hypoglycemia | Avoid concurrent use if possible; monitor and consider dose adjustments |
| Psyllium | Psyllium may delay absorption of glucose from meals, leading to less postprandial hyperglycemia and potentially allowing a reduced dosage of the antidiabetic agent | Avoid concurrent use if possible; monitor and consider dose adjustments |

### Adverse Reactions: Insulin Aspart

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Injection site reactions, weight gain, hypoglycemia | Pruritus, rash, lipodystrophy | Severe hypersensitivity, insulin resistance |

**Efficacy Monitoring Parameters.** Preprandial blood glucose between 70 and 130 mg/dL, $HbA_{1c}$ <7%.

**Toxicity Monitoring Parameters.** Symptoms of hypoglycemia include nausea, sweating, and loss of consciousness, tremor

**Key Patient Counseling Points.** Monitor blood glucose in frequent intervals (2-4 times per day); if <70 mg/dL, eat candy or sugar and contact prescriber. Store in refrigerator. Dispose needles in sharps container. Do not share needles; this increases the risk of transmission of infectious diseases. Rotate injection sites.

**Clinical Pearls.** Insulin requirements may change during periods of stress (illness) or with increased activity; monitor and adjust. This is the fastest acting insulin.

# INSULIN DETEMIR: Levemir

**Class:** Insulin, Long-Acting

**Dosage Forms.** **Injection Solution:** 100 units/mL; **Pen (Administration Device):** 100 units/mL

**Common FDA Label Indication and Dosing.**

1. Diabetes mellitus, type 1 and 2: Dosing is individualized to patient needs

**Off-Label Uses.** Not required

**MOA.** Insulin promotes cellular uptake of glucose, fatty acids, and amino acids, and their conversion to glycogen, triglycerides, and proteins.

**Drug Characteristics: Insulin Detemir**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Onset: 2 h, no peak, duration: 14-24 h (dose dependant) |
| **Dose Adjustment Renal** | Not required | **Distribution** | 98% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | 50% hepatically metabolized |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 30% with a half-life of 5-7 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

**Medication Safety Issues: Insulin Detemir**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| FlexPen, FlexTouch | No | No | Yes | FlexFill | Avoid sliding scale |

Novo Nordisk 100 units/mL pictured

### Drug Interactions: Insulin Detemir

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Beta-blockers | Altered glucose metabolism and increased risk of hypoglycemia | Avoid propranol; use others with caution and increased monitoring |
| Fluoroquinolones | Altered glucose metabolism and increased risk of hypoglycemia and hyperglycemia | Avoid concurrent use if possible; monitor and consider dose adjustments |
| MAOIs | Stimulation of insulin secretion, hypoglycemic effects | Avoid concurrent use if possible; monitor and consider dose adjustments |
| Somatostatin analogues | Altered glucose metabolism and increased risk of hypoglycemia | Avoid concurrent use if possible; monitor and consider dose adjustments |
| Psyllium | Psyllium may delay absorption of glucose from meals, leading to less postprandial hyperglycemia and potentially allowing a reduced dosage of the antidiabetic agent | Avoid concurrent use if possible; monitor and consider dose adjustments |

### Adverse Reactions: Insulin Detemir

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Injection site reactions, weight gain, hypoglycemia | Pruritus, rash | Severe hypersensitivity, insulin resistance |

**Efficacy Monitoring Parameters.** Pre-prandial blood glucose between 70 and 130 mg/dL, $HbA_{1c}$ <7%.

**Toxicity Monitoring Parameters.** Symptoms of hypoglycemia include nausea, sweating, and loss of consciousness, tremor.

**Key Patient Counseling Points.** Monitor blood glucose in frequent intervals (2-4 times per day); if <70 mg/dL, eat candy or sugar and contact prescriber. Store in refrigerator. Dispose needles in sharps container. Do not share needles; this increases the risk of transmission of infectious diseases. Rotate injection sites. Not for IV or IM use. Do not share pens, even if needles are changed.

**Clinical Pearls.** Insulin requirements may change during periods of stress (illness) or with increased activity; monitor and adjust.

# INSULIN GLARGINE: Lantus

**Class:** Insulin, Long-Acting

**Dosage Forms. Injection Solution:** 100 units/mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Diabetes mellitus, type 1 and 2: Dosing is individualized to patient needs

**Off-Label Uses.** None

**MOA.** Insulin promotes cellular uptake of glucose, fatty acids, and amino acids, and their conversion to glycogen, triglycerides, and proteins.

Sanofi-Aventis pictured

**Drug Characteristics: Insulin Glargine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Onset: 4-5 h, peak: none, duration: 22-24 h |
| **Dose Adjustment Renal** | Not required | **Distribution** | Unknown |
| **Dialyzable** | Not dialyzable | **Metabolism** | Metabolized to form active metabolites: M1 (21A-Gly-insulin) and M2 (21A-Gly-des-30B-Thr-insulin) 50% |
| **Pregnancy Category** | C | **Elimination** | Duration of effect 10-24 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

**Medication Safety Issues: Insulin Glargine**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| SoloStar | No | No | Yes | Latanoprost, Latuda, Xalatan | Avoid sliding scale |

### Drug Interactions: Insulin Glargine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Beta-blockers | Altered glucose metabolism and increased risk of hypoglycemia | Avoid propranol; use others with caution and increased monitoring |
| Fluoroquinolones | Altered glucose metabolism and increased risk of hypoglycemia and hyperglycemia | Avoid concurrent use if possible; monitor and consider dose adjustments |
| MAOIs | Stimulation of insulin secretion, hypoglycemic effects | Avoid concurrent use if possible; monitor and consider dose adjustments |
| Somatostatin analogues | Altered glucose metabolism and increased risk of hypoglycemia | Avoid concurrent use if possible; monitor and consider dose adjustments |
| Psyllium | Psyllium may delay absorption of glucose from meals, leading to less postprandial hyperglycemia and potentially allowing a reduced dosage of the antidiabetic agent | Avoid concurrent use if possible, monitor and consider dose adjustments |

### Adverse Reactions: Insulin Glargine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Injection site reactions, weight gain, hypoglycemia | Pruritus, rash, lipodystrophy | Severe hypersensitivity, insulin resistance |

**Efficacy Monitoring Parameters.** Preprandial blood glucose between 70 and 130 mg/dL, $HbA_{1c}$ <7%.

**Toxicity Monitoring Parameters.** Symptoms of hypoglycemia include nausea, sweating, and loss of consciousness, tremor

**Key Patient Counseling Points.** Monitor blood glucose in frequent intervals (2-4 times per day); if <70 mg/dL, eat candy or sugar and contact prescriber. Store in refrigerator. Dispose needles in sharps container. Do not share needles; this increases the risk of transmission of infectious diseases. Rotate injection sites.

**Clinical Pearls.** Insulin requirements may change during periods of stress (illness) or with increased activity; monitor and adjust. Following subcutaneous administration, insulin glargine forms a microprecipitate in the fatty tissue from which small amounts of insulin are released slowly, resulting in a relatively constant concentration/time profile over 24 h with no pronounced peak.

# INSULIN LISPRO: Humalog, Humalog KwikPen

**Class:** Insulin, Rapid-Acting

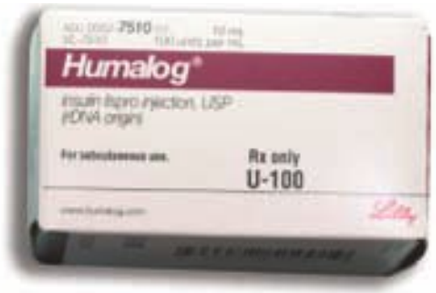
**Dosage Forms.** **Injection Solution:** 100 units/mL; **Pen (Administration Device):** 100 units/mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Diabetes mellitus, type 1 and 2: Dosing is individualized to patient needs

**Off-Label Uses.** None

**MOA.** Insulin promotes cellular uptake of glucose, fatty acids, and amino acids, and their conversion to glycogen, triglycerides, and proteins.

Lilly pictured  100 units/mL

**Drug Characteristics: Insulin Lispro**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Onset: 15-30 min, peak: 1-2 h, duration 3-4 h |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 0.26 L/kg |
| **Dialyzable** | Not dialyzable | **Metabolism** | 50% hepatically metabolized |
| **Pregnancy Category** | C | **Elimination** | Half-life of 0.5-1 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

**Medication Safety Issues: Insulin Lispro**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| Mix 50/50, KwikPen | HumaLOG | No | Yes | Humira, HumaLIN N, HumaLIN R, NovoLOG | Avoid sliding scale |

### Drug Interactions: Insulin Lispro

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Beta-blockers | Altered glucose metabolism and increased risk of hypoglycemia | Avoid propranol; use others with caution and increased monitoring |
| Fluoroquinolones | Altered glucose metabolism and increased risk of hypoglycemia and hyperglycemia | Avoid concurrent use if possible; monitor and consider dose adjustments |
| MAOIs | Stimulation of insulin secretion, hypoglycemic effects | Avoid concurrent use if possible; monitor and consider dose adjustments |
| Somatostatin analogues | Altered glucose metabolism and increased risk of hypoglycemia | Avoid concurrent use if possible; monitor and consider dose adjustments |
| Psyllium | Psyllium may delay absorption of glucose from meals, leading to less postprandial hyperglycemia and potentially allowing a reduced dosage of the antidiabetic agent | Avoid concurrent use if possible, monitor and consider dose adjustments |

### Adverse Reactions: Insulin Lispro

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Injection site reactions, weight gain, hypoglycemia | Hypokalemia, lipodystrophy | Severe hypersensitivity, insulin resistance |

**Efficacy Monitoring Parameters.** Pre-prandial blood glucose between 70 and 130 mg/dL, $HbA_{1c}$ <7%.

**Toxicity Monitoring Parameters.** Symptoms of hypoglycemia include nausea, sweating, and loss of consciousness, tremor

**Key Patient Counseling Points.** Monitor blood glucose in frequent intervals (2-4 times per day); if <70 mg/dL, eat candy or sugar and contact prescriber. Store in refrigerator. Dispose needles in sharps container. Do not share needles; this increases the risk of transmission of infectious diseases. Rotate injection sites.

**Clinical Pearls.** Insulin requirements may change during periods of stress (illness) or with increased activity; monitor and adjust. Injection of insulin lispro into an abdominal versus posterior upper arm or lateral thigh area site results in more rapid absorption. Faster acting than regular insulin.

# IPRATROPIUM/ALBUTEROL: Combivent, Various

**Class:** Anticholinergic/Selective $\beta_2$-Agonist Combination

**Dosage Forms.** **Metered-Dose Inhaler (MDI):** 18 mcg/90 mcg ipratropium/albuterol per actuation; **Inhalation Solution:** 0.5 mg/2.5 mg ipratropium/albuterol per 3 mL; **Spray:** 20 mcg/100 mcg ipratropium/albuterol per inhalation

**Common FDA Label Indication, Dosing, and Titration.**

1. Chronic obstructive pulmonary disease: Adults, 2 inhalations qid (*max* 12 inhalations/d) or 3 mL via nebulizer qid (*max* 6 doses/d)

**Off-Label Uses.**

1. Asthma exacerbation: Adults, ipratropium 0.5 mg with albuterol 2.5 mg via nebulized usually given once

**MOA.** Albuterol is a selective $\beta_2$-adrenergic agonist that produces bronchodilation, vasodilation, uterine relaxation, skeletal muscle stimulation, peripheral vasodilation, and tachycardia. Ipratropium is a competitive antagonist of acetylcholine at peripheral, but not central, muscarinic receptors. It appears to produce bronchodilation by inhibition of cholinergic receptors on bronchial smooth muscle.

Boehringer Ingelheim pictured

**Drug Characteristics: Ipratropium/Albuterol**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | About 90% of an inhaled dose is swallowed; F = 6.9% following inhalation |
| **Dose Adjustment Renal** | Not required | **Distribution** | Albuterol protein binding 10% |
| **Dialyzable** | Not dialyzable | **Metabolism** | Albuterol is conjugatively metabolized to an active metabolite; ipratropium is partially metabolized to 8 inactive metabolites |
| **Pregnancy Category** | C | **Elimination** | Albuterol renal elimination is 80-100% with a half-life of 4 h; ipratropium has minimal renal elimination, 48% in feces, with a half-life of 2 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to albuterol, ipratropium, or any other components of the product, or to atropine or its derivatives, or levalbuterol; hypersensitivity to soya lecithin or related food products (eg, soybean, peanut products) | **Black Box Warnings** | None |

### Medication Safety Issues: Ipratropium/Albuterol

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Combivir, Serevent | No |

### Drug Interactions: Ipratropium/Albuterol

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Other anticholinergic agents | Additive effect with ipratropium | Avoid concurrent use |
| Other short-acting sympathomimetics | Additive effect with albuterol | Avoid concurrent use |
| Beta-blockers | May decrease effectiveness of albuterol and produce bronchospasms | Avoid use of nonselective beta-blocker in patients with asthma; monitor PFTs if cardioselective beta-blockers are clinically indicated |
| Diuretics (non-potassium sparing) | May potentiate hypokalemia | Monitor potassium levels |
| Digoxin | May decrease digoxin levels | Monitor digoxin levels |
| MAOI and tricyclic antidepressants | May potentiate albuterol effect on cardiovascular system | Consider alternative therapy |

### Adverse Reactions: Ipratropium/Albuterol

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Bronchitis, upper respiratory tract infections | Angina, tachycardia, nausea, cough, headache, dyspnea, tremor, nervousness, insomnia, urinary retention, blurred vision | Angle-closure glaucoma, pneumonia, hypersensitivity reactions, paradoxical bronchospasm |

**Efficacy Monitoring Parameters.** Resolution of COPD symptoms, improved PFTs.

**Toxicity Monitoring Parameters.** Use alternative therapy or seek emergency treatment if paradoxical bronchospasms occur.

**Key Patient Counseling Points.** Instruct patient on appropriate inhaler technique. Wash the mouthpiece in warm water and air dry thoroughly daily (may cease to deliver medication if mouthpiece becomes blocked). Store the inhaler at room temperature; avoid excessive humidity; do not freeze. Each canister contains 200 inhalations. Keep track of number of inhalations administered and discard canister after 200 inhalations have been used. Nebulizer technique: use entire vial of inhalation solution immediately after opening to avoid contamination; deliver over 5-15 min. Seek medical attention if the prescribed dose does not provide relief or if symptoms worsen.

**Clinical Pearls.** Because of anticholinergic effect of ipratropium, use with caution in patients with bladder neck obstruction, narrow-angle glaucoma, or BPH.

# IRBESARTAN: Avapro, Various

**Class:** Angiotensin II Receptor Antagonist

**Dosage Forms. Oral Tablet:** 75 mg, 150 mg, and 300 mg

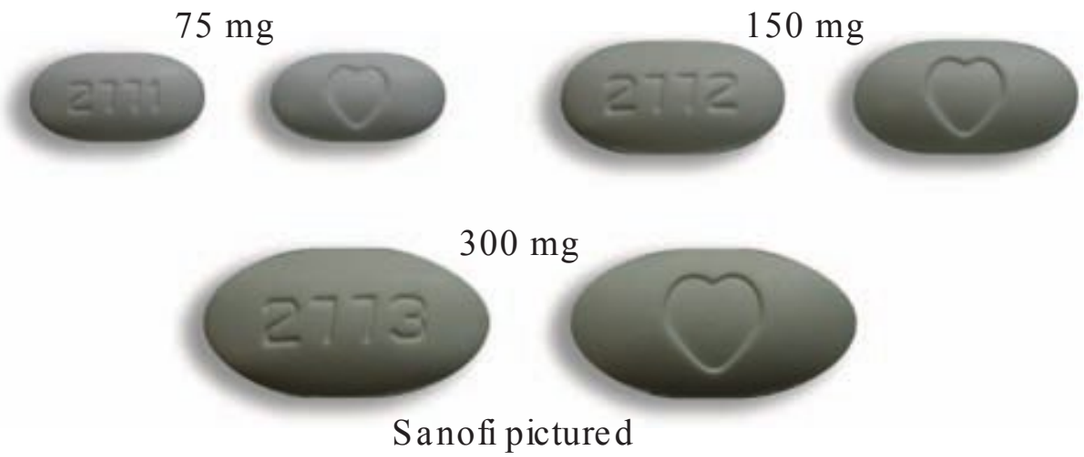
**Common FDA Label Indication, Dosing, and Titration.**

1. Diabetic nephropathy in patients with type 2 diabetes and hypertension: Adults, 75-300 mg po daily; titrate to target dose of 300 mg daily
2. Hypertension: Adults, initial, 150-300 mg po daily

**Off-Label Uses.**

1. Left ventricular hypertrophy: Adults, 150-300 mg po daily
2. Hypertension, renal impairment: Adults, 150-300 mg po daily

**MOA.** Irbesartan is a selective, reversible, competitive antagonist of the angiotensin II receptor (AT1), which is responsible for the physiologic effects of angiotensin II including vasoconstriction, aldosterone secretion, sympathetic outflow, and stimulation of renal sodium reabsorption.



Sanofi pictured

**Drug Characteristics: Irbesartan**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 80%, food does not affect absorption |
| **Dose Adjustment Renal** | Patients receiving hemodialysis, initial dose 75 mg po daily | **Distribution** | Vd = 53-93 L; 90% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Minor CYP2C9 substrate. Moderate inhibitor of CYP2C8 and CYP2C9 |
| **Pregnancy Category** | C (1st trimester), D (2nd and 3rd trimesters) | **Elimination** | Renal elimination is 20% and fecal elimination is 80% with a half-life 11-15 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity or pregnancy | **Black Box Warnings** | Pregnancy |

**Medication Safety Issues: Irbesartan**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Anaprox | No |

### Drug Interactions: Irbesartan

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Potassium-sparing diuretics | Increased risk of hypotension, hyperkalemia | Avoid concurrent use or monitor BP and serum potassium levels |
| CYP2C8 and 2C9 substrates | Decreased metabolism of substrates and increased toxicity of substrates | Avoid concurrent use or consider substrate dose reduction |
| ACE-Is | Increased risk of hypotension, hyperkalemia, nephrotoxicity | Avoid concurrent use or monitor BP, SCr, and potassium levels |
| Potassium supplements, salt substitutes | Increased risk of hyperkalemia and cardiac arrhythmias | Avoid concurrent use or monitor serum potassium levels |
| NSAIDs | Decreased antihypertensive and natriuretic effect of irbesartan, increased risk of nephrotoxicity | Avoid concurrent use or monitor BP and SCr levels |
| Diuretics | Increased risk of postural hypotension due to hypovolemia | Monitor BP; rise from seated position slowly |
| Lithium | Increased risk of lithium toxicity | Monitor serum lithium levels |

### Adverse Reactions: Irbesartan

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Headache | Diarrhea, dizziness, fatigue, heartburn, hyperkalemia, hypotension, nephrotoxicity, tachycardia | Angioedema, birth defects, hepatotoxicity, rhabdomyolysis |

**Efficacy Monitoring Parameters.** Decreased BP. Monitor BP weekly; may require 2-4 wk for full effect.

**Toxicity Monitoring Parameters.** Report signs/symptoms of hypotension, tachycardia. Baseline and periodic electrolyte panel, renal function tests, and urine protein are recommended.

**Key Patient Counseling Points.** Seek medical attention if angioedema (swelling of the face, eyes, lips, tongue, or throat), excessive fluid loss (vomiting, diarrhea, or excessive perspiration), hyperkalemia (confusion, body weakness, uneven heartbeat, or numbness/tingling in hands or feet), reduction in urination, jaundice, or skin rash occurs. Avoid pregnancy. Avoid abrupt discontinuation. Use potassium supplements or salt substitutes only under medical supervision. This medicine may cause dizziness. Avoid alcohol or driving.

**Clinical Pearls.** Safety and efficacy have not been established in children.

# ISOSORBIDE MONONITRATE: Imdur, ISMO, Monoket, Various

**Class:** Long-Acting Nitrate, Anti-anginal

**Dosage Forms.** **Oral Tablet, Extended Release:** 30 mg, 60 mg, 120 mg; **Oral Tablet, Immediate Release:** 10 mg, 20 mg

Kremers Urban generic 20 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Angina, prophylaxis: Adults, Extended Release, initial, 30-60 mg po daily, may titrate to maintenance of 120-240 mg po daily; Immediate Release, 20 mg bid separated 7 h apart to decrease tolerance development

**Off Label Uses**. None

**MOA.** Isosorbide mononitrate (ISMN) is the active 5-mononitrate metabolite of isosorbide dinitrate. Nitroglycerin and other organic nitrates are converted to nitric oxide (NO) by vascular endothelium. NO activates guanylate cyclase, increasing cyclic GMP that in turn decreases intracellular calcium, resulting in direct relaxation of vascular smooth muscle.

**Drug Characteristics: Isosorbide Mononitrate**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 93%, food slows rate (but not extent) of absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 0.6L; <5% protein bound |
| **Dialyzable** | Yes (hemodialysis) | **Metabolism** | >95% hepatic, CYP3A4/5 substrate |
| **Pregnancy Category** | C | **Elimination** | Renal elimination of metabolites is 96% with a half-life of 6 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to nitrates, concurrent use with erectile dysfunction meds | **Black Box Warnings** | None |

**Medication Safety Issues: Isosorbide Mononitrate**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | XR formulation | No | Imuran, Inderal LA, K-Dur | No |

### Drug Interactions: Isosorbide Mononitrate

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inducers | Increased metabolism of isosorbide mononitrate decreases isosorbide efficacy | Monitor for toxicity and consider dose increases of isosorbide mononitrate |
| CYP3A4/5 inhibitors | Decreased metabolism of isosorbide mononitrate increases risk of isosorbide mononitrate toxicity | Monitor for efficacy and consider dose decreases of isosorbide mononitrate |
| Phosphodiesterase inhibitors (erectile dysfunction medications) | Excessive hypotension | Concurrent use contraindicated; separate sildenafil and vardenafil from nitrates by 24 h; tardenafil from nitrates by 48 h |

### Adverse Reactions: Isosorbide Mononitrate

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Dizziness, headache | Bradycardia, f ushing, hypotension, nausea, orthostatic hypotension, tachycardia, vomiting | Severe hypotension, syncope |

**Efficacy Monitoring Parameters.** Decreased use of sublingual nitroglycerin, reduction in angina episodes.

**Toxicity Monitoring Parameters.** Report signs/symptoms of hypotension, problematic headaches, or decreasing efficacy (drug tolerance) to prescriber.

**Key Patient Counseling Points.** It is best to take this medicine on an empty stomach with at least half a glass of water. Swallow the extended-release tablet whole. Do not break, crush, or chew it. This medicine can cause headaches, which is a sign that the medicine is working. Acetaminophen may be used to relieve the headache. Talk with your doctor if the headache is severe. This medicine can cause dizziness. Avoid driving, using machines, or doing anything else that could be dangerous if not alert. Stand up slowly if this medicine causes light-headedness from orthostatic hypotension. Do not stop using this medicine suddenly without asking a health-care provider. The dose may need to be slowly decreased before stopping it completely. Avoid concomitant use of erectile dysfunction medications as this may increase risk of severe hypotension. Avoid drinking alcohol while taking this drug.

**Clinical Pearls.** Safety and efficacy have not established in children. Combining long-acting nitrates with antihypertensive medications can increase risk of hypotension. To avoid tolerance, include an 8-h nitrate-free interval in every 24-h period.

# KETOCONAZOLE TOPICAL: Nizoral, Various

Teva generic 2% cream pictured

**Class:** Imidazole Antifungal

**Dosage Forms.** **Topical Cream:** 2%, **Topical Foam:** 2%, **Topical Gel:** 2%, **Topical Shampoo:** 1% (OTC), 2% (by prescription)

**Common FDA Label Indication, Dosing, and Titration.**

1. Candidiasis of skin: Apply 2% cream topically once daily for 2 wk
2. Dandruff: Apply 1% shampoo topically to wet hair, lather, rinse thoroughly, and repeat; use every 3-4 d for up to 8 wk; then as needed to control dandruff
3. Pityriasis versicolor: Apply 2% shampoo topically to damp skin and a wide surrounding margin, lather, leave on skin for 5 min, then rinse, *or* apply 2% cream to affected areas once daily × 2 wk
4. Seborrheic dermatitis: Apply cream, gel, and foam topically to the affected area bid for 4 wk or until clinical clearing
5. Tinea corporis: Apply 2% cream topically once daily for 2 wk
6. Tinea cruris: Apply 2% cream topically once daily for 2 wk
7. Tinea pedis: Apply 2% cream topically once daily for 6 wk

**Off-Label Uses.** None

**MOA.** Ketoconazole inhibits biosynthesis of ergosterol or other sterols, damaging the fungal cell wall membrane and altering its permeability.

## Drug Characteristics: Ketoconazole Topical

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Minimal absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Minimal absorption |
| **Dialyzable** | Not dialyzable | **Metabolism** | Minimal absorption |
| **Pregnancy Category** | C | **Elimination** | Minimal absorption |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

## Medication Safety Issues: Ketoconazole Topical

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| A-D | No | No | No | Nasarel, Neoral, Nitrol | No |

**Drug Interactions: Ketoconazole Topical.** None known with topical product; many interactions with oral formulation

## Adverse Reactions: Ketoconazole Topical

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Application site reaction with foam | Dry skin, burning, stinging at site of application | Rash, hair loss |

**Efficacy Monitoring Parameters.** Resolution of erythema and pruritus. Improvement in erythema and pruritus usually occurs within 3-5 d. If no improvement is seen after 1 wk of treatment for tinea cruris or tinea corporis or after 2 wk of treatment for tinea pedis, then the diagnosis should be reviewed.

**Toxicity Monitoring Parameters.** Seek medical attention if severe skin irritation or rash.

**Key Patient Counseling Points.** Apply thin layer to affected area of skin. Skin should be intact. Do not get it in your eyes, nose, mouth, or vagina. Do not wash the areas where you applied this medicine for at least 3 h after application. Cosmetics (makeup or sunscreens) may be put on the affected areas 20 min after application. Topical products are alcohol based and flammable immediately after application.

**Clinical Pearls.** Topical products typically not effective in toenail onychomycosis. Resistant infections typically require oral therapy.

# LABETALOL: Normodyne, Various

**Class:** α/β-Adrenergic Blocker

**Dosage Forms. Oral Tablet:** 100 mg, 200 mg, 300 mg

Sandoz generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Hypertension: Adults, initial, 100 mg po bid; may titrate in 100 mg increments po bid every 2-3 d to maintenance dose of 200-400 mg po bid, *max* dose 2400 mg daily

**Off-Label Uses.**

1. Hypertension: Children, initial, 1-3 mg/kg/d po in 2 divided doses; *max* 10-12 mg/kg/d or 600 mg po bid
2. Hypertension, urgency: 200-400 mg po depending on initial BP

**MOA.** Labetalol is an adrenergic receptor blocking drug that has selective $\alpha_1$- and nonselective β-adrenergic receptor blocking actions.

**Drug Characteristics: Labetalol**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Reduce dose by 50% if hepatic failure | **Absorption** | F = 25%; food increases absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 3-16 L/kg; 50% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | >90% hepatic and primarily via glucuronide conjugation |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 55-60% (5% unchanged) and 50% in feces, with a half-life of 5-8 h |
| **Lactation** | Compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity; bronchial asthma or related bronchospastic condition; severe sinus bradycardia, 2nd- or 3rd-degree AV block; overt heart failure; cardiogenic shock, conditions associated with severe and prolonged hypotension | **Black Box Warnings** | None |

**Medication Safety Issues: Labetalol**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | Yes (IV only) | Betaxolol, lamoTRIgine, Lipitor | No |

### Drug Interactions: Labetalol

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Alpha-/Beta-agonists | Labetalol may enhance the vasopressor effect of alpha-/beta-agonist | Avoid concurrent use or monitor BP |
| Alpha1-blockers, fentanyl | Additive orthostatic hypotension | Avoid concurrent use or monitor BP |
| Beta-blockers, amiodarone, dronedarone | Increased risk of bradycardia, heart block, sinus arrest | Avoid concurrent use in patients with sick sinus syndrome or AV block |
| Antidiabetic drugs | Decreased glycemic control | Monitor blood glucose levels |
| Calcium channel blockers | Increased risk of hypotension and/or bradycardia and AV block | Avoid concurrent use |

### Adverse Reactions: Labetalol

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Dizziness, fatigue, nausea | Bradyarrhythmias, constipation, diaphoresis, diarrhea, disorder of glucose regulation, dyspnea, headache, impotence, increased liver enzymes, orthostatic hypotension, somnolence, wheezing | Hepatotoxicity, bronchospasm |

**Efficacy Monitoring Parameters.** Decreased BP.

**Toxicity Monitoring Parameters.** Signs/symptoms of peripheral edema, increased HR, signs/symptoms of liver damage.

**Key Patient Counseling Points.** Report signs/symptoms of hypotension with initial dosing and dose changes. Avoid alcohol while taking drug. May cause dizziness. Avoid driving, using machinery, or doing anything else that could be dangerous if not alert. Instruct patient to rise slowly from a sitting/supine position, as labetalol may cause orthostatic hypotension. Report signs/symptoms of bronchospasm, slow HR, hepatotoxicity, or syncope. Advise diabetic patients to carefully follow blood sugar levels as beta-blockers may mask symptoms of hypoglycemia. Advise patients against sudden discontinuation of drug as this may cause rebound hypertension.

**Clinical Pearls.** Safety and efficacy not established in pediatric patients <6 y of age. Is not a first-line agent for managing hypertension, thiazides, calcium channel blockers are preferred for initial management

# LACOSAMIDE: Vimpat

**Class:** Anticonvulsant, Miscellaneous. C-V

**Dosage Forms. Oral Tablet:** 50 mg, 100 mg, 150 mg, 200 mg; **Oral Solution:** 10 mg/mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Partial onset seizure: Initial, 100 mg po bid, may titrate by 50 mg increments to *max* of 200 mg po bid

**Off-Label Uses.** None

**MOA.** Lacosamide stabilizes hyperexcitable neuronal membranes and inhibits neuronal firing

**Drug Characteristics: Lacosamide**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | *Max* dose 300 mg in mild to moderate hepatic dysfunction, avoid in severe hepatic dysfunction | **Absorption** | F = 100% |
| **Dose Adjustment Renal** | CrCl ≤30 ml/min, *max* dose is 300 mg | **Distribution** | Vd = 0.6 L/kg |
| **Dialyzable** | Removed by hemodialysis | **Metabolism** | Hepatic, CYP3A4/5, 2C9 and 2C19 substrate |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 95% (40% unchanged) with a half-life of 13 h |
| **Lactation** | Excretion into breast milk unknown, weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

**Medication Safety Issues: Lacosamide**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Zonisamide | No |

### Drug Interactions: Lacosamide

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP2C9, CYP3A4/5 inhibitors | Decreased lacosamide metabolism increases risk of lacosamide toxicity | Consider dose decreases of lacosamide if concurrent strong CYP3A4/5 or CYP2C9 inhibitors or poor renal or hepatic function, monitor and consider dose reduction if concurrent moderate inhibitors |
| CYP2C9, CYP3A4/5 inducers | Increased lacosamide metabolism decreases lacosamide efficacy | Consider dose increases of lacosamide if concurrent strong CYP3A4/5 or CYP2C9 inhibitors, monitor and consider dose increase if concurrent moderate inhibitors |

### Adverse Reactions: Lacosamide

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Dizziness, fatigue, ataxia, nausea, tremor, diplopia | Syncope, drowsiness, diarrhea, pruritus, nystagmus, increased liver enzymes | Acute psychosis, bradycardia, hepatotoxicity, agranulocytosis, suicidiality |

**Efficacy Monitoring Parameters.** Decreased seizures.

**Toxicity Monitoring Parameters.** Obtain ECG prior to initiating therapy in patients with underlying risk of conduction disorders. CBC, LFTs and SCr at initiation and periodically during therapy.

**Key Patient Counseling Points.** May be taken without regard to food but at same time of day. Take with food if GI distress. For the oral solution, measure carefully with oral syringe. Seek medical attention if seizure frequency increases or seizures worsen, abnormal heartbeat or extreme dizziness.

**Clinical Pearls.** May be used as monotherapy or added to other antiseizure medications for patients with resistant epilepsy. Start at 50 mg when used in combination.

# LAMOTRIGINE: Lamictal, Various

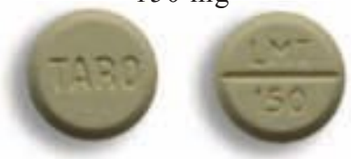
**Class:** Phenyltriazine Anticonvulsant

**Dosage Forms.** **Oral Chewable Tablet:** 2 mg, 5 mg, 25 mg; **Oral Tablet:** 25 mg, 100 mg, 150 mg, 200 mg; **Oral Tablet, Extended Release:** 25 mg, 50 mg, 100 mg, 200 mg, 250 mg, 300 mg; **Oral Dispersible Tablet:** 25 mg, 50 mg, 100 mg, 200 mg

200 mg

Teva generic pictured

150 mg




Taro generic pictured

100 mg

Taro generic pictured

25 mg

Teva generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Bipolar I disorder: Adults, 100-400 mg po daily
2. Partial seizure, adjunct or monotherapy, tonic-clonic seizure, Lennox-Gastaut syndrome, adjunctive: Adults and Children ≥12 y of age, Immediate Release, 100-500 mg/d po in 2 divided doses, Extended Release, 200-600 mg po daily; Children 2-12 y of age: Immediate Release, 1-15 mg/kg/d po in 1 or 2 divided doses, *max* 400 mg/d

**Off-Label Uses.** None

**MOA.** Lamotrigine is a phenyltriazine derivative unrelated to other marketed antiepileptic drugs (AEDs). Lamotrigine inhibits voltage-dependent sodium channels, thereby stabilizing neuronal membranes and reducing the release of excitatory neurotransmitters such as glutamate and aspartate.

**Drug Characteristics: Lamotrigine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Moderate-severe without ascites, reduce dose by 25%; severe with ascites, reduce dose by 50% | **Absorption** | F = 98%, no effect of food on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 0.9-1.3 L; 55% protein bound |
| **Dialyzable** | Yes (hemodialysis), 20% removed | **Metabolism** | 90% hepatic and occurs by glucuronidation |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 94% with a half-life of 25-70 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | Skin reactions |

### Medication Safety Issues: Lamotrigine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| ODT, XR | LamoTRIgine, LaMICtal | Extended-release formulation, oral dispersible tablet | No | Labetalol, LamISIL, lamiVUDine, levothyroxine, Lomotil | No |

### Drug Interactions: Lamotrigine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Enzyme inducers, rifampin, carbamazepine | Increased lamotrigine metabolism decreases lamotrigine efficacy | Monitor seizure control and consider dose increase of lamotrigine |
| Escitalopram | Increased risk of myoclonus through additive effect on calcium channels | Caution with concurrent use |
| Ethinyl estradiol and other estrogen-based birth control products | Decreased lamotrigine concentrations via increased metabolism | Use an alternative form of birth control or consider dose increase of lamotrigine |
| Risperidone | Increased risperidone plasma concentrations and risk of adverse effects via unknown mechanism | Monitor and use with caution |

### Adverse Reactions: Lamotrigine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Rash, ataxia, somnolence, headache, diplopia, rhinitis, nausea, vomiting, insomnia | Vertigo, anxiety, depression, dysmenorrhea | Stevens-Johnson syndrome, anemia, leukopenia, disseminated intravascular coagulation, thrombocytopenia, liver failure, aseptic meningitis, suicidal thoughts |

**Efficacy Monitoring Parameters.** Seizure severity and frequency if taken for seizures. Decrease in manic or depressive symptoms if for bipolar disorder.

**Toxicity Monitoring Parameters.** Seek medical attention if yellowing of skin or eyes, unusual bruising or bleeding, blistering skin rash, or shortness of breath.

**Key Patient Counseling Points.** Seek medical attention if rash develops. Slow titration necessary to minimize side effects. Avoid alcohol. Talk to your health-care provider if you become or plan to become pregnant. Review driving restrictions for patients with seizures. Place oral disintegrating tablet formulation on tongue and allow to dissolve.

**Clinical Pearls.** Rash is more common in children, when quickly titrated and with high starting doses. Rash usually occurs 2-8 wk after start of therapy. Extended-release products are not approved for use in children <13 y of age. Bipolar patients have an increased risk of suicide during first 24 wk of therapy. Avoid abrupt discontinuation, increases risk of seizures. Medication guide required at dispensing.

# LANSOPRAZOLE: Prevacid, Various

**Class:** Proton Pump Inhibitor

**Dosage Forms. Oral Capsule, Delayed Release:** 15 mg, 30 mg; **Oral Disintegrating Tablet:** 15 mg, 30 mg; **Powder for Oral Suspension:** 3 mg/mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Duodenal ulcer disease: 15 mg po daily × up to 4 wk
2. Gastric ulcer disease, treatment: 30 mg po daily × up to 8 wk
3. *Helicobacter pylori* GI tract infection, triple therapy: 30 mg po bid × 10-14 d in combination with amoxicillin 1000 mg and clarithromycin 500 mg po bid
4. Erosive esophagitis, GERD, treatment: Children 1-11 y of age and ≤30 kg, 15 mg po daily × 12 wk; Children >30 kg, 30 mg po daily × 12 wk; Children ≥12 y of age and Adults, 30 mg po daily × 8-16 wk
5. Zollinger-Ellison syndrome: 60 mg po bid up to 180 mg/d

**Off-Label Uses.**

1. Heartburn ≥2 d/wk: 15 mg po daily for up to 14 d (OTC labeling)
2. Drug-induced GI disturbance: 15 mg po daily

Takeda generic 30 mg pictured

Novartis 15 mg pictured

**MOA.** Lansoprazole is a proton pump inhibitor (PPI) that, when protonated in the secretory canaliculi of the parietal cells, covalently binds to $H^{++}$/K+-ATPase (proton pump), which is the final pathway for acid secretion.

**Drug Characteristics: Lansoprazole**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Consider dose adjustments in severe liver disease | **Absorption** | F = 80%, brief delay in reaching peak if taken with food, but no effect of food on overall absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 14-18 L; 97% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | 70-75% hepatic, CYP2C19 and CYP3A4/5 substrate |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 15-25% with a half-life of 90 min |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | Caution with CYP2C19 poor metabolizers |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

**Medication Safety Issues: Lansoprazole**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| 24 HR; SoluTab | No | Do not crush, chew, or open delayed release capsule or SoluTab | No | Aripiprazole, dexlansoprazole | No |

### Drug Interactions: Lansoprazole

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Antacids | Increase gastric pH and prevent dissolution of lansoprazole granules, reducing bioavailability of lansoprazole | Administer lansoprazole at least 1 h after antacid therapy |
| Clopidogrel | May decrease the effect of clopidogrel on platelet inhibition, resulting in cardiovascular events (MI, stroke, death) | Avoid concurrent use; consider alternative acid-reducing agent such as $H_2$ inhibitor |
| CYP2C19 and CYP3A4/5 inducers | Increased metabolism of lansoprazole, decreased efficacy | Avoid concurrent use or increase dose of lansoprazole |
| CYP2C19 and CYP3A4/5 inhibitors | Decreased metabolism of lansoprazole and increased risk of lansoprazole toxicity | Avoid concurrent use or decrease dose of lansoprazole |
| pH-dependent drugs (erlotinib, mycophenolate, etc) | As lansoprazole lowers gastric pH, absorption of drugs that require acid environment is reduced | Avoid concurrent use |

### Adverse Reactions: Lansoprazole

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Diarrhea, headache | Stevens-Johnson syndrome, rhabdomyolysis, acute interstitial nephritis, *Clostridium diff cle* diarrhea, hypomagnesemia |

**Efficacy Monitoring Parameters.** Resolution of GI discomfort, resolution of ulcers shown on endoscopy; for treatment of *H. pylori*, negative urea breath test.

**Toxicity Monitoring Parameters.** Seek medical attention if severe headache or blistering skin rash occurs.

**Key Patient Counseling Points.** Should be taken on an empty stomach 1 h before eating. Should not be taken with antacids. For those unable to swallow capsules, capsules may be opened and sprinkled on 1 tablespoon of applesauce if intact granules swallowed immediately.

**Clinical Pearls.** Multiple *H. pylori* regimens exist that include different combinations of PPIs and antibiotics; counsel patient to complete full regimen if prescribed for *H. pylori* management. Other PPI and $H_2$ antagonists available OTC; warn patients not to take multiple products concurrently to avoid additive risk of adverse effects. Increased risk of bone fracture with long-term use, use with caution in those with osteoporosis. Medication guide required at dispensing.

# LATANOPROST: Xalatan, Various

**Class:** Prostaglandin, Antiglaucoma Agent

**Dosage Forms.** **Ophthalmic Solution:** 0.005%

**Common FDA Label Indication, Dosing, and Titration.**

1. Ocular hypertension, open-angle glaucoma: 1 drop in affected eye(s) daily in the evening

**Off-Label Uses.** None

**MOA.** Latanoprost is a prostaglandin F2-alpha analog. It is believed to reduce IOP by increasing the outflow of aqueous humor. Studies suggest that the main mechanism of action is increased uveoscleral outflow, but the exact mechanism is unknown.

**Drug Characteristics: Latanoprost**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Absorbed through the cornea where the isopropyl ester prodrug is hydrolyzed to the acid form to become biologically active. Systemic absorption following ocular instillation is very low |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 0.16 L/kg |
| **Dialyzable** | Not dialyzable | **Metabolism** | Metabolized within the cornea; any entering systemic circulation is metabolized in the liver, extent unknown |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 88-98% with a half-life of 17 min |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

Pfizer 0.005% solution pictured

L

### Medication Safety Issues: Latanoprost

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Lantus, Travatan, Xalacom | No |

### Drug Interactions: Latanoprost

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Pilocarpine | Coadministration decreases access of latanoprost to the receptor and increases resistance to flow through the uveoscleral pathway | Bedtime dose of pilocarpine should be given at least 10 min (preferably 1 h) after latanoprost |

### Adverse Reactions: Latanoprost

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Blurred vision, itching, sensation of foreign body in eye, hyperpigmentation of eyelid, iris pigmentation | Dry eye, eyelid edema | Macular retinal edema, diplopia, keratitis |

**Efficacy Monitoring Parameters.** Reduction in IOP.

**Toxicity Monitoring Parameters.** Seek medical attention if symptoms of ocular irritation are severe.

**Key Patient Counseling Points.** Wash hands and remove contact lenses before using the medicine. For administration, lie down or tilt your head back. With your index finger, pull down the lower lid of your eye to form a pocket. Hold the dropper close to your eye with the other hand. Drop the correct number of drops into the pocket made between your lower lid and eyeball. Gently close your eyes. Place your index finger over the inner corner of your eye for 1 min. Do not rinse or wipe the dropper or allow it to touch anything, including your eye. Put the cap on the bottle right away.

**Clinical Pearls.** If used concurrently with pilocarpine, separate dose by 1 h if possible. Separate administration from other ophthalmic products by at least 5 min. Advise patients that there is a risk of permanent increased iris pigmentation associated with instillation of this product. Do not administer more than once daily to avoid loss of therapeutic effect. Store intact bottles under refrigeration. Opened bottles may be stored at room temperature for 6 wk.

# LEVALBUTEROL: Xopenex HFA

**Class:** Selective $\beta_2$-Agonist; Bronchodilator

**Dosage Forms. Metered Dose Inhaler:** 0.045 mg/actuation; **Nebulization Solution:** 0.31 mg/3 mL, 0.63 mg/3 mL, 1.25 mg/3 mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Asthma, bronchospasm: Adults and Children ≥4 y of age, MDI, 2 inhalations q4-6h prn (*max* 2 inhalations q4h); by nebulizer, 0.63 mg TID (*max* 1.25 mg TID)

**Off-Label Uses.**

1. Asthma, acute exacerbation: Children ≥4 y of age, MDI, 4-8 inhalations q20min × 3 doses, then q1-4h prn; Adults, MDI, 4-8 inhalations po q20min up to 4 h, then q1-4h prn; by nebulizer, 1.25-2.5 mg q20min × 3 doses, then q1-4h prn

**MOA.** Activation of $\beta_2$-adrenergic receptors on airway smooth muscle leads to the activation of adenylate cyclase and to an increase in the intracellular concentration of cyclic-3′, 5′-adenosine monophosphate (cyclic AMP). The increase in cyclic AMP is associated with the activation of protein kinase A, which in turn inhibits the phosphorylation of myosin and lowers intracellular ionic calcium concentrations, resulting in muscle relaxation. Levalbuterol relaxes the smooth muscles of all airways, from the trachea to the terminal bronchioles.

Sepracor pictured

## Drug Characteristics: Levalbuterol

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 30% after oral administration |
| **Dose Adjustment Renal** | Not required | **Distribution** | After inhalation, Vd is ~1900 L |
| **Dialyzable** | Not dialyzable | **Metabolism** | Oral doses undergo rapid metabolism in the GI tract; hepatic metabolism of inhaled doses |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 80-100% with a half-life of 5-7 min |
| **Lactation** | Compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

## Medication Safety Issues: Levalbuterol

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| HFA | No | No | No | Xanax | No |

### Drug Interactions: Levalbuterol

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Other short-acting sympathomimetics | May potentiate levalbuterol effect | Avoid concurrent use |
| Beta-blockers | May decrease effectiveness of levalbuterol and produce bronchospasm | Avoid use of nonselective beta-blockers in patients with asthma; monitor PFTs if cardioselective beta-blockers clinically indicated |

### Adverse Reactions: Levalbuterol

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Vomiting | Chest pain, palpitations, tachyarrhythmia, tremor, pharyngitis, rhinitis | Paradoxical bronchospasm, anaphylaxis, cardiac dysrhythmias |

**Efficacy Monitoring Parameters.** Resolution of asthma symptoms and improvement in PFTs.

**Toxicity Monitoring Parameters.** BP, HR.

**Key Patient Counseling Points.** Instruct patient on proper inhaler technique. Wash the mouthpiece and air dry thoroughly at least once a week (may cease to deliver medication if mouthpiece becomes blocked). Store the inhaler at room temperature, away from heat and direct light. Do not freeze. Do not keep this medicine inside a car where it could be exposed to extreme heat or cold. Contact prescriber if the need to use more levalbuterol to control symptoms than usual as this may indicate asthma deterioration.

**Clinical Pearls.** The National Heart, Lung and Blood Institute asthma guidelines recommend SABA as the drug of choice for treating acute asthma symptoms and exacerbations. SABA are not recommended for regularly scheduled, daily, long-term use.

# LEVETIRACETAM: Keppra, Keppra XR, Various

Mylan generic
250 mg pictured

Mylan generic
500 mg pictured

Teva generic
1000 mg pictured

**Class:** Anticonvulsant

**Dosage Forms.** **Tablet:** 250 mg, 500 mg, 750 mg, 1000 mg; **Tablet, Extended Release:** 500 mg, 750 mg; **Oral Solution:** 100 mg/mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Myoclonic seizure, adjunct: Children ≥12 y of age and Adults, initial, 500 mg po bid, titrate to target dose of 3000 mg/d
2. Partial seizure, adjunct: Children ≥16 y of age and Adults, immediate release, initial, 500 mg po bid, *max* 3000 mg/d; extended release, initial, 1000 mg po qd, *max* 3000 mg/d; Children 4-15 y of age, immediate release, initial, 10 mg/kg po bid, *max* 60 mg/kg/d
3. Tonic-clonic seizure, primary generalized, adjunct: Children ≥16 y of age and Adults, initial, 500 mg po bid, titrate to target dose of 3000 mg/d; Children 6-15 y of age, initial, 10 mg/kg po bid, titrate to target dose of 60 mg/kg/d

**Off-Label Uses.** None

**MOA.** Levetiracetam is a pyrrolidine derivative that is structurally unrelated to other AEDs. Its mechanism of action is unclear and does not relate to any known mechanisms of neuronal excitation or inhibition. The action of levetiracetam in animal models of seizures and epilepsy is unique from other AEDs.

**Drug Characteristics: Levetiracetam**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 100%; minor effect of food on absorption |
| **Dose Adjustment Renal** | CrCl <30 mL/min, reduce dose by 67%; CrCl = 30-50 mL/min, reduce dose by 50% | **Distribution** | <10% protein bound |
| **Dialyzable** | CrCl <30 mL/min, reduce dose by 67%; CrCl = 30-50 mL/min, reduce dose by 50% | **Metabolism** | Minimal and via hydrolysis |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 66% unchanged and 20-25% in feces, with a half-life of 6-8 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

### Medication Safety Issues: Levetiracetam

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| Keppra Keppra XR | LevETIRAcetam | Do not crush ER tablets | No | LevOCARNitine, levofloxacin | No |

### Drug Interactions: Levetiracetam

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Carbamazepine | Increased risk of carbamazepine toxicity | Use caution with concomitant therapy; monitor for side effects |

### Adverse Reactions: Levetiracetam

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Asthenia, fatigue, headache, somnolence, vomiting | Abnormal behavior, agitation, depression, diarrhea, dizziness, hostile behavior, irritability, loss of appetite, mood swings, nausea, nasopharyngitis, neck pain | Pancytopenia, hepatotoxicity, suicidal thoughts, suicide |

**Efficacy Monitoring Parameters.** Reduction in the frequency and severity of seizures.

**Toxicity Monitoring Parameters.** Emergence or worsening of depression, suicidal behavior or ideation, or unusual changes in behavior, WBC, LFTs.

**Key Patient Counseling Points.** Instruct patient to swallow extended-release tablet whole; do not chew, break, or crush. Avoid activities requiring mental alertness or coordination until drug effects are realized. Report mood swings, agitation, hostile behavior, suicidal ideation, or unusual changes in behavior. Avoid sudden discontinuation of drug, may increase seizure activity.

**Clinical Pearls.** Safety and efficacy of tablets and solution not established in children <4 y of age. Safety and efficacy of extended-release tablet not established in children <16 y of age. Patients weighing <20 kg should be dosed with the oral solution. Data suggest an increased risk of suicidal behavior or ideation may exist in patients receiving therapy with AEDs. Pregnancy: up to a 50% dose increase during 3rd trimester with subsequent dose reduction after delivery may be necessary. Do not stop abruptly, increased risk of seizures. Dispense with medication safety guideline.

# LEVOCETIRIZINE: Xyzal

**Class:** Antihistamine

**Dosage Forms.** **Oral Solution:** 2.5 mg/5 mL; **Oral Tablet:** 5 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Idiopathic urticaria, perennial or seasonal allergic rhinitis: Children 6 mo to 5 y of age, 1.25 mg po daily; Children 6-11 y of age, 2.5 mg po daily; Children ≥12 y of age and Adults, 5 mg po daily; doses should be given in the evening

Sanofi-Aventis 5 mg pictured

**Off-Label Uses.** None

**MOA.** Levocetirizine, an enantiomer of cetirizine, is a low-sedating, long-acting $H_1$-receptor antagonist that is a metabolite of hydroxyzine. It competitively inhibits the interaction of histamine with $H_1$ receptors, thereby preventing the allergic response.

**Drug Characteristics: Levocetirizine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 85%, limited effect of food on absorption |
| **Dose Adjustment Renal** | CrCl = 30-50 mL/min, 2.5 mg po every other day; CrCl = 10-29 mL/min, 2.5 mg po twice per wk; CrCl <10 mL/min, avoid | **Distribution** | Vd = 0.4 L/kg with 95% protein binding |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic metabolism, <14% |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 85% (80% unchanged) with a half-life of 7-8 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to cetirizine, levocetirizine, hydroxyzine, patients with CrCl <10 mL/min, children <12 y with any renal impairment, any patient on hemodialysis | **Black Box Warnings** | None |

**Medication Safety Issues: Levocetirizine**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Cetirizine | No |

### Drug Interactions: Levocetirizine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CNS depressants (opioids, benzodiazepines, alcohol) | Possible increase in sedation effects | Use concurrently with caution |

### Adverse Reactions: Levocetirizine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Diarrhea in children | Sedation, headache, dry mouth, fatigue, and nausea | Agitation, seizures |

**Efficacy Monitoring Parameters.** Improvement in rhinitis or urticaria symptoms.

**Toxicity Monitoring Parameters.** Seek medical attention for signs of severe CNS toxicity; monitor SCr.

**Key Patient Counseling Points.** Patients should avoid activities requiring mental alertness or coordination until drug effects are known, as drug may cause dizziness or sedative effects.

**Clinical Pearls.** An expensive alternative to racemic version (cetirizine) which is available generically and over the counter. Limited evidence suggesting any advantage over racemic compound.

# LEVOFLOXACIN: Levaquin, Various

**Class:** Fluoroquinolone Antibiotic

**Dosage Forms. Oral Solution:** 25 mg/mL; **Oral Tablet:** 250 mg, 500 mg, 750 mg

Ortho-McNeil-Janssen pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Bacterial prostatitis, chronic: 500 mg po daily × 28 d
2. Bacterial sinusitis, acute: 750 mg po daily × 5 d
3. Bronchitis, chronic, acute bacterial exacerbation: 500 mg po daily × 7 d
4. Community acquired pneumonia: 500-750 mg po daily × 7-14 d
5. Infection of skin and/or subcutaneous tissue: (uncomplicated) 500 mg po daily × 7-14 d
6. Pyelonephritis, acute: 250 mg po daily × 10 d

**Off-Label Uses.**

1. Chlamydial infection: 500 mg po daily × 7 d
2. Traveler's diarrhea: 500 mg po daily × 1-3 d

**MOA.** Levofloxacin is a fluoroquinolone that inhibits bacterial DNA gyrase, an enzyme responsible for the unwinding of DNA for transcription and subsequent supercoiling of DNA for packaging into chromosomal subunits. It is highly active against aerobic, gram-negative bacilli.

## Drug Characteristics: Levofloxacin

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 99%, no food effect, take without regard to meals |
| **Dose Adjustment Renal** | CrCl 20-50 mL/min, reduce dose by 50%; CrCl 5-19 mL/min, extend interval to 48 h | **Distribution** | Bile, blister, CSF, gynecologic tissues, lung, prostate, synovial fluid, sputum, tonsils |
| **Dialyzable** | Not dialyzable | **Metabolism** | Not metabolized |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 87% with a half-life of 6-8 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to ciprofloxacin or other quinolones; concomitant tizanidine administration | **Black Box Warnings** | Myasthenia gravis; tendon rupture |

## Medication Safety Issues: Levofloxacin

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | LevETIRAcetam | No |

### Drug Interactions: Levofoxacin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Antidiabetics | Hypogycemic or hyperglycemic episodes, mechanism unknown | Caution with concurrent use, monitor plasma glucose and consider dose adjustments of antidiabetic agent |
| Aluminum, calcium, and calcium-fortified foods, didanosine, iron | Decreased absorption of fluoroquinolones caused by chelation | Separate administration by 2 h before or 6 h after |
| Class III antiarrhythmic agents or other agents that effect the QTc interval | Additive potential for QTc prolongation | Contraindicated |
| Corticosteroids | Increased risk if tendon rupture | Counsel patients to discontinue levofoxacin and seek medical attention if tendon pain or rupture |
| NSAIDs | Increased risk of seizures via inhibition of GABA resulting in CNS stimulation | Avoid NSAIDs if possible |
| Warfarin | Increased risk of bleeding | Increased monitoring of INR and warfarin adjustments |

### Adverse Reactions: Levofoxacin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Photosensitivity | Nausea and vomiting, rash, myalgia, arthralgia, tendinitis, headache | Stevens-Johnson syndrome, renal failure, severe hypersensitivity, anemia, neutropenia, thrombocytopenia, seizure, cardiac arrest, cardiac arrhythmias, liver failure, tendon rupture, psychosis, glucose abnormalities, *C. diffcile* colitis |

**Efficacy Monitoring Parameters.** Resolution of signs and symptoms of infection.

**Toxicity Monitoring Parameters.** Baseline SCr.

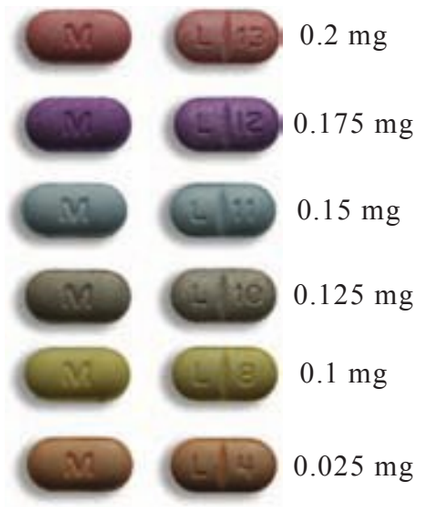
**Key Patient Counseling Points.** Seek medical attention if decreased urination, yellowing of eyes, blistering skin rash or extreme fatigue, unusual bruising or bleeding, shortness of breath or chest pain, or tendon pain. Take with or without food, but not with milk, yogurt, or other dairy products or calcium-fortified products (some juices and breads). If using antacids, sucralfate, or mineral supplements and multivitamins with calcium, iron, or zinc, take levofloxacin at least 2 h before or 6 h after these medicines.

**Clinical Pearls.** Not approved in children <18 y of age. Oral and IV dosing is interchangeable. Increased risk of tendon rupture in patients >60 y of age. Medication guide required at dispensing.

# LEVOTHYROXINE: Synthroid, Various

**Class:** Thyroid Supplement

**Dosage Forms.** **Oral Tablet:** 25 mcg, 50 mcg, 75 mcg, 88 mcg, 100 mcg, 112 mcg, 125 mcg, 137 mcg, 150 mcg, 175 mcg, 200 mcg, 300 mcg; **Oral Capsule:** 13 mcg, 25 mcg, 50 mcg, 75 mcg, 100 mcg, 112 mcg, 125 mcg, 137 mcg, 150 mcg



Mylan generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Hypothyroidism: Oral, maintenance, individualized based on clinical response and serum TSH levels; Adults, 25-300 mcg po daily; Infants 0-3 mo of age, 10-15 mcg/kg/d po daily, Infants 3-6 mo of age, 8-10 mcg/kg/d po daily, Infants 6-12 mo of age, 6-8 mcg/kg/d po daily, Children 1-5 y of age, 5-6 mcg/kg/d po daily, Children 6-12 y of age, 4-5 mcg/kg/d po daily, Children ≥12 y of age, growth and puberty incomplete) 2-3 mcg/kg/d po daily, Children ≥12 y of age, growth and puberty complete, 1.7 mcg/kg/d
2. Thyroid-stimulating hormone suppression, pituitary: Thyroid cancer, doses >2 mcg/kg/d po are usually required to suppress TSH <0.1 milliunits/L

**Off-Label Uses.**

1. Toxicity due to radiotherapy; use same age-based dosing as hypothyroidism

**MOA.** Levothyroxine sodium is a synthetic thyroid hormone. The endogenous thyroid hormones, T3 and T4, diffuse into the cell nucleus and bind to thyroid receptor proteins attached to DNA. This hormone nuclear receptor complex activates gene transcription and synthesis of messenger RNA and cytoplasmic proteins.

**Drug Characteristics: Levothyroxine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 40-80%, increases with fasting |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 8.7-9.7 L; >99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Approximately 80% of levothyroxine sodium is deiodinated into T3 in the liver, kidney, and other tissues. It can also be metabolized by conjugation with glucuronides and sulfates and then enter into enterohepatic recirculation |
| **Pregnancy Category** | A | **Elimination** | Renal excretion is 50% with a half-life of 7 d |
| **Lactation** | Compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity, nontoxic diffuse goiter or nodular thyroid disease, thyrotoxicosis, acute MI, treatment of obesity or weight loss, uncorrected adrenal insufficiency; may precipitate acute adrenal crisis | **Black Box Warnings** | Not for weight reduction |

## Medication Safety Issues: Levothyroxine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | LamoTRIgine, Lanoxin, levofloxacin, liothyronine | No |

## Drug Interactions: Levothyroxine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Aluminum, calcium- and magnesium-containing antacids, iron, sucralfate, orlistat, etc | Decreased absorption of levothyroxine | Separate administration by 4 h |
| Estrogens | Estrogen-induced increases in serum thyroxine-binding globulin concentration | Monitor and consider increasing dose of levothyroxine |
| Eltrombopag | Inhibition of OATP1B1-mediated elimination of levothyroxine by eltrombopag | Monitor and consider decreasing dose of levothyroxine |
| Imatinib | Decreased levothyroxine effectiveness and worsening of hypothyroidism | Monitor and consider increasing dose of levothyroxine |
| Phenytoin, rifampin, simvastatin | Increased levothyroxine clearance | Monitor and consider increasing dose of levothyroxine |
| Warfarin | Enhanced anticoagulant effect | Monitor and consider warfarin dose adjustment |

## Adverse Reactions: Levothyroxine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Appetite decreased, anxiety, diarrhea, insomnia | Aggravation of preexisting cardiovascular disease, hyperthyroidism |

**Efficacy Monitoring Parameters.** Serum TSH, T(3), and T(4) levels. T(3) normal range is 100-200 ng/dL. T(4) normal range is 4.5-11.2 mcg/dL. Free T4 normal range is 0.7-1.8 ng/dL. TSH level should be between 0.5 and 3.0 mIU/L in those treated for a thyroid disorder. Resolution of symptoms of hypothyroidism, fatigue, edema, hair loss, cold intolerance, and lethargy.

**Toxicity Monitoring Parameters.** Monitor patients with preexisting cardiovascular disease for exacerbation of symptoms.

**Key Patient Counseling Points.** May require 6-8 wk for symptomatic improvement. Avoid abrupt discontinuation. Take on an empty stomach, with water at least 30 min before food. Avoid antacids and iron within 4 h of dose.

**Clinical Pearls.** Not recommended for weight loss. May cause serious adverse effects and death in euthymic patients using it for weight loss.

# LIDOCAINE TOPICAL PATCH: Lidoderm

Endo 5% patch pictured

**Class:** Local Anesthetic

**Dosage Forms.** **Topical Patch:** 5%

**Common FDA Label Indication, Dosing, and Titration.**

1. Postherpetic neuralgia and localized pain: 1-3 patches topically simultaneously for up to 12 h within a 24-h period

**Off-Label Uses.** None

**MOA.** Lidocaine is an amide-type local anesthetic agent and is suggested to stabilize neuronal membranes by inhibiting the ionic fluxes required for the initiation and conduction of impulses. The penetration of lidocaine in patch form into intact skin is sufficient to produce an analgesic effect, but less than the amount necessary to produce a complete sensory block.

## Drug Characteristics: Lidocaine Topical Patch

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Severe hepatic dysfunction, use fewer patches, for shorter periods of time, and/or with longer treatment-free intervals | **Absorption** | Only 3% of administered dose is absorbed systemically when applied to intact skin |
| **Dose Adjustment Renal** | Not required | **Distribution** | Not absorbed |
| **Dialyzable** | Yes | **Metabolism** | Not absorbed |
| **Pregnancy Category** | B | **Elimination** | Not absorbed |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

## Medication Safety Issues: Lidocaine Topical Patch

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | No |

**Drug Interactions: Lidocaine Topical Patch.** Minimal systemic absorption, none known.

## Adverse Reactions: Lidocaine Topical Patch

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Skin irritation, somnolence | Hypotension, nausea, vomiting, confusion, dizziness, headache, paresthesia, constipation, tremor | Cardiac arrest, cardiac dysrhythmia, seizure, methemoglobinemia |

**Efficacy Monitoring Parameters.** Relief from pain.

**Toxicity Monitoring Parameters.** Application of too many patches, for too long a period of time, and/or without adequate drug-free period may increase toxicity; application to broken skin or covering with occlusive dressing may lead to toxicity, particularly cardiac dysrhythmia.

**Key Patient Counseling Points.** Instruct patients on the appropriate application process. Leave patches on skin for no more than12 h within a 24-h period. Caution patients to administer only as directed, to intact skin, without covering with occlusive dressing or tight clothes.

**Clinical Pearls.** Patches may be cut into smaller sizes prior to removal of release liner to refine dose to meet patients' needs. Patients should be instructed to fold used patches after removal so that the adhesive side sticks to itself and safely discard used patches or pieces of cut patches where children and pets cannot get to them. Accidental ingestion of used patches can lead to serious adverse effects.

# LINAGLIPTIN: Tradjenta

**Class:** Dipeptidyl peptidase IV inhibitor

**Dosage Forms. Oral Tablet:** 5 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Diabetes, type 2: 5mg po daily

**Off-Label Uses.** None

**MOA.** Binds to and inhibits the dipeptidyl peptidase IV enzyme, resulting in prolonged incretin levels. Incretin hormones regulate glucose metabolism by increasing insulin secretion and release.

**Drug Characteristics: Linagliptin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 30% |
| **Dose Adjustment Renal** | Not required | **Distribution** | Protein binding 70-80% |
| **Dialyzable** | Unknown | **Metabolism** | Hepatic, CYP3A4/5 substrate, P-glycoprotein substrate |
| **Pregnancy Category** | B | **Elimination** | 80% in the feces unchanged. Half-life is 12 h, enzyme binding can persist >100 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

**Medication Safety Issues: Linagliptin**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | Yes | No | No |

### Drug Interactions: Linagliptin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inhibitors | Decreased linagliptin metabolism increases risk of linagliptin toxicity | Avoid strong CYP3A4/5 inhibitors, moderate inhibitors, monitor carefully and consider linagliptin dose reduction |
| CYP3A4/5 inducers | Increased linagliptin metabolism decreases linagliptin efficacy | Avoid strong CYP3A4/5 inducers, monitor carefully and consider linagliptin dose increases |
| P-glycoprotein inhibitors | Decreased linagliptin transport increases risk of linagliptin toxicity | Monitor carefully and consider linagliptin dose reduction |
| P-glycoprotein inducers | Increased linagliptin transport decreases linagliptin efficacy | Monitor carefully and consider linagliptin dose increases |
| Corticosteroids, thiazide diuretics | May decrease the hypoglycemic effect of linagliptin | Monitor and consider dose adjustments of linagliptin |

### Adverse Reactions: Linagliptin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Hypoglycemia | Headache, weight gain, diarrhea, arthralgia | Acute pancreatitis, anaphylaxis, angioedema, hypersensitivity |

**Efficacy Monitoring Parameters.** Preprandial blood glucose between 70 and 130 mg/dL, $HbA_{1c}$ <7%

**Toxicity Monitoring Parameters.** Severe abdominal pain, hypoglycemia

**Key Patient Counseling Points.** Monitor blood glucose frequently (2-4 times per day); if <70 mg/dL eat candy or juice and contact prescriber. Take with or without food, but at same time each day.

**Clinical Pearls.** Metformin is first-line therapy for type 2 diabetes and has been shown to be more effective than DPP-4 monotherapy. Linagliptin may be added as a 2nd agent in patients not controlled on metformin or as first-line therapy in patients with contraindications for metformin, such as renal dysfunction.

# LIRAGLUTIDE: Victoza

**Class:** Glucagon-Like Peptide-1-Receptor Agonist

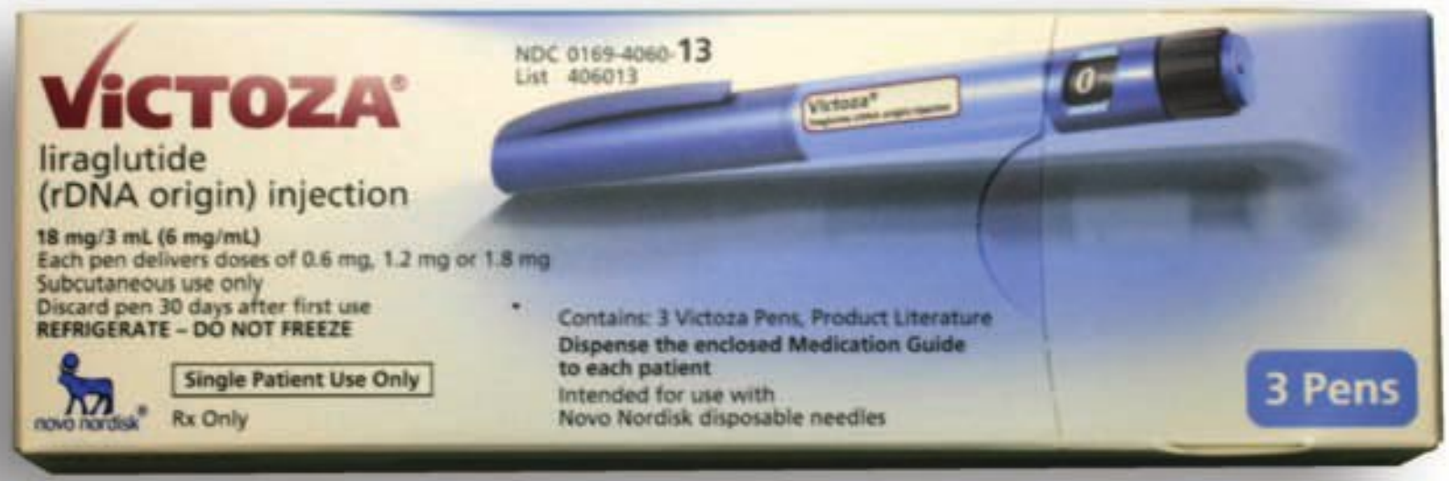
**Dosage Forms. Solution, Pen Injector:** 18 mg/3 mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Diabetes, type 2: 0.6 mg sq once daily for 1 wk, then increase to 1.2 mg sq once daily

**Off-Label Uses.** None

**MOA.** Analog of glucagon-like peptide-1, which increases glucose-dependent insulin secretion, decreases inappropriate glucagon secretion, slows gastric emptying, and decreased food intake.




**Drug Characteristics: Liraglutide**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Use with caution in patients with severe hepatic dysfunction | **Absorption** | F = 55% |
| **Dose Adjustment Renal** | Use with caution in patients with severe renal dysfunction | **Distribution** | Vd = 13L, protein binding >98% |
| **Dialyzable** | Unknown | **Metabolism** | Metabolized by dipeptidyl peptidase IV |
| **Pregnancy Category** | C | **Elimination** | 5% in the feces, 6% in urine, Half-life is 13 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity, multiple endocrine neoplasia syndrome type 2, history or family history of medullary thyroid carcinoma | **Black Box Warnings** | Increased risk of thyroid cancer |

### Medication Safety Issues: Liraglutide

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | Yes | No | No |

### Drug Interactions: Liraglutide

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Corticosteroids, thiazide diuretics | May decrease the hypoglycemic effect of liraglutide | Monitor and consider dose adjustments of liraglutide |

### Adverse Reactions: Liraglutide

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Nausea, diarrhea, vomiting | Headache, hyperbilirubinemia, antibody development, injection site reactions | Acute renal failure, thyroid carcinoma, exacerbation of chronic renal failure, hypoglycemia, pancreatitis, hypersensitivity |

**Efficacy Monitoring Parameters.** Pre-prandial blood glucose between 70 and 130 mg/dL, $HbA_{1c}$ <7%

**Toxicity Monitoring Parameters.** Severe abdominal pain, SCr, LFTs

**Key Patient Counseling Points.** Monitor blood glucose frequently (2-4 times per day); if <70 mg/dL eat candy or juice and contact prescriber. Administer in upper arm, thigh, or abdomen. Change needle for each injection, do not share pens, even if needle is changed. If also using insulin, administer with separate injection in a non-adjacent area. Can be injected without regard to meals.

**Clinical Pearls.** Metformin is first-line therapy for type 2 diabetes. Liraglutide may be added as a 2nd agent in patients not controlled on metformin. An advantage of liraglutide over other therapies is lack of weight gain and no hypoglycemia.

# LISDEXAMFETAMINE: Vyvanse

**Class:** Amphetamine, CNS Stimulant. C-II

**Dosage Forms. Oral Capsule:** 20 mg, 30 mg, 40 mg, 50 mg, 60 mg, 70 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Attention-deficit hyperactivity disorder (ADHD): 30 mg po daily in the morning, may titrate in 10-20 mg/d increments at weekly intervals to *max* dose of 70 mg po daily; discontinue if improvement not observed after 1 mo of dosage titration.

30 mg 40 mg 50 mg 60 mg

Shire generic pictured

**Off-Label Uses.** None

**MOA.** Lisdexamfetamine is converted to dextroamphetamine. The mechanism of action of dextroamphetamine in the treatment of ADHD is unknown. Amphetamines may block the reuptake of norepinephrine and dopamine at the presynaptic neuron and thus increase the release of norepinephrine and dopamine into the extraneuronal space.

**Drug Characteristics: Lisdexamphetamine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 100%, food has no effect on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 3.5-4.6 L/kg; 60% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive metabolism in the blood by hydrolytic activity of red blood cells to dextroamphetamine and l -lysine |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 96% and 0.3% in feces, with a half-life of <1 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity/idiosyncrasy to sympathomimetic amines; MAOIs; symptomatic cardiovascular disease or advanced arteriosclerosis; moderate-severe hypertension; hyperthyroidism; glaucoma; agitated states; history of drug dependence | **Black Box Warnings** | Risk of abuse, misuse, diversion |

### Medication Safety Issues: Lisdexamphetamine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Do not chew capsule, but may be opened and dissolved in water | No | Visanne, ViVAXIM | No |

### Drug Interactions: Lisdexamphetamine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Tricyclic antidepressants | Increased risk of hypertension, other cardiac effects, and CNS stimulation | Use caution with concomitant therapy; monitor BP and for side effects |
| MAOIs | Increased risk of hypertensive crisis (headache, hyperpyrexia, hypertension) | Concomitant use contraindicated |

### Adverse Reactions: Lisdexamphetamine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Dystonia, insomnia, hallucinations, irritability, loss of appetite, upper abdominal pain, xerostomia | Agitation, anxiety, decreased growth and development, diarrhea, dizziness, headache, increased BP, increased HR, nausea, rash, vomiting, weight loss | Chest pain, new onset or worsening of existing psychotic disorders, stroke, sudden cardiac death, tachycardia |

**Efficacy Monitoring Parameters.** Improvement of mental and behavioral symptoms of ADHD (inappropriate inattention, impulsivity, hyperactivity, and cognitive performance).

**Toxicity Monitoring Parameters.** Palpitations, near syncope, or syncope; may be indicative of a cardiac condition. BP and HR should be evaluated at baseline, during routine follow-up within 1-3 mo, and at follow-up visits every 6-12 mo.

**Key Patient Counseling Points.** Take dose in the morning with or without food. Growth rate and weight may need to be monitored more frequently for children using this drug. Report new or worsened psychiatric problems (behavior and thought problems, bipolar illness, aggressive behavior or hostility). Also report chest pain, palpitations, dyspnea, or signs/symptoms of cardiac dysrhythmia, myocardial infarction, or cerebrovascular accident. Capsule may be opened and the entire contents dissolved in a glass of water, stirring until dispersed completely and consuming entire mixture immediately.

**Clinical Pearls.** Amphetamines have a high potential for abuse, and administration for prolonged periods of time may lead to drug dependence and must be avoided. Misuse of amphetamines may cause sudden death and serious cardiovascular adverse events. A complete family and patient history for conditions associated with sudden cardiac death is required and current use of any other prescription or over-the-counter medications needs to be determined. A complete physical evaluation of the patient for hypertension, cardiac murmurs, physical findings associated with Marfan syndrome, and signs of irregular cardiac rhythms should be conducted. Medication guide required at dispensing.

# LISINOPRIL: Prinivil, Zestril, Various

**Class:** ACE-I, Antihypertensive

**Dosage Forms.** **Oral Tablet:** 2.5 mg, 5 mg, 10 mg, 20 mg, 30 mg, 40 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Acute myocardial infarction: 5-10 mg po daily × 6 wk
2. Heart failure: 2.5-5 mg po daily, may titrate to 40 mg/d
3. Hypertension: Adults, 10 mg po daily, may titrate to 80 mg/d; Children 6-16 y of age, 0.07 mg/kg (*max* 5 mg/d) po daily, may titrate to 0.61 mg/kg/d (*max* 40 mg/d)

**Off-Label Uses.** None

**MOA.** Lisinopril is a competitive ACE-I. It also reduces serum aldosterone, leading to decreased sodium retention, potentiates the vasodilator kallikrein–kinin system, and can alter prostanoid metabolism, inhibit the sympathetic nervous system, and inhibit the tissue renin–angiotensin system.

**Drug Characteristics: Lisinopril**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 25% (F = 16% in heart failure), no effect of food on absorption |
| **Dose Adjustment Renal** | CrCl 10-30 mL/min: initial dose 5 mg/d; CrCl <10 mL/min: initial dose is 2.5 mg/d; dialysis patients: initial dose is 2.5 mg/d, supplemental dose equivalent to 20% of daily dose after hemodialysis | **Distribution** | 25% protein bound |
| **Dialyzable** | Yes (hemodialysis and peritoneal) | **Metabolism** | Not metabolized |
| **Pregnancy Category** | C (1st trimester), D (2nd and 3rd trimesters) | **Elimination** | Renal elimination is 50-70% with a half-life of 12 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to lisinopril or other ACE-Is, history of ACE-I-induced angioedema, and hereditary or idiopathic angioedema, concurrent use with aliskerin in diabetic patients | **Black Box Warnings** | Pregnancy |

Teva generic pictured

### Medication Safety Issues: Lisinopril

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Fosinopril, Lioresal, ZyPREXA, RisperDAL | No |

### Drug Interactions: Lisinopril

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Angiotensin-receptor blockers, potassium-sparing diuretics | Increased risk of hypotension, hyperkalemia, nephrotoxicity | Avoid concurrent use or monitor BP, SCr, and potassium levels |
| Azathioprine | Increased risk of myelosuppression | Avoid concurrent use, or monitor for anemia or leukopenia |
| Cyclosporine | Increased risk of nephrotoxicity | Avoid concurrent use or monitor SCr levels |
| Diuretics | Increased risk of postural hypotension due to hypovolemia | Monitor BP; rise from seated position slowly |
| NSAIDs | Decreased antihypertensive and natriuretic effect of lisinopril, increased risk of nephrotoxicity | Avoid concurrent use or monitor BP and SCr |
| Potassium supplements, salt substitutes | Increased risk of hyperkalemia and cardiac arrhythmias | Avoid concurrent use or monitor serum potassium levels |

### Adverse Reactions: Lisinopril

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Diarrhea, dizziness, dry cough, headache, hypotension, hyperkalemia, nausea, nephrotoxicity, rash, tachycardia, vomiting | Angioedema, birth defects, liver failure |

**Efficacy Monitoring Parameters.** Decreased BP.

**Toxicity Monitoring Parameters.** Signs/symptoms of angioedema (swelling of the face, eyes, lips, tongue, or throat), severe persistent cough, hypotension; monitor baseline and periodic electrolytes, SCr, BUN, and urine protein.

**Key Patient Counseling Points.** Avoid pregnancy. Use potassium supplements or salt substitutes only under medical supervision. May cause dizziness that may worsen if dehydrated.

**Clinical Pearls.** Observe patients who are volume depleted for at least 2 h after taking the initial dose of lisinopril. As effective as atenolol in the treatment of hypertension. Recommended as first line therapy with HCTZ for HTN.

# LITHIUM CARBONATE: Eskalith, Eskalith-CR, Lithobid, Various

**Class:** Antimanic

**Dosage Forms.** **Oral Capsule:** 150 mg, 300 mg, 600 mg; **Oral Tablet:** 300 mg; **Oral Tablet, Extended Release:** 300 mg, 450 mg; **Oral Solution**: 300 mg/5 mL (as a citrate)

Roxane generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Bipolar disorder, maintenance therapy: Adults and Children >12 y of age, extended release, 900-1800 mg/d po in 2-3 divided doses; immediate release, initial 300 mg po daily, may titrate to 900-1800 mg po in 3-4 divided doses
2. Bipolar disorder, manic episode: Adults and Children >12 y of age, extended release, 1800 mg/d po in 2-3 divided doses; immediate release, 600 mg po tid

**Off-Label Uses.**

1. Depression: Adults and Children >12 y of age, extended release, 600-1200 mg/d po in 2-3 divided doses; immediate release, 300 mg po bid-qid

**MOA.** Lithium's mechanism of anti-manic effect is unknown; it alters the actions of several second-messenger systems (eg, adenylate cyclase and phosphoinositol). Alters cation transport across cell membrane in nerve and muscle cells and influences reuptake of serotonin and/or norepinephrine; second-messenger systems involving the phosphatidylinositol cycle are inhibited

**Drug Characteristics: Lithium**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 90-100%, food has no effect on absorption |
| **Dose Adjustment Renal** | CrCl 10-50 mL/min, give 50-75% of the usual dose; CrCL <10 mL/min, give 25-50% of usual dose at the normal dosing interval | **Distribution** | Vd = 1.4 L/kg, no protein binding |
| **Dialyzable** | Yes, a maintenance dose should be given following hemodialysis | **Metabolism** | Not metabolized |
| **Pregnancy Category** | D | **Elimination** | Renal elimination is 89-98% and <1% fecal elimination, with a half-life of 14-24 h (up to 2.43 d with long-term therapy) |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Severe debilitation, dehydration, or sodium depletion; significant cardiovascular disease; significant renal impairment; concomitant diuretic therapy | **Black Box Warnings** | Lithium levels required |

**Medication Safety Issues: Lithium**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| CR | No | Do not chew or crush ER formulations | No | Estratest | No |

### Drug Interactions: Lithium

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Acetazolamide, sodium bicarbonate | Decreased lithium concentrations and effectiveness | Monitor lithium efficacy and serum concentrations |
| ACE-Is, ARBs, diuretics | Increased risk of lithium toxicity and/or nephrotoxicity | Avoid concomitant use of ACI-Is and ARBs; diuretics are contraindicated |
| Agents that prolong QT interval | Additive cardiotoxicity | Avoid concurrent use or monitor ECGs |
| Antipsychotic drugs, clozapine | Increased risk of adverse effects and extrapyramidal symptoms | Monitor for adverse effects |
| MAOIs | Increased risk of malignant hyperpyrexia | Avoid concomitant use; allow 2 wk to elapse between discontinuation of MAOIs and initiation of lithium |
| SSRIs, linezolid | Increased lithium concentrations and/or an increased risk of serotonin syndrome | Monitor for adverse effects and lithium serum concentrations |

### Adverse Reactions: Lithium

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Cardiac dysrhythmias, fine tremor, hypothyroidism, leukocytosis, thrombocytosis, xerostomia | Ataxia, blurred vision, diarrhea, EEG changes, ECG changes, headache, muscle weakness, nausea, oliguria, polyuria, somnolence, tinnitus, vomiting | Hypotension, nephrotoxicity, seizure, hypercalcemia, hyperparathyroidism |

**Efficacy Monitoring Parameters.** Reduction in manic symptoms, prevention of manic and depressive episodes. Drug levels: between 1 and 1.5 mEq/L for acute mania and 0.6 and 1.2 mEq/L for long-term control; serum concentrations should not exceed 2.0 mEq/L during acute therapy. Drug levels should be drawn just prior to the next dose.

**Toxicity Monitoring Parameters.** Kidney and thyroid function, hydration status, sodium levels. Periodic EEG and ECG exams if medically warranted.

**Key Patient Counseling Points.** Swallow extended-release tablets whole; do not crush or chew. Avoid activities requiring mental alertness or coordination until drug effects are realized. Report signs/symptoms of toxicity, which may vary depending on the degree of toxicity. These may include diarrhea, vomiting, tremor, ataxia, drowsiness, muscle weakness, lack of coordination, giddiness, blurred vision, tinnitus, or large volumes of dilute urine. Maintain adequate fluid intake and normal salt intake.

**Clinical Pearls.** Safety and effectiveness in patients <12 y of age have not been established. Lithium toxicity is closely related to serum lithium levels and can occur at doses close to therapeutic levels. Ability to tolerate lithium is greater during the acute manic phase and decreases when manic symptoms subside. Do not confuse dosing in mEq versus mg. Doses should be in mg (300 mg = 8 mEq).

# LORAZEPAM: Ativan, Various

Sandoz generic pictured

Watson generic pictured

**Class:** Benzodiazepine, Short or Intermediate Acting. C-IV

**Dosage Forms.** **Oral Tablet:** 0.5 mg, 1 mg, 2 mg; **Oral Solution:** 2 mg/mL, 4 mg/mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Anxiety: Adults, 1 mg po bid-tid
2. Insomnia, due to anxiety or situational stress: Adults and Children >12 y of age, 2-4 mg po hs

**Off-Label Uses**

1. Alcohol withdrawal syndrome: Initial, 2 mg po qid, then 1 mg qid × 8 doses

**MOA.** Enhance the postsynaptic effect of the inhibitory neurotransmitter, GABA.

**Drug Characteristics: Lorazepam**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 90-93%, no effect of food on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 1.3 L/kg; 85% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensively metabolized via glucuronidation |
| **Pregnancy Category** | D | **Elimination** | Renal elimination is 88% with a half-life of 12 h in adults; increased half-life in other age groups |
| **Lactation** | Compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to benzodiaz-epines, narrow-angle glaucoma | **Black Box Warnings** | None |

### Medication Safety Issues: Lorazepam

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| Intensol | LORazepam | No | No | ALPRAZolam, clonazePAM | Avoid benzodiazepines (any type) for treatment of insomnia, agitation, or delirium |

### Drug Interactions: Lorazepam

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Alfentanil, opioids, and other respiratory depressants | Additive respiratory depression | Avoid if possible and consider dose reductions of both agents |
| Amitriptyline | Additive psychomotor defects | Monitor and advise patient |
| Ethinyl estradiol and other estrogen-based birth control products | Increased lorazepam metabolism and decreased effectiveness | May require higher dose of lorazepam |
| Valproic acid | Decreased metabolism of lorazepam | Reduce lorazepam dose by 50% |

### Adverse Reactions: Lorazepam

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Drowsiness, impaired motor coordination, retrograde amnesia | Asthenia, dizziness, blurred vision, depression | Seizures, mania, depression, withdrawal symptoms |

**Efficacy Monitoring Parameters.** Reduction in anxiety symptoms, alcohol withdrawal symptoms (BP, tremor), onset of sleep.

**Toxicity Monitoring Parameters.** Seek medical attention if severe drowsiness, thoughts of suicide, or seizures; monitor BP, HR.

**Key Patient Counseling Points.** May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol.

**Clinical Pearls.** May be benzodiazepine of choice in impaired liver function and for nursing mothers. Use caution in elderly, appear more sensitive to the effects; dose reductions of 50% have been recommended. Avoid abrupt discontinuation after chronic use, may cause seizures. Safety not established for children <12 y of age.

# LOSARTAN: Cozaar, Various

**Class:** Angiotensin II Receptor Antagonist, Antihypertensive

**Dosage Forms.** **Oral Tablet:** 25 mg, 50 mg, 100 mg

Merck 100 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Hypertension: Adults, initial 50 mg po daily, may titrate to 25-100 mg po daily or bid; Children ≥6 y of age, 0.7 mg/kg po daily, *max* 50 mg po daily
2. Heart failure: Initial, 12.5 mg po daily, maintenance 50 mg po daily
3. Reduce risk of cerebrovascular accident, in hypertensive patients with left ventricular hypertrophy; prophylaxis, diabetic nephropathy: Initial, 50 mg po daily, may titrate to 100 mg podaily
4. Diabetic nephropathy: Initial, 50 mg daily, may titrate based on BP up to 100 mg po daily

**Off-Label Uses.**

1. Cardiovascular event risk, reduction: Adults, 50-100 mg po daily
2. Isolated systolic hypertension, left ventricular hypertension, nondiabetic kidney disease: 50 mg po daily

**MOA.** Losartan is a selective, reversible, competitive antagonist of the angiotensin II receptor (AT1), which is responsible for the physiologic effects of angiotensin II including vasoconstriction, aldosterone secretion, sympathetic outflow, and stimulation of renal sodium reabsorption.

## Drug Characteristics: Losartan

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Starting dose, 25 mg po daily, *max* 100 mg/d | **Absorption** | F = 33%, food slows absorption and decreases Cmax by 10% |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 34 L; 99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | 14% hepatic, CYP2C9 and CYP3A4/5 substrate |
| **Pregnancy Category** | C (1st trimester), D (2nd and 3rd trimesters) | **Elimination** | Renal elimination is 35% and fecal elimination is 60% with a half-life 2 h (6-9 h for active metabolite, 5-carboxylic acid) |
| **Lactation** | Not recommended | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to losartan or other angiotensin II receptor antagonists, pregnancy | **Black Box Warnings** | Pregnancy |

## Medication Safety Issues: Losartan

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Colace, Coreg | No |

### Drug Interactions: Losartan

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| ACE-Is, potassium-sparing diuretics | Increased risk of hypotension, hyperkalemia, nephrotoxicity | Avoid concurrent use or monitor BP, SCr, and potassium levels |
| Aliskiren | Increased risk of hyperkalemia | Monitor serum potassium level |
| CYP2C9 and CYP3A4/5 inhibitors | Decreased losartan metabolism and increased risk of losartan toxicity | Monitor BP; consider dose reductions of losartan |
| CYP2C9 and CYP3A4/5 inducers | Increased losartan metabolism and decreased losartan efficacy | Monitor BP; consider dose increases of losartan |
| Diuretics | Increased risk of postural hypotension due to hypovolemia | Monitor BP; rise from seated position slowly |
| Potassium supplements, salt substitutes | Increased risk of hyperkalemia and cardiac arrhythmias | Avoid concurrent use or monitor serum potassium level |
| Nonsteroidal anti-inf ammatory drugs | Decreased antihypertensive and natriuretic effect of losartan, increased risk of nephrotoxicity | Avoid concurrent use or monitor BP and SCr levels |

### Adverse Reactions: Losartan

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Headache | Anorexia, back pain, constipation, dizziness, dyspepsia, hypotension, hyperkalemia, leg pain, muscle cramps, myalgia, nausea, nephrotoxicity, rash, tachycardia | Angioedema, birth defects, hepatotoxicity, rhabdomyolysis |

**Efficacy Monitoring Parameters.** Decreased BP.

**Toxicity Monitoring Parameters.** Signs/symptoms of peripheral edema. Baseline and periodic electrolyte panel, renal function tests, and urine protein are recommended.

**Key Patient Counseling Points.** Avoid pregnancy. Avoid sudden discontinuation; rebound hypertension can occur. Use potassium supplements or salt substitutes only under medical supervision. May cause dizziness that may worsen if dehydrated. Seek medical attention if angioedema, excessive fluid loss, hyperkalemia, reduction in urination, or jaundice occurs.

**Clinical Pearls.** Observe patients who are volume depleted for at least 2 h after taking the initial dose and consider a lower starting dose.

# LOTEPREDNOL: Alrex, Lotemax

**Class:** Corticosteroid, Ophthalmic

**Dosage Forms.** **Suspension, Ophthalmic:** 0.2%, 0.5%; **Ointment, Ophthalmic:** 0.5%; **Gel, Ophthalmic:** 0.5%

**Common FDA Label Indication, Dosing, and Titration.**

1. Temporary relief of seasonal allergic conjunctivitis: Instill 1 drop of 0.2% suspension qid
2. Inflammatory conditions: Instill 1-2 drops of 0.5% suspension in conjunctival sac of affected eye qid
3. Postoperative inflammation: Apply 1/2 inch of gel or 1-2 drops of 0.5% gel or suspension into conjunctival sac of affected eye qid continuing 24 h before surgery and for 2 wk after surgery

**Off-Label Uses.** None

**MOA.** Corticosteroids inhibit the inflammatory response including edema, capillary dilation, leukocyte migration, and scar formation

### Drug Characteristics: Loteprednol

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Minimal |
| **Dose Adjustment Renal** | Not required | **Distribution** | Not absorbed |
| **Dialyzable** | Unknown | **Metabolism** | Not absorbed |
| **Pregnancy Category** | C | **Elimination** | Not absorbed |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity, active eye infection | **Black Box Warnings** | None |

### Medication Safety Issues: Loteprednol

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | No |

**Drug Interactions: Loteprednol:** None known

### Adverse Reactions: Loteprednol

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Headache, burning on instillation, discharge, dry eyes, itching, photophobia, abnormal vision/blurring | Irritation, corneal abnormalities, eyelid erythema, increased IOP | Cataract formation, changes in visual acuity, optic nerve damage, secondary eye infection |

**Efficacy Monitoring Parameters.** Relief or prevention of redness, irritation and other inflammatory symptoms

**Toxicity Monitoring Parameters.** Assess for increased IOP if >10 d of treatment, signs and symptoms of infection

**Key Patient Counseling Points.** Suspension: Shake well before use. Take out contact before use, may put contacts back in 10 min after using suspension. Tilt head and drop into eye. Keep eyes closed after use and put pressure on inside corner of the eye. Ointment: Do not use contacts while using this product. To administer, gently pull down lower lid, and squeeze in gel. Let go of eyelid, but keep eye closed for 1-2 min. Gel: Turn upside down and shake once. Do not use contacts while using this product. Tilt head and drop into eye. Keep eyes closed after use and put pressure on inside corner of the eye. If using for both eyes, do not use same bottle in both eyes.

**Clinical Pearls.** Patients with allergic conjunctivitis should be advised to avoid triggers, rubbing their eyes, and reduce contact use. Cool compresses and refrigerated artificial tears can also reduce redness and irritation.

# LOVASTATIN: Altoprev, Mevacor, Various

**Class:** HMG-CoA Reductase Inhibitor

**Dosage Forms. Oral Tablet:** 10 mg, 20 mg, 40 mg; **Oral Tablet, Extended Release:** 20 mg, 40 mg, 60 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Coronary arteriosclerosis, hypercholesterolemia, primary and mixed: Initial, 20 mg po daily, maintenance 10-80 mg po daily or in 2 divided doses; *max* 80 mg/d; Extended-release tablet: 20-60 mg po qhs
2. Familial hypercholesterolemia, heterozygous: Children 10-17 y of age, initial, 10 po daily, maintenance 10-40 mg po daily; *max* 40 mg/d

Sandoz generic pictured

**Off-Label Uses.** None

**MOA.** HMG-CoA reductase inhibitors competitively inhibit conversion of HMG-CoA to mevalonate, an early rate-limiting step in cholesterol synthesis.

**Drug Characteristics: Lovastatin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Active liver disease or unexplained persistent elevation of liver enzymes, avoid use | **Absorption** | F = <5% with immediate release, improved to 30% with ER, food decreases absorption |
| **Dose Adjustment Renal** | CrCl <30mL/min, use caution if giving doses >20 mg/d | **Distribution** | >95% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | 80-85% hepatic, CYP3A4/5 substrate |
| **Pregnancy Category** | X | **Elimination** | Renal elimination is <10% with a half-life of 2 h |
| **Lactation** | Contraindicated | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to lovastatin, active liver disease, pregnancy and lactation, concomitant use with HIV protease inhibitors, and unexplained persistent elevation of liver enzymes | **Black Box Warnings** | None |

**Medication Safety Issues: Lovastatin**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Do not crush or chew ER formulations | No | AtorvaSTATin | No |

### Drug Interactions: Lovastatin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inhibitors | Decreased lovastatin metabolism increase risk of lovastatin toxicity | Avoid concurrent use or monitor for myopathy and measure creatine kinase levels, *max* dose of lovastatin 20 mg/d for strong inhibitors (40 mg/d with verapamil, a moderate inhibitor). Protease inhibitors are contraindicated |
| CYP3A4/5 inducers | Increased lovastatin metabolism decreases lovastatin efficacy | Avoid concurrent use, or monitor lipids and consider dose increases of lovastatin |
| Fibrates, niacin | Increased risk of myopathy or rhabdomyolysis | Avoid concurrent use or monitor for myopathy and measure creatine kinase levels. Use lower doses of statins |

### Adverse Reactions: Lovastatin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Abdominal pain, constipation, diarrhea, headache, increased liver enzymes, myalgia, nausea, rash, hyperglycemia | Rhabdomyolysis, hepatotoxicity, increased risk of diabetes |

**Efficacy Monitoring Parameters.** Reduction in total cholesterol, LDL-cholesterol, and triglyceride levels; increase in HDL-cholesterol levels. Assess at baseline and periodically during treatment.

**Toxicity Monitoring Parameters.** Signs/symptoms of rhabdomyolysis (myalgias, dark urine, arthralgias, fatigue) or hepatotoxicity. LFTs, blood glucose, and $HbA_{1c}$ should be performed at baseline, 6-12 wk after initiation of therapy, and periodically thereafter. Serum creatine kinase should be measured in patients experiencing muscle pain and in those receiving other drugs associated with myopathy.

**Key Patient Counseling Points.** Immediate-release tablets should be taken with the evening meal. Extended-release tablets should be taken at bedtime. Swallow extended-release tablets whole; do not chew, crush, or cut. Avoid alcohol, grapefruit, and grapefruit juice. Report signs/symptoms of rhabdomyolysis, jaundice (yellowing of skin or eyes), or renal failure. There are multiple significant drug-drug interactions with lovastatin. Consult a health-care professional prior to starting any new prescription or OTC medications. Lovastatin does not take the place of lifestyle changes (diet, exercise) to lower cholesterol levels.

**Clinical Pearls.** Safety and efficacy of extended-release tablets not established in pediatric patients. Use increases risk of diabetes, especially in the elderly.

# LUBIPROSTONE: Amitiza

**Class:** Chloride Channel Activator

**Dosage Forms. Oral Capsule:** 8 mcg, 24 mcg

**Common FDA Label Indication, Dosing, and Titration.**

1. Chronic idiopathic constipation: 24 mcg po bid
2. Irritable bowel syndrome with constipation: Females >18 y of age, 8 mcg po bid
3. Opioid induced constipation: 24 mcg po bid

**Off-Label Uses.** None

**MOA.** Lubiprostone is a bicyclic fatty acid that acts at the apical portion of the intestine as a chloride channel activator, which increases intestinal fluid secretion. When used for opioid-induced constipation activation of the chloride channel bypasses the antisecretory effects of opioids

**Drug Characteristics: Lubiprostone**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Moderate, reduce dose to 16 mcg bid; Severe, reduce dose to 8 mcg bid | **Absorption** | Poorly absorbed |
| **Dose Adjustment Renal** | Not required | **Distribution** | >94% protein bound |
| **Dialyzable** | Unknown | **Metabolism** | Rapid and extensive in stomach and jejunum by carbonyl reductase to active metabolite |
| **Pregnancy Category** | C | **Elimination** | Half-life of 0.9 -1.4 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity, bowel obstruction | **Black Box Warnings** | None |

**Medication Safety Issues: Lubiprostone**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Do not crush or chew | No | No | No |

**Drug Interactions: Lubiprostone**

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Methadone | May decreases lubiprostone activation of chloride channels resulting in decreased lubiprostone efficacy | Monitor therapy and consider alternative constipation treatments |

**Adverse Reactions: Lubiprostone**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Headache, nausea, diarrhea | Edema, dizziness, dyspnea, fatigue, abdominal pain, f atulence, vomiting, xerostomia | Anorexia, GERD, tachycardia |

**Efficacy Monitoring Parameters.** Relief of constipation.

**Toxicity Monitoring Parameters.** Baseline LFTs, physical exam and history to rule out bowel obstruction.

**Key Patient Counseling Points.** Take with food and water to reduce risk of nausea. Seek medical attention chest pain, shortness of breath or severe GI symptoms. Dyspnea, described as chest tightness, has been reported and generally occurs with the 1st dose and resolves after a few hours without intervention.

**Clinical Pearls.** Not approved for males with irritable bowel syndrome, despite what you may see advertised directly to consumers.

# MARAVIROC: Selzentry

**Class:** Antiretroviral Agent, CCR5 Antagonist

**Dosage Forms. Oral Tablet:** 150 mg, 300 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Treatment of CCR5-tropic HIV-1 infection, in combination with other antiretroviral agents: Adults, 300 mg po bid

**Off-Label Uses.** None

**MOA.** Selectively and reversibly binds to the chemokine (C-C motif receptor 5 [CCR5]) coreceptors located on human CD4 cells. CCR5 antagonism prevents interaction between the human CCR5 coreceptor and the gp120 subunit of the viral envelope glycoprotein, thereby inhibiting gp120 conformational change required for CCR5-tropic HIV-1 fusion with the CD4 cell and subsequent cell entry.

Viir Healthcare pictured

**Drug Characteristics: Maraviroc**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Use with caution if moderate or severe hepatic impairment | **Absorption** | F = 23-33%, food decreases absorption by 30-60% |
| **Dose Adjustment Renal** | Reduce dose to 150 mg bid if CrCl <30 mL/min; avoid if on interacting meds | **Distribution** | CSF |
| **Dialyzable** | No | **Metabolism** | Hepatic, CYP3A4/5 and ABCB1 major substrate |
| **Pregnancy Category** | B | **Elimination** | 20% unchanged in feces, 14-34% renally eliminated as parent, half-life 14-18 h |
| **Lactation** | Weight risks and benefits | **Pharmacogenetics** | Requires trophism test for the presence of CCR5 on patient CD4 cells |
| **Contraindications** | Patients with CrCl <30 mL/min or ESRD who are taking potent CYP3A4/5 inhibitors or inducers | **Black Box Warnings** | Hepatotoxicity |

**Medication Safety Issues: Maraviroc**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Yes | Yes | No | No |

### Drug Interactions: Maraviroc

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inhibitors | Decreased maraviroc metabolism and increased risk of maraviroc toxicity | Reduce dose of maraviroc to 150 mg bid if strong CYP3A5/5 inhibitor, monitor and consider dose reduction with moderate CYP3A4/5 inhibitors |
| CYP3A4/5 inducers | Increased maraviroc metabolism and decreased maraviroc efficacy | Increase dose of maraviroc to 600 mg bid with strong inducers |

### Adverse Reactions: Maraviroc

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Fever, rash, cough | Hypertension, insomnia, anxiety, fatigue, benign skin neoplasms, neutropenia, elevated LFTs, constipation, herpes infection | Coronary artery disease, angina, jaundice, hepatic failure, seizures |

**Efficacy Monitoring Parameters.** HIV viral load, CD4 count, tropism assay, HIV resistance testing.

**Toxicity Monitoring Parameters.** LFTs, bilirubin.

**Key Patient Counseling Points.** Take with or without food. Do not chew or crush tablet. Does not prevent transmission of HIV, practice safe sex, do not share needles, etc. May cause drowsiness, avoid driving and concurrent CNS depressants.

**Clinical Pearls.** Not recommended for children <16 y of age. HIV may enter the cell via CCR5, CXCR4, or both receptors (called dual or mixed). Maraviroc is only indicated for HIV viruses that only use CCR5 for cell entry. Does not cure HIV. Medication guide required at dispensing.

# MEASLES, MUMPS, RUBELLA VACCINE, LIVE: MMR-II

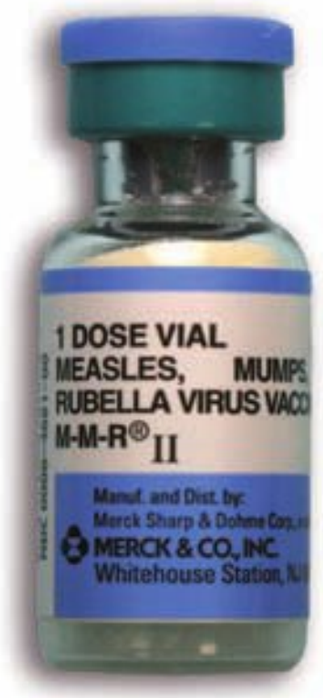
**Class:** Vaccine

**Dosage Forms.** **Lyophilized Powder for Subcutaneous Injection:** 0.5 mL after reconstitution with supplied diluent; also available in combination with varicella vaccine

**Common FDA Label Indication, Dosing, and Titration.**

1. Prevention of measles, mumps, and rubella infections: Adults, 1 dose (2nd dose indicated for adults who are at high risk); Children, 1 dose at age 12 mo with a 2nd dose at age 4-6 y, prior to entering school

**Off-Label Uses.** None



Merck pictured

**Drug Characteristics: Measles, Mumps, Rubella Vaccine, Live**

| | | | |
|---|---|---|---|
| **Pregnancy Category** | C | **ADME** | None known |
| **Lactation** | Generally considered safe during lactation | **Pharmacogenetics** | Not yet clinically relevant |
| **Contraindications** | Hypersensitivity to MMR vaccine or a component of the vaccine (egg, gelatin, neomycin); immunosuppression; pregnancy | **Black Box Warnings** | None |

**Medication Safety Issues: Measles, Mumps, Rubella Vaccine, Live**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| MMR-II, MMRV | No | No | No | None | No |

**Drug Interactions: Measles, Mumps, Rubella Vaccine, Live**

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Moderate- to high-dose corticosteroids | Immunosuppression reduces vaccine efficacy and patients are at increased risk of measles infection | Delay MMR vaccine administration until corticosteroid therapy has been discontinued |
| Immunosuppressing agents | Immunosuppression reduces vaccine efficacy and patients are at increased risk of measles infection | Delay MMR vaccine administration until immunosuppressive therapy has been discontinued |
| Immune globulin or blood products | Interference with immune response to live vaccines | Delay MMR vaccine administration for a period of time depending on type and dose of immune globulin or blood product |

**Adverse Reactions: Measles, Mumps, Rubella Vaccine, Live**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Fever, arthralgia (adult females) | Rash | Thrombocytopenia, anaphylaxis, Guillain-Barré syndrome, febrile seizure |

**Efficacy Monitoring Parameters.** Prevention of measles, mumps, and rubella infections; although antibody concentrations might be measured, routine measurement for vaccine response is not recommended.

**Toxicity Monitoring Parameters.** Monitor for syncope after administration.

**Key Patient Counseling Points.** Some children may experience mild fever and rash 7-10 d after vaccine administration. Avoid pregnancy for 28 d following vaccine administration.

**Clinical Pearls.** Individuals born before 1957 can be considered immune unless a female of childbearing potential. Administer to females found to be seronegative to rubella following completion of pregnancy. If not administered simultaneously, MMR must be separated by at least 4 wk from other live vaccines. Ensure that international travelers are appropriately immunized. Avoid confusion with MMRV, which also contains varicella vaccine. Administer 2nd dose at least 28 d after 1st dose.

# MECLIZINE: Antivert, Dramamine, Various

**Class:** Antihistamine, Antiemetic

**Dosage Forms.** **Oral Tablet:** 12.5 mg, 25 mg, 32 mg; **Oral Tablet, Chewable:** 25 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Motion sickness: 25-50 mg po 1 h before departure, may repeat q24h prn
2. Vertigo: 25-100 mg po daily in 1-3 divided doses, depending on clinical response

**Off-Label Uses.** None

**MOA.** Meclizine is an antihistamine that suppresses the vasodepressor response to histamine while only slightly inhibiting acetylcholine.

Rugby generic 25 mg pictured

**Drug Characteristics: Meclizine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Not known |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 7 L/kg |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, minor CYP2D6 substrate |
| **Pregnancy Category** | B | **Elimination** | Excreted in urine and feces, half-life of 6 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

**Medication Safety Issues: Meclizine**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Anzemet, Axert | No |

**Drug Interactions: Meclizine**

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CNS depressants (opioids, benzodiazepines, alcohol) | Possible increase in sedation effects | Use concurrently with caution |

**Adverse Reactions: Meclizine**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Sedation, headache, dry mouth, fatigue, and nausea | |

**Efficacy Monitoring Parameters.** Improvement in nausea or vertigo symptoms.

**Toxicity Monitoring Parameters.** Seek medical attention for signs of severe CNS toxicity.

**Key Patient Counseling Points.** Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery. Patients should avoid alcoholic beverages while taking this drug. Because of its potential anticholinergic action, this drug should be used with caution in patients with asthma, glaucoma, or enlargement of the prostate gland.

**Clinical Pearls.** Meclizine is available over the counter in many different products, and by prescription. Caution should be used to avoid duplication of therapy and patients should be advised on product selection.

# MEDROXYPROGESTERONE: Provera, Various

**Class:** Progestin Hormone

**Dosage Forms.** **Oral Tablet:** 2.5 mg, 5 mg, 10 mg; **Oral Suspension:** 104 mg/0.65 mL, 150 mg/mL, 400 mg/mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Abnormal uterine bleeding unrelated to menstrual cycle: 5-10 mg po daily × 5-10 d starting on days 16 or 21 of the menstrual cycle
2. Prevention of estrogen-induced endometrial hyperplasia: 5-10 mg po daily for 12-14 d starting on days 1 or 16 of the menstrual cycle, when estrogen is being administered
3. Secondary physiologic amenorrhea: 5-10 mg po daily × 5-10 d

**Off-Label Uses.**

1. Breast cancer, endometrial carcinoma: Dose is individualized

Barr generic pictured

**MOA.** Medroxyprogesterone transforms proliferative into secretory endometrium. Androgenic and anabolic effects have been noted, but the drug is apparently devoid of significant estrogenic activity.

**Drug Characteristics: Medroxyprogesterone**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Mild or moderate hepatic dysfunction, reduce dose or dose frequency; severe, contraindicated | **Absorption** | F = 0.6-10%, food increases AUC and Cmax |
| **Dose Adjustment Renal** | Not required | **Distribution** | 86-90% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, CYP3A4/5 substrate; induces CYP3A4/5 |
| **Pregnancy Category** | X | **Elimination** | Primarily renal elimination (metabolites) with a half-life of 11-16 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to medroxyprogesterone, abnormal genital bleeding, history of estrogen- or progesterone-dependent neoplasia, active or history of DVT or PE, severe liver dysfunction, known or suspected pregnancy | **Black Box Warnings** | Cardiovascular, dementia risk, loss of BMD (Depo-Provera) |

### Medication Safety Issues: Medroxyprogesterone

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | MedroxyPROGESTERone | No | No | Covera, methylPREDNISolone | No |

### Drug Interactions: Medroxyprogesterone

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inducers | Increased medroxyprogesterone metabolism reduces medroxyprogesterone effectiveness | Consider dose increases of medroxyprogesterone |
| CYP3A4/5 inhibitors | Decreased medroxyprogesterone metabolism increases risk of medroxyprogesterone toxicity | Consider dose decreases of medroxyprogesterone |
| CYP3A4/5 substrates | Increased substrate metabolism may decrease effectiveness of substrates | Monitor and consider increasing dose of substrate |
| Corticosteroids | Clearance of corticosteroid reduced by inhibition of corticosteroid metabolism by the medroxyprogesterone resulting in steroid toxicity | Monitor for corticosteroid toxicity and reduce dose if necessary |
| Warfarin | Medroxyprogesterone may increase or decrease warfarin effectiveness; mechanism unknown | Monitor INR |

### Adverse Reactions: Medroxyprogesterone

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Weight gain, headache, amenorrhea, breast tenderness | Abdominal pain, asthenia, feeling nervous, breakthrough bleeding | Deep venous thrombosis, thrombophlebitis, osteoporosis, pulmonary embolism |

**Efficacy Monitoring Parameters.** Resolution of clinical signs of abnormal bleeding.

**Toxicity Monitoring Parameters.** Baseline pelvic and breast exam at therapy initiation; monitor BMD; diagnostic evaluation to rule out malignancy in the event of persistent or recurring vaginal bleeding.

**Key Patient Counseling Points.** Menstrual bleeding should occur 3-7 d after last dose. Patients should report if menstruation does not occur within 7 d after last dose.

**Clinical Pearls.** Injectable formulation of medroxyprogesterone is administered every 3 mo for contraception and for pain associated with endometriosis. Combination of estrogens and progestins should not be used for the prevention of cardiovascular disease. Increased risk of myocardial infarction, stroke, invasive breast cancer, PE, and DVT has been shown in postmenopausal women.

# MELOXICAM: Mobic, Various

**Class:** NSAID

**Dosage Forms.** **Oral Tablet:** 7.5 mg, 15 mg; **Oral Suspension:** 7.5 mg/5 mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Osteoarthritis: 7.5 mg po daily, may titrate to *max* of 15 mg/d
2. Rheumatoid arthritis: 7.5 mg po daily, may titrate to *max* of 15 mg/d
3. Juvenile rheumatoid arthritis: Children ≥2 y of age, 0.125 mg/kg po daily, may titrate to *max* of 7.5 mg/d

**Off-Label Uses.** None

**MOA.** Nonselective inhibitor of COX-1 and COX-2, and reversibly alters platelet function and prolongs bleeding time.

Mylan generic pictured

**Drug Characteristics: Meloxicam**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 89%, food has minimal effect on absorption |
| **Dose Adjustment Renal** | Avoid if CrCl <20 mL/min | **Distribution** | Vd = 10-16 L; 99% protein bound |
| **Dialyzable** | Not dialyzable, *max* dose 7.5 mg/d | **Metabolism** | Hepatic, minor substrate of CYP3A4/5 |
| **Pregnancy Category** | C (D ≥30 weeks gestation) | **Elimination** | Renal elimination with a half-life of 15-20 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Sensitivity to meloxicam; concurrent ketorolac, pentoxifylline use, asthma, allergic-type reaction following other NSAID use, CABG | **Black Box Warnings** | Cardiovascular and GI risk, CABG |

**Medication Safety Issues: Meloxicam**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | Avoid chronic use unless other alternatives are not effective and patient can take gastroprotective agent |

### Drug Interactions: Meloxicam

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Aspirin, low-molecular-weight heparins, SSRIs, NSAIDs, pentoxifylline | Additive GI toxicity and increased risk of bleeding | Concurrent ketorolac, pentoxifylline contraindicated; others, monitor for GI toxicity |
| ACE-Is, ARBs, beta-blockers, loop and thiazide diuretics | Decreased diuretic and antihypertensive efficacy via decreased renal prostaglandin production | Monitor and consider alternative therapy |
| Cholestyramine | Decreased absorption of meloxicam | Separate administration by 1-2 h |
| Cyclosporine, tacrolimus | Increased risk of cyclosporine, tacrolimus toxicity, unknown mechanism | Monitor cyclosporine and tacrolimus levels and consider dose adjustments |
| Pemetrexed | Decreased renal clearance and increased toxicity of pemetrexed | Avoid concurrent use in patients with renal dysfunction |
| Sulfonylureas | Increased risk of hypoglycemia via inhibition of sulfonylurea metabolism | Monitor FPG and adjust as necessary |
| Warfarin | Both substrates for CYP2C9, competitive metabolism | Monitor INR and adjust warfarin dose |

### Adverse Reactions: Meloxicam

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Edema, itching, rash, GI distress, dizziness, tinnitus, ototoxicity | Stevens-Johnson syndrome, GI bleeding, thrombosis, elevated liver functions, acute renal failure, congestive heart failure, aplastic anemia |

**Efficacy Monitoring Parameters.** Decreased pain and improved range of motion.

**Toxicity Monitoring Parameters.** CBC, LFTs, SCr, fecal occult blood tests if chronic use. Seek medical attention if severe skin rash, black tarry stools, chest pains, yellowing of eyes or skin, or change in urination.

**Key Patient Counseling Points.** Take with food or milk to decrease GI upset. For suspension, shake gently before using.

**Clinical Pearls.** Elderly patients are at increased risk of GI ulceration. Use lowest effective dose for shortest possible duration; after observing initial response, adjust dose and frequency to meet individual patient's needs.

# MEMANTINE: Namenda

**Class:** *N*-Methyl-d-Aspartate (NMDA) Receptor Antagonist

**Dosage Forms.** **Oral Solution:** 10 mg/5 mL; **Oral Tablet:** 5 mg, 10 mg; **Oral Capsule, Extended Release:** 7 mg, 14 mg, 21 mg, 28 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Alzheimer disease: 5 mg po daily, may titrate dose no more than once per week to target dose of 10 mg po bid

Forest Laboratories 10 mg pictured

**Off-Label Uses.** None

**MOA.** Activation of NMDA receptors by glutamate is believed to contribute to the symptomatology of Alzheimer disease. Memantine is believed to act as an uncompetitive (open-channel) NMDA receptor antagonist that binds preferentially to the NMDA receptor–operated cation channels. There is no evidence that memantine prevents or slows neurodegeneration in patients with Alzheimer disease.

**Drug Characteristics: Memantine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 100%, no effect of food on absorption |
| **Dose Adjustment Renal** | CrCl <30 mL/min, target dose of 5 mg po bid | **Distribution** | Vd = 9-11 L; 45% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | 50% and occurs by glucuronidation |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 50% (unchanged) with a half-life of 60-80 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

**Medication Safety Issues: Memantine**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| XR | No | Do not chew or crush XR capsule | No | Mesalamine | No |

**Drug Interactions: Memantine.** None known

**Adverse Reactions: Memantine**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Hypertension, hypotension, syncope, vomiting, dizziness, headache, cough, pain | Stevens-Johnson syndrome, deep venous thrombosis, hepatitis, liver failure, cerebrovascular accident, grand mal seizure, transient ischemic attack, acute renal failure |

**Efficacy Monitoring Parameters.** Improvement in cognitive function and ability to take part in activities of daily living.

**Toxicity Monitoring Parameters.** Seek medical attention if severe adverse effects occur; BP, eye exams, LFTs, electrolytes, SCr.

**Key Patient Counseling Points.** May be taken with or without food.

**Clinical Pearls.** There is sparse evidence that this product is clinically effective in the treatment of Alzheimer disease. It may slow progression but does not reverse or improve symptoms once present.

# MENINGOCOCCAL VACCINE: Menactra, Menveo, Menomune, MenHibrix

**Class:** Vaccine

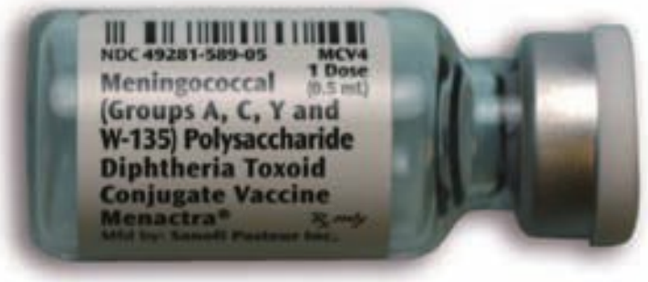
**Dosage Forms.** **Solution for Intramuscular Injection:** Quadrivalent conjugate vaccine (serogroups A,C,Y,W-135; MCV4) 0.5 mL (Menactra, Menveo); Bivalent conjugate vaccine (serogroups C and Y; MenHibrix); **Solution for Subcutaneous Injection:** Polysaccharide vaccine (MPSV4) 0.5 mL (Menomune)

**Common FDA Label Indication, Dosing, and Titration.**

1. Prevention of invasive meningococcal disease caused by serotypes A, C, Y, W-135: Adults, single dose of MCV4 or MPSV4 (through age 55 y for MCV4); Children 2 mo of age, use 4 dose series of Menveo at age 2, 4, 6, and 12 mo; Children 9-23 mo of age, 2 doses of Menactra; Children ≥2 y of age, a single dose of either Menactra or Menveo
2. Prevention of invasive meningococcal disease caused by serotypes C and Y

**Off-Label Uses.**

1. Prevention of invasive meningococcal disease caused by serotypes A, C, Y, W-135: Routine immunization of adolescents 11-12 y of age and a 2nd dose at 16 y of age
2. Prevention of invasive meningococcal disease caused by serotypes A, C, Y, W-135 in individuals at high risk of invasive meningococcal disease or those at ongoing risk of exposure, in individuals with complement deficiencies, asplenia, HIV, individuals who work with *N. meningitides* in the laboratory: MCV4, 2 doses 3 mo apart and then every 5 y
3. Prevention of invasive meningococcal disease caused by serotypes A, C, Y, W-135 for military recruits, travelers to or people who live in epidemic areas or endemic countries or 1st-year college students up to 21 y of age who live in dormitory and did not receive a dose at 16 y of age: MCV4, single dose




Sanofi Pasteur pictured

Sanofi Pasteur pictured

**Drug Characteristics: Meningococcal Vaccine**

| | | | |
|---|---|---|---|
| **Pregnancy Category** | MCV4, B; MPSV4, B | **ADME** | Not known |
| **Lactation** | Infant risk is minimal | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to meningococcal vaccine or a component of the vaccine | **Black Box Warnings** | None |

**Medication Safety Issues: Meningococcal Vaccine**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| CRM, D | No | No | No | None | No |

### Drug Interactions: Meningococcal Vaccine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Moderate- to high-dose corticosteroids | Immunosuppression may decrease therapeutic effect | Delay meningococcal vaccine administration until corticosteroid therapy has been discontinued if possible; clinical judgment |
| Immunosuppressing agents: cyclosporine, tacrolimus, azathioprine, methotrexate | Immunosuppression may decrease therapeutic effect | Delay meningococcal vaccine administration until immunosuppressive therapy has been discontinued if possible; clinical judgment |

### Adverse Reactions: Meningococcal Vaccine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Injection site reactions, including erythema and soreness. Irritability, abnormal crying, decreased appetite, diarrhea, malaise, fatigue headache, asthenia | Rash, nausea, arthralgia, myalgia, fever | Febrile seizure, anaphylaxis, Guillain-Barré syndrome |

**Efficacy Monitoring Parameters.** Prevention of invasive meningococcal disease.

**Toxicity Monitoring Parameters.** Monitor for syncope after administration.

**Key Patient Counseling Points.** Used to prevent meningitis and other serious infections. In addition to recommended primary vaccination, patients at risk for infection (asplenic, immune compromised) should receive boosters every 5 y; first-year college students up through age 21 y living in dormitories should be vaccinated if not vaccinated on or after their 16th birthday. Infants at high risk of invasive infection (asplenia, immune compromised) should be immunized starting at age 2 mo with Menveo. Optional MenACWY for healthy infants.

**Clinical Pearls.** MenACWY-CRM is used to describe Menveo, while MenACWY-D is used to describe Menactra. MenACWY is used to describe all vaccines in this category. Use caution to avoid confusing products. MCV4 should be used to immunize individuals aged 2 mo (Menveo) or 9 mo (Menactra) up to age 55 y. Use MPSV4 for individuals ≥56 y of age who require immunization. MCV4 is administered IM, while MPSV4 is administered SQ. Immunized individuals remain at risk for invasive disease caused by *N. meningitides* serogroup B.

# METAXALONE: Skelaxin, Various

**Class:** Centrally Acting Skeletal Muscle Relaxant

**Dosage Forms. Oral Tablet:** 800 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Musculoskeletal pain or spasm: 800 mg po tid-qid

**Off-Label Uses.** None

**MOA.** The mechanism of action of metaxalone in humans has not been established, but may be due to general CNS depression. Metaxalone has no direct action on the contractile mechanism of striated muscle, the motor end plate, or the nerve fiber.

King Pharmaceuticals 800 mg pictured

**Drug Characteristics: Metaxalone**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Use lower initial doses and increase dose carefully | **Absorption** | F is unknown, food enhances absorption |
| **Dose Adjustment Renal** | Use lower initial doses and increase dose carefully | **Distribution** | Vd = 800 L |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic metabolism, substrate of multiple CYP enzymes |
| **Pregnancy Category** | D | **Elimination** | Renal elimination with a half-life of 8-9 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to metaxalone, significantly impaired renal or hepatic function | **Black Box Warnings** | None |

**Medication Safety Issues: Metaxalone**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Mesalamine, metolazone | Avoid. Most muscle relaxants poorly tolerated by older adults, because of anticholinergic adverse effects, sedation, increased risk of fractures |

**Drug Interactions: Metaxalone**

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CNS depressants (opioids, benzodiazepines, alcohol) | Additive sedative effects | Avoid concurrent use or monitor carefully for signs of toxicity |

### Adverse Reactions: Metaxalone

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Nausea, vomiting, dizziness, headache, somnolence | Hemolytic anemia, leukopenia, jaundice, immune hypersensitivity reaction, maculopapular rash |

**Efficacy Monitoring Parameters.** Reduction in pain and muscle spasms.

**Toxicity Monitoring Parameters.** Monitor LFTs and CBC periodically.

**Key Patient Counseling Points.** Patients should avoid activities requiring mental alertness or coordination until drug effects are known, as drug may cause dizziness or sedative effects.

**Clinical Pearls.** Metaxalone is used for the relief of discomfort associated with acute, painful musculoskeletal conditions in adults and should be used for only short periods (up to 2 or 3 wk). Not for use in children <12 y of age. Use with caution in elderly who may be more susceptible to adverse effects.

# METFORMIN: Glucophage, Various

**Class:** Biguanide, Hypoglycemic

**Dosage Forms.** **Oral Tablet:** 500 mg, 850 mg, 1000 mg; **Oral Tablet, Extended Release:** 500 mg, 750 mg, 1000 mg; **Oral Solution:** 500 mg/5 mL

**Common FDA Label Indication, Dosing and Titration.**

1. Diabetes mellitus, type 2: Adults, immediate release, 500-1000 mg po bid, may titrate to *max* dose 2250 mg/d; extended release, 500-2000 mg po daily, may titrate to *max* dose 2000 mg/d; Children ≥10 y of age, immediate release, 500-1000 mg po bid, may titrate to *max* dose 2000 mg/d

**Off-Label Uses.** None

**MOA.** Metformin is a biguanide antihyperglycemic agent. It does not affect insulin secretion; rather, it reduces hepatic glucose production and enhances glucose utilization by muscle.

Teva generic 850 mg pictured

Teva generic 1000 mg pictured

Teva generic 500 mg ER pictured

Barr generic 750 mg ER pictured

**Drug Characteristics: Metformin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Severe hepatic insufficiency, avoid use | **Absorption** | F = 40-60%; immediate release: absorption reduced with food; extended release and oral solution: absorption enhanced with food |
| **Dose Adjustment Renal** | SCr >1.4 mg/dL, contraindicated | **Distribution** | Vd = 654 L; not protein bound |
| **Dialyzable** | Yes | **Metabolism** | Not metabolized |
| **Pregnancy Category** | B | **Elimination** | 90% renal elimination with a half-life of 7-12 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to metformin, contrast media, SCr >1.4 mg/dL, metabolic acidosis | **Black Box Warnings** | Lactic acidosis |

**Medication Safety Issues: Metformin**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| Glucophage and Glucophage XR | MetFORMIN | Do not chew or crush ER formulation | Yes | MetroNIDAZOLE | No |

### Drug Interactions: Metformin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Acetrizoic acid and other contrast media | Increased risk of lactic acidosis and renal failure | Contraindicated |
| Beta-blockers | Altered glucose metabolism and increased risk of hypoglycemia | Avoid propranol; use others with caution and increased monitoring |
| Cationic drugs, amiloride, cimetidine, cephalexin | Competition for proximal renal tubular secretion and reduced metformin clearance | Monitor and consider dose adjustments of both agents |
| Fluoroquinolones | Altered glucose metabolism and increased risk of hypoglycemia and hyperglycemia | Avoid concurrent use if possible; monitor and consider dose adjustments |
| MAOIs | Stimulation of insulin secretion, hypoglycemic effects | Avoid concurrent use if possible; monitor and consider dose adjustments |
| Psyllium | Psyllium may delay absorption of glucose from meals, leading to less postprandial hyperglycemia and potentially allowing a reduced dosage of the antidiabetic agent | Avoid concurrent use if possible; monitor and consider dose adjustments |

### Adverse Reactions: Metformin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Diarrhea, malabsorption, nausea, cobalamin deficiency, asthenia, vomiting, f atulence | Headaches, indigestion | Lactic acidosis, weight loss, hepatoxicity, hemolytic anemia, hypersensitivity |

**Efficacy Monitoring Parameters.** Pre-prandial blood glucose between 70 and 130 mg/dL, $HbA_{1c}$ <7%.

**Toxicity.** Renal function, CBC, $B_{12}$ levels. Seek medical attention if severe skin rash, muscle weakness or pain, yellowing of eyes or skin, unusual bruising, or bleeding.

**Key Patient Counseling Points.** Monitor blood glucose in frequent intervals (2-4 times per day); if <70 mg/dL, eat candy or sugar and contact prescriber. Take with morning meal if daily dosing. Take with morning and evening meal if bid. Drink plenty of liquids to improve elimination of metformin. Avoid alcohol; this increases the risk of lactic acidosis.

**Clinical Pearls.** Patient having procedure with iodinated contrast: withhold metformin prior to or at the time of the procedure and for 48 h following the procedure. Restart metformin only after kidney function has been reevaluated and found to be normal. Take extended-release product with food or milk. Immediate release may be taken with food, if GI upset occurs. Metformin is first-line therapy for type 2 diabetes. Metformin does not cause hypoglycemia when used as a single agent. Response typically not seen at doses <1500 mg/d.

# METHADONE: Dolophine, Various

**Class:** Opioid Analgesic. C-II

**Dosage Forms.** **Oral Tablet:** 5 mg, 10 mg; **Oral Tablet for Suspension:** 40 mg; **Oral Solution:** 5 mg/5 mL, 10 mg/5 mL, 10 mg/1 mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Pain, chronic (moderate-severe): Opioid naive patients, 2.5 mg po q8h, may titrate to response
2. Drug detoxification, opioid abuse: 15-30 mg po q8h, titrate to response; when used for treatment of opioid addiction (detoxification or maintenance), may only be dispensed by certified opioid treatment programs

Roxane generic 10 mg pictured

**Off-Label Uses.** None

**MOA.** Methadone is a phenylethylamine opioid agonist qualitatively similar to morphine but with a chemical structure unrelated to the alkaloid-type structures of the opium derivatives. Analgesic activity of (R)-methadone is 8-50 times that of (S)-methadone, and (R)-methadone has a tenfold higher affinity for opioid receptors.

**Drug Characteristics: Methadone**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 85% with minimal food effect |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 3.6 L/kg; 85-90% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, CYP2B6 and 3A4/5 substrate. Moderate CYP2D6 inhibitor |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 10-20% with a half-life of 20-24 h |
| **Lactation** | Usually compatible, peak concentration 4-5h after dose | **Pharmacogenetics** | None known |
| **Contraindications** | Bronchial asthma, hypersensitivity to opioids, paralytic ileus, respiratory depression, hypercarbia | **Black Box Warnings** | Accidental ingestion; drug abuse; opioid addiction/use; QT prolongation; respiratory depression; tablets contain excipients |

**Medication Safety Issues: Methadone**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| Intensol | No | Tablet for suspension | Yes | Dexmethylphenidate, Mephyton | No |

## Drug Interactions: Methadone

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Amiodarone, agents that prolong the QT interval | Additive QT prolongation | Avoid concurrent use |
| Barbiturates, benzodiazepines, centrally acting muscle relaxants, opioids, phenothiazines | Additive CNS depression | Monitor and consider dose adjustments |
| Buprenorphine, opioid agonists/antagonists, opioid antagonists | Precipitation of withdrawal symptoms | Avoid concurrent use with opioids |
| CYP3A4/5 and CYP2B6 inducers | Increased methadone metabolism and decreased methadone efficacy | Consider methadone dose increases |
| CYP3A4/5 and CYP2B6 inhibitors | Decreased methadone metabolism increases risk of methadone toxicity | Consider methadone dose decreases |
| CYP2D6 substrates | Reduced metabolism of substrates and increased toxicity | Avoid concurrent use or consider dose reduction of substrates |
| Didanosine | Decreased didanosine absorption | Separate use by 1-2 h |
| MAOIs | Additive respiratory depression, increased risk of serotonin syndrome | Contraindicated |

## Adverse Reactions: Methadone

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Constipation, GI distress, hypotension, dizziness, sedation | Arrhythmias, edema, dyspnea, respiratory depression | Stevens-Johnson syndrome, physical dependence, tolerance, QT prolongation |

**Efficacy Monitoring Parameters.** Relief of pain. Relief of signs and symptoms associated with narcotic addiction.

**Toxicity Monitoring Parameters.** Seek medical attention if severe skin rash, excessive drowsiness, decreased breathing, severe constipation, chest pain, or dizziness; vital signs.

**Key Patient Counseling Points.** Use a stool softener and stimulant combination or laxative for preventing constipation. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol and other CNS depressants. Seek medical attention if short of breath or extremely drowsy. Breast-feeding women should monitor child for signs of sedation and respiratory depression.

**Clinical Pearls.** Tolerance and physical dependence may occur with chronic use; avoid abrupt discontinuation. High interpatient variability in absorption, metabolism, and relative analgesic potency of methadone requires careful dose initiation and titration. Fatal respiratory depression has occurred; the highest risk is at initiation and with dosage increases. For oral administration only; excipients to deter use by injection are contained in tablets. Do not chew or swallow tablet for suspension—dissolve in liquid and drink. Keep away from children and pets. Medication guide required at dispensing. Included in REMS program requiring additional education for prescribers.

# METHOCARBAMOL: Robaxin, Various

Qualitest generic pictured

**Class:** Centrally Acting Skeletal Muscle Relaxant

**Dosage Forms. Oral Tablet:** 500 mg, 750 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Musculoskeletal pain or spasm: 1500 mg po qid × 48-72 h, may titrate to 750 mg po q4h, or 1500 mg po tid or 1000 mg po qid

**Off-Label Uses.** None

**MOA.** The mechanism of action of methocarbamol in humans has not been established, but may be due to general CNS depression. It has no direct action on the contractile mechanism of striated muscle, the motor end plate, or the nerve fiber.

**Drug Characteristics: Methocarbamol**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Use lower doses initially and increase dose carefully in patients with hepatic failure | **Absorption** | Food has no effect on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Protein binding 45-50% |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic via dealkylation and hydroxylation |
| **Pregnancy Category** | C | **Elimination** | Renal elimination of metabolites with a half-life of 1-2 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

**Medication Safety Issues: Methocarbamol**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Mephobarbital, Skelaxin | Avoid. Most muscle relaxants poorly tolerated by older adults, because of anticholinergic adverse effects, sedation, increased risk of fractures |

**Drug Interactions: Methocarbamol**

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CNS depressants (opioids, benzodiazepines, alcohol) | Additive sedative effects | Avoid concurrent use or monitor carefully for signs of toxicity |

### Adverse Reactions: Methocarbamol

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Flushing, pruritus, rash, urticaria, nausea, vomiting, dizziness, headache, nystagmus, somnolence, vertigo, blurred vision, conjunctivitis | Bradyarrhythmia, hypotension, syncope, leukopenia, anaphylactoid reaction |

**Efficacy Monitoring Parameters.** Reduction in pain and muscle spasms.

**Toxicity Monitoring Parameters.** Seek medical attention if idiosyncratic symptoms such as extreme weakness, transient quadriplegia, dizziness, and confusion occur within minutes or hours after 1st dose; vital signs.

**Key Patient Counseling Points.** Patients should avoid activities requiring mental alertness or coordination until drug effects are known, as drug may cause dizziness or sedative effects.

**Clinical Pearls.** Methocarbamol is used for the relief of discomfort associated with acute, painful musculoskeletal conditions in adults and should be used for only short periods (up to 2 or 3 wk). Drug may color urine brown, black, or green. Injectable form available, used for spasticity associated with tetanus.

# METHOTREXATE: Trexall, Various

**Class:** Antimetabolite

**Dosage Forms. Oral Tablet:** 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg

Dava generic 2.5 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Non-Hodgkin lymphoma, advanced (Burkitt lymphoma, stages I and II): 10-25 mg/d po for 4-8 d for several courses with a 7-10 d rest period
2. Psoriasis (Severe): initial, 2.5-5 mg q12h × 3 doses/wk, may titrate dose to 10-25 mg/wk po
3. Rheumatoid arthritis, severe: 7.5-15 mg po once weekly, may titrate by 5 mg/wk every 2-3 wk to *max* 20-30 mg/wk
4. Juvenile rheumatoid arthritis, polyarticular course: 10 mg/m$^2$ po once weekly, may titrate to clinical response

**Off-Label Uses.**

1. Many cancers: Dose varies with cancer, stage, and concurrent chemotherapy

**MOA.** Reversibly inhibits dihydrofolate reductase (DHFR). Dihydrofolates are reduced to tetrahydrofolates by DHFR before they are used in DNA synthesis. Methotrexate interferes with DNA synthesis, repair, and cellular replication.

**Drug Characteristics: Methotrexate**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Bilirubin = 3.1-5 mg/dL, reduce dose by 25%; bilirubin >5 mg/dL, avoid | **Absorption** | Dose-dependent, doses <40 mg/m$^2$, F = 42%; doses >40 mg/m$^2$, F = 17% |
| **Dose Adjustment Renal** | CrCl = 10-50 mL/min, reduce dose by 50%; CrCl <10 mL/min: avoid | **Distribution** | Vd = 0.4-0.8 L/kg; 50% protein bound |
| **Dialyzable** | Yes, hemodialysis | **Metabolism** | Intracellular polyglutamation, excreted by P-glycoprotein |
| **Pregnancy Category** | X | **Elimination** | Renal elimination is 48-100% with a dose-dependent half-life of 4-10 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to methotrexate, pregnancy, nursing, preexisting blood dyscrasias in patients treated for psoriasis and rheumatoid arthritis | **Black Box Warnings** | Acute renal failure; ascites; bone marrow suppression; dermatologic toxicity; diarrhea; hepatotoxicity; lymphomas; NSAIDs; opportunistic infections; pneumonitis; renal impairment; tumor lysis syndrome; CBC w/diff, platelet, liver, and renal lab testing mandatory |

## Medication Safety Issues: Methotrexate

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | Yes | Mercaptopurine, methylPREDNISolone | No |

## Drug Interactions: Methotrexate

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Aspirin, dantrolene, loop diuretics, NSAIDs, penicillins, PPIs, salicylates, trimethoprim, sulfisoxazole | Competition for renal tubular secretion, increased methotrexate toxicity and nephrotoxicity | Avoid concurrent use, or consider methotrexate dose reductions. NSAIDs are contraindicated. |
| BCG vaccine, other live vaccines and immunostimulants | Increased risk of infection from live vaccine | Contraindicated |
| Eltrombopag | Inhibition of OATP1B1 by eltrombopag results in decreased methotrexate clearance and increased toxicity | Avoid concurrent use, or consider methotrexate dose reductions |
| Leucovorin, folic acid | Leucovorin is a reduced folate that counteracts the anticancer effects of methotrexate | Avoid concurrent use, unless using as a rescue agent |

## Adverse Reactions: Methotrexate

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Myelosuppression, nausea, vomiting, alopecia, stomatitis, photosensitivity, rash | Elevated LFTs, diarrhea | Acute renal failure, liver failure, interstitial lung disease, Stevens-Johnson syndrome, secondary malignancies (lymphomas), opportunistic infections |

**Efficacy Monitoring Parameters.** Resolution of symptoms of psoriasis. Decreased pain and improved range of motion in rheumatoid arthritis. Shrinkage or disappearance of tumor. Methotrexate levels may be monitored and used to adjust leucovorin.

**Toxicity Monitoring Parameters.** Baseline and periodic CBC, SCr, LFTs, negative pregnancy test. Seek medical attention if severe mouth ulcerations, fever >101.5°F, shortness of breath, changes in urination, yellowing of eyes or skin, unusual bruising, or bleeding.

**Key Patient Counseling Points.** Causes nausea and vomiting; ensure patients have antiemetics and know how to take them. Avoid sun exposure. May take with food.

**Clinical Pearls.** Baseline and regular CBC w/diff, platelet, liver, and renal lab testing are mandatory. High-dose methotrexate requires urine alkalinization with sodium bicarbonate infusions to enhance methotrexate excretion and requires leucovorin administration started 24 h after methotrexate to rescue normal cells. Elimination is reduced in patients with ascites and/or pleural effusions related to third spacing, resulting in prolonged half-life and toxicity. Concomitant methotrexate administration with radiotherapy may increase the risk of soft tissue necrosis and osteonecrosis. Numerous dosing regimens are used; do not confuse daily and weekly dosing strategies.

# METHYLPHENIDATE: Ritalin, Various

**Class:** CNS Stimulant. C-II

**Dosage Forms.** **Oral Tablet:** 5 mg, 10 mg, 20 mg; **Oral Tablet, Chewable:** 2.5 mg, 5 mg, 10 mg; **Oral Tablet, Extended Release:** 10 mg, 18 mg, 20 mg, 27 mg, 36 mg, 54 mg; **Oral Capsule, Extended Release:** 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg; **Oral Capsule Extended Release, 24 h:** 10 mg, 20 mg, 30 mg, 40 mg; **Oral Solution:** 5 mg/5 mL, 10 mg/5 mL; **Oral Suspension:** 25 mg/5 mL; **Patch:** 10 mg/9 h, 15 mg/9 h, 20 mg/9 h, 30 mg/9 h

Sandoz generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Attention-deficit hyperactivity disorder: Adults, immediate-release tablets, solution, and chewable tablets, 10-60 mg/d po divided 2-3 times daily, preferably 30-45 min before meals; Children ≥6 y of age, initial, 5 mg po bid, may titrate in increments of 5-10 mg at weekly intervals; doses above 60 mg/d not recommended
2. Attention-deficit hyperactivity disorder, no prior methylphenidate therapy: Adults and Children ≥6 y of age, extended release, 20 mg po daily, may titrate in increments of 10 mg at weekly intervals; *max* 60 mg/d
3. Narcolepsy: Adults, immediate-release tablets, solution, and chewable tablets, 10-60 mg/d po divided 2-3 times daily; sustained release; Adults and Children ≥6 y of age, 20-60 mg/d po divided q8h

**Off-Label Uses.**

1. Depression: 5-30 mg po daily

**MOA.** Amphetamines are non-catecholamine sympathomimetic amines with CNS stimulant activity. Amphetamines are thought to block the reuptake of norepinephrine and dopamine into the presynaptic neuron and increase the release of these monoamines into the extraneuronal space.

**Drug Characteristics: Methylphenidate**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 22-25%, minimal food effect |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 2.6 L/kg; 10-30% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive metabolism, predominately via de-esterification |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 78-98% with a half-life of 3 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to amphetamines, anxiety, agitation, concurrent MAOIs, drug dependence, glaucoma, tics or history of Tourette syndrome, hypertension, angina, heart failure, concurrent isof urane anesthetics | **Black Box Warnings** | Abuse and dependence potential |

### Medication Safety Issues: Methylphenidate

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| CD, ER, XL, LA, SR | No | Do not crush or chew ER formulations | No | Methadone | No |

### Drug Interactions: Methylphenidate

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Amitriptyline, citalopram, TCAs | Enhanced amphetamine effects from the release of norepinephrine (hypertension, CNS stimulation) | Avoid concurrent use |
| Citalopram, SSRIs | Increased risk of serotonin syndrome (muscle rigidity, tachycardia, agitation) | Avoid concurrent use if possible, monitor for serotonin syndrome if used together |
| MAOIs | Hypertensive crisis | Contraindicated within 14 d |

### Adverse Reactions: Methylphenidate

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Weight loss, loss of appetite, headache, insomnia, irritability | Anxiety, tachycardia, nausea, vomiting | Seizures, spasmodic movement, anemia, thrombocytopenia, psychosis, mania, drug dependence, suicidal thoughts, priapism |

**Efficacy Monitoring Parameters.** Resolution of signs of ADHD, patients should have improved attention span and reduced impulsivity.

**Toxicity Monitoring Parameters.** BP, HR, and weight. CBC. Seek medical attention if chest pain, seizures, heart palpitations, change in behavior or personality, or hostility. Growth in children.

**Key Patient Counseling Points.** Avoid late evening doses due to resulting insomnia. Swallow the extended-release capsule whole. Do not crush, break, or chew it. If you cannot swallow the extended-release capsule, you may open it and pour the medicine into a small amount of soft food such as pudding, yogurt, or applesauce. Stir this mixture well and swallow it without chewing. Avoid abrupt discontinuation. For the patch, apply same time each day, alternating hips. Remove after 9 h.

**Clinical Pearls.** Amphetamines have a high potential for abuse, and administration for prolonged periods of time may lead to drug dependence and must be avoided. Misuse of amphetamines may cause sudden death and serious cardiovascular adverse events. Treatment may include drug holidays to assess ongoing need of medication, decrease tolerance, and limit growth suppression. Avoid confusion of multiple different brand names and formulations. Medication guide required at dispensing. Some generic versions of the extended-release product are BX rated and are not interchangeable.

# METHYLPREDNISOLONE: Medrol, Various

**Class:** Adrenal Corticosteroid

**Dosage Forms.** **Oral Tablet:** 2 mg, 4 mg, 8 mg, 16 mg, 32 mg

**Common FDA Label Indication and Dosing.**

Dosing for indications listed below: Adults, 4-48 mg po daily; Children, specific dosing parameters not specified; for all patients, adjust dose according to patient response

1. Allergic states (eg, asthma, etc)
2. Dermatologic diseases (eg, exfoliative erythroderma, etc)
3. Endocrine disorders (eg, adrenocortical insufficiency, etc)
4. Gastrointestinal diseases (eg, regional enteritis, ulcerative colitis, etc)
5. Hematologic disorders (eg, acquired hemolytic anemia, etc)
6. Neoplastic diseases (eg, palliative management of leukemias and lymphomas, etc)
7. Nervous system (eg, multiple sclerosis, cerebral edema, etc)
8. Renal diseases (eg, idiopathic nephrotic syndrome, systemic lupus erythematosus, etc)
9. Respiratory diseases (eg, idiopathic eosinophilic pneumonia, etc)
10. Rheumatic disorders (eg, rheumatoid arthritis, etc)

Sandoz generic 4 mg pictured

**Off-Label Uses.** None

**MOA.** Corticosteroids are naturally occurring and synthetic adrenocortical steroids cause varied metabolic effects, modify the body's immune responses to diverse stimuli, and are used primarily for their anti-inflammatory effects in disorders of many organ systems.

**Drug Characteristics: Methylprednisolone**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Well absorbed |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 1.5 L/kg |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, CYP3A4/5 substrate |
| **Pregnancy Category** | C | **Elimination** | Primarily renal elimination with a half-life of 2-3 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to methylprednisolone or other glucocortosteroids, administration of live vaccines, fungal infections | **Black Box Warnings** | None |

### Medication Safety Issues: Methylprednisolone

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | MethylPREDNISolone | No | No | PrediniSONE | No |

### Drug Interactions: Methylprednisolone

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inhibitors | Decreased methylprednisolone metabolism increases risk of methylprednisolone toxicity | Monitor for toxicity and reduce methylprednisolone dose if necessary |
| CYP3A4/5 inducers | Increased methylprednisolone metabolism decreases methylprednisolone efficacy | Monitor for efficacy and consider methylprednisolone dose increases |
| Fluoroquinolones | Concurrent use of steroids and fluoroquinolones can increase risk of tendon rupture, especially in elderly | Avoid concurrent use, or monitor carefully for tendon rupture |
| Phenytoin | Phenytoin increases methylprednisolone metabolism; methylprednisolone can increase or decrease phenytoin metabolism | Monitor methylprednisolone efficacy and phenytoin concentrations |
| Warfarin | Steroids can either increase or decrease INR in patients taking warfarin | Monitor INR carefully |

### Adverse Reactions: Methylprednisolone

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| GI upset | Hypertension, atrophic condition of skin, impaired skin healing, osteoporosis, depression, euphoria, pulmonary tuberculosis, hyperglycemia | Primary adrenocortical insufficiency, Cushing syndrome, decreased body growth, increased risk of infection |

**Efficacy Monitoring Parameters.** Improvement or resolution of clinical signs and symptoms; monitor for decrease in ESR, or improvement of PFT.

**Toxicity Monitoring Parameters.** Monitor for signs of hyperglycemia, osteoporosis, adrenocortical insufficiency, and infection; frequency and severity of adverse effects are dependent on the length of treatment and dose.

**Key Patient Counseling Points.** For short-term treatment, inform patients to take doses with meals to prevent GI upset. For high-dose or longer-term treatment, inform patients to monitor for signs of hyperglycemia, osteoporosis, adrenocortical insufficiency, and infection.

**Clinical Pearls.** Available in a variety of dosage forms for various indications, including ophthalmic preparations. Use lowest effective dose and discontinue as soon as possible to avoid serious long-term adverse effects. Injectable formulations sold by compounding pharmacies have been associated with outbreak of fatal fungal infections.

# METOCLOPRAMIDE: Reglan, Various

**Class:** Dopamine Antagonist

**Dosage Forms.** **Oral Tablet:** 5 mg, 10 mg; **Oral Solution:** 5 mg/5 mL, 10 mg/2 mL 10 mg/10 mL; **Oral Dispersible Tablet:** 5 mg

NorthStar Rx generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Diabetic gastroparesis: 10 mg po 30 min before meals and at bedtime × 2-8 wk; *max* 12 wk duration
2. Gastroesophageal reflux disease: Adults, 10-15 mg po qid 30 min before meals and at bedtime; Neonates, 0.15 mg/kg po q6h; Infants, 0.1 mg/kg po tid-qid 10-30 min before meals and at hs, *max* dose 0.3-0.75 mg/kg/d × 2 wk to 6 mo

**Off-Label Uses.**

1. Decreased lactation: 30-45 mg po daily × 7-15 d or 10-15 mg po tid × 7-15 d
2. Nondiabetic gastroparesis: 10 mg po 30 min before meals and at hs for 2-8 wk; *max* 12 wk duration

**MOA.** Metoclopramide stimulates motility of the upper GI tract without stimulating gastric, biliary, or pancreatic secretions. Its mode of action is unclear. It seems to sensitize tissues to the action of acetylcholine. It is also a dopamine receptor antagonist at dose >5 mg/kg.

**Drug Characteristics: Metoclopramide**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 80%, minimal food effect |
| **Dose Adjustment Renal** | CrCl = 10-50 mL/min, reduce dose by 25%; CrCl <10 mL/min, reduce dose by 50% | **Distribution** | Vd = 3.5 L/kg; 30% protein bound |
| **Dialyzable** | 2-38% by hemodialysis | **Metabolism** | Hepatic, minor CYP1A2 and CYP2D6 substrate |
| **Pregnancy Category** | B | **Elimination** | Renal 75-80%, with a half-life of 5-6 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity, GI hemorrhage, mechanical obstruction or perforation, pheochromocytoma, concomitant use with drugs likely to cause extrapyramidal reactions, epilepsy | **Black Box Warnings** | Tardive dyskinesia |

**Medication Safety Issues: Metoclopramide**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| ODT | No | Dispersible tablet | No | Metolazone, metoprolol, metroNIDAZOLE | Avoid, unless for gastroparesis |

### Drug Interactions: Metoclopramide

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Amitriptyline, antipsychotics, bupropion, TCAs | Increased risk of neuroleptic malignant syndrome and extrapyramidal symptoms | Contraindicated |
| Cabergoline, dopamine agonists | Decreased effect of dopamine agonists | Avoid concurrent use |
| Cyclosporine, levodopa, tacrolimus | Increased absorption and toxicity | Avoid concurrent use or monitor cyclosporine or tacrolimus levels and adjust dosage; avoid concurrent levodopa |
| Didanosine | Increased didanosine plasma concentrations | Avoid concurrent use |
| Digoxin, posaconazole | Decreased GI absorption and decreased efficacy of digoxin, posaconazole | Avoid concurrent use or monitor digoxin levels and adjust dosage |
| MAOIs | Increased risk of hypertensive crisis | Avoid concurrent use |
| Linezolid, SSRIs | Increased risk serotonin syndrome | Avoid concurrent use |

### Adverse Reactions: Metoclopramide

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Asthenia, somnolence | Dizziness, headache | Malignant hypertension, arrhythmias, galactorrhea, amenorrhea, gynecomastia, and impotence secondary to hyperprolactinemia, agranulocytosis, dystonia, extrapyramidal reactions, tardive dyskinesia |

**Efficacy Monitoring Parameters.** Reduction in nausea and vomiting.

**Toxicity Monitoring Parameters.** Seek medical attention if elevated BP, heart palpitation, fluid retention, unusual bruising or bleeding, or involuntary jerking movements.

**Key Patient Counseling Points.** Take this medicine on an empty stomach, 30 min before each meal and at bedtime. Not for long-term use. If using the oral dispersible tablet, make sure your hands are dry. Place the tablet in your mouth. It should melt quickly. After the tablet has melted, swallow or take a drink of water.

**Clinical Pearls.** Extrapyramidal reactions may consist of torticollis, facial spasms, urinary retention, and tetanus-like reactions. Young patients receiving high doses are at increased risk. Most patients respond to anticholinergic agents such as benztropine. Tardive dyskinesia is reported with the use of metoclopramide tablets. The symptoms of tardive dyskinesia are characterized by involuntary movements of the tongue, face, mouth, or jaw.

# METOPROLOL: Toprol XL, Various

**Class:** β-Adrenergic Blocker, Cardioselective

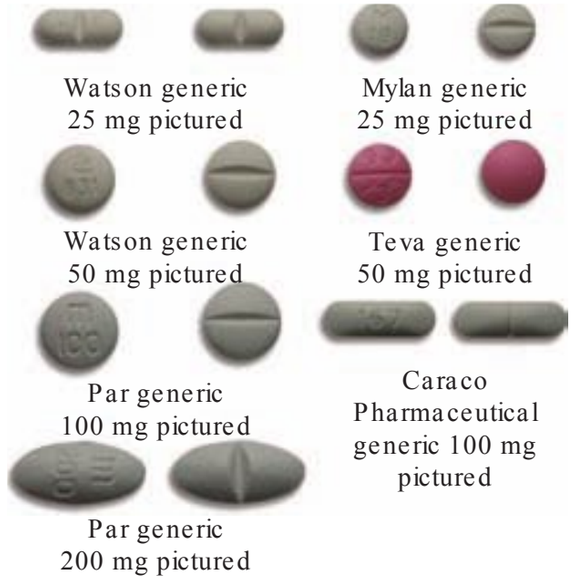
**Dosage Forms. Oral Tablet:** 25 mg, 50 mg, 100 mg; **Oral Tablet, Extended Release:** 25 mg, 50 mg, 100 mg, 200 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Angina: Adults, 50 mg po bid or 100 mg extended release po daily, may titrate to 100-400 mg total daily dose
2. Heart failure: Adults, NYHA Class II, 25 mg po daily for 2 wk, may titrate to *max* 200 mg/d; NYHA Class III-IV, 12.5 mg po daily for 2 wk, may titrate to *max* 200 mg/d
3. Hypertension: Adults, initial, immediate release, 50 mg po bid, may titrate up to 450 mg po per day in 2-3 divided doses; initial, extended release, 25-100 mg po daily, may titrate to 100-400 mg once daily; Children >6 y of age, 1 mg/kg po daily, may titrate to *max* 50 mg/d

**Off-Label Uses.**

1. Acute myocardial infarction: Adults, immediate release, 25-50 mg po q6-12h, convert to bid dosing over 2-3 d, or to daily extended release dosing with a *max* dose of 200 mg po daily
2. Atrial fibrillation-cardioversion: Adults, 50-200 mg po daily
3. Cardiac dysrhythmia: Adults, immediate release, 25–100 mg po bid; extended release, 50-400 mg po daily



Watson generic 25 mg pictured

Mylan generic 25 mg pictured

Watson generic 50 mg pictured

Teva generic 50 mg pictured

Par generic 100 mg pictured

Caraco Pharmaceutical generic 100 mg pictured

Par generic 200 mg pictured

**MOA.** Metoprolol is a cardioselective β-adrenergic blocker used in arrhythmias, hypertension, angina pectoris, and heart failure. It is also effective in decreasing post-MI mortality.

**Drug Characteristics: Metoprolol**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Liver disease, use slow-dose titration | **Absorption** | F = 65-70%; food increases Cmax and AUC |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 3-5 L; 12% protein bound |
| **Dialyzable** | Yes, give maintenance dose after dialysis completed | **Metabolism** | Hepatic, CYP2D6 substrate |
| **Pregnancy Category** | C | **Elimination** | Renal elimination of metabolite is 95% with a half-life of 3-7 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | Use with caution in known CYP2D6 poor metabolizers |
| **Contraindications** | Hypersensitivity; severe bradycardia, 2nd- or 3rd-degree AV block, sick sinus syndrome; decompensated heart failure; cardiogenic shock | **Black Box Warnings** | Abrupt withdrawal |

## Medication Safety Issues: Metoprolol

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| XL | No | Do not crush or chew ER formulation<br>ER formulation is scored and can be broken in half | Yes (IV only) | TEGretol, Topamax | No |

## Drug Interactions: Metoprolol

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Alpha-blockers, fentanyl | Increased risk of hypotension | Monitor BP |
| Amiodarone, dronedarone | Increased risk of bradycardia, heart block, sinus arrest | Avoid concurrent use in patients with sick sinus syndrome or AV block |
| Antidiabetic drugs | Decreased glycemic control | Monitor blood glucose levels |
| Calcium channel blockers, quinidine | Increased risk of hypotension and/or bradycardia and atrioventricular block | Avoid concurrent use |
| Clonidine | Exaggerated clonidine withdrawal response | Avoid abrupt withdrawal of clonidine while on concomitant beta-blocker therapy |
| CYP2D6 inhibitors | Decreased metoprolol metabolism increases risk of metoprolol toxicity | Initiate metoprolol at lower doses, monitor HR and BP |
| NSAIDs, venlafaxine | Decreased antihypertensive effect of metoprolol | Avoid concurrent use or monitor BP |

## Adverse Reactions: Metoprolol

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Dizziness, fatigue, hypotension | Arthralgia, bradyarrhythmias, bronchospasm, cold extremities, diarrhea, depression, dyspnea, disorder of glucose regulation, headache, heart block, impotence, nausea, rash, somnolence, syncope, vomiting | Heart failure |

**Efficacy Monitoring Parameters.** Decreased BP, reduction in chest pain, decreased number of weekly angina attacks, reduction in use of prophylactic nitroglycerin to relieve chest pain, improvement in signs/symptoms of heart failure.

**Toxicity Monitoring Parameters.** Signs/symptoms of heart failure, decreased HR. Monitor serum electrolytes, and renal function at baseline and periodically.

**Key Patient Counseling Points.** Take on an empty stomach and avoid alcohol. Avoid abrupt discontinuation, exacerbations of angina may occur. Instruct patients to report signs/symptoms of hypotension, heart failure, or exacerbation of angina with initial dosing and dose changes. This medicine may cause dizziness. Avoid driving, using machinery, or doing anything else that could be dangerous if not alert. Advise diabetic patients to carefully follow blood sugar levels as beta-blockers may mask symptoms of hypoglycemia.

**Clinical Pearls.** Avoid concomitant use of calcium channel blockers, as concomitant use may significantly affect HR or rhythm. Increase dose weekly when titrating for HTN/angina but every 2 wk for HF. Injectable metoprolol is also used for cardioversion in atrial fibrillation patients.

# METRONIDAZOLE: Flagyl, Various

**Class:** Nitroimidazole Antibiotic, Antiprotozoal

**Dosage Forms. Oral Capsule:** 375 mg; **Oral Tablet, Extended Release:** 750 mg; **Oral Tablet:** 250 mg, 500 mg

Barr generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Abscess, anaerobic: 7.5 mg/kg po q6h; *max* 4 g/d
2. Amebic dysentery, acute: Adults, 750 mg po tid × 5-10 d; Children, 35-50 mg/kg/d po in 3 divided doses for 10 d; *max* 750 mg/dose
3. Bacterial vaginosis: Extended-release tablets, 750 mg po daily × 7 d
4. Trichomoniasis (for patient and sex partner): 2 g po × 1 dose or 250 mg po q8h × 7 d or 1 g bid × 2 doses

**Off-Label Uses.**

1. *C. difficile* diarrhea, including pseudomembranous colitis, mild-moderate initial episode or 1st recurrence: 500 mg po tid × 10-14 d
2. *H. pylori* GI tract infection: 500 mg po bid in combination with clarithromycin and a PPI ("triple therapy")

**MOA.** Metronidazole is a synthetic nitroimidazole active against *T. vaginalis* (trichomoniasis), *E. histolytica* (amebiasis), and *G. lamblia* (giardiasis); it is bactericidal against nearly all obligate anaerobic bacteria including *B. fragilis*.

**Drug Characteristics: Metronidazole**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Severe hepatic dysfunction, consider dose reduction by 50% | **Absorption** | F = 100%, food effects rate, but not extent of absorption |
| **Dose Adjustment Renal** | CrCl <10 mL/min, reduce dose by 50% | **Distribution** | Abscess, bronchial f uids, peritoneal, saliva, crosses BBB |
| **Dialyzable** | Yes, supplement after hemodialysis, Peritoneal dialysis—no adjustment | **Metabolism** | Hepatic (30-60%) and occurs by glucuronidation. Moderate CYP3A4/5 inhibitor |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 60-80% of unchanged drug with a half-life of ~8 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to metronidazole, 1st trimester of pregnancy | **Black Box Warnings** | Carcinogenic |

### Medication Safety Issues: Metronidazole

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| ER | MetroNIDAZOLE | Do not crush or chew ER formulation | No | Mebendazole, meropenem, metFORMIN, methotrexate, metoclopramide, miconazole | No |

### Drug Interactions: Metronidazole

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Antiarrhythmic agents, TCAs | Increased risk of QT prolongation and other cardiac events | Avoid concurrent use if possible; if used together, monitor carefully and consider dose reductions |
| Amprenavir oral solution | Contains propylene glycol, an increased risk of propylene glycol toxicity | Solution contraindicated (reaction does not occur with amprenavir capsules) |
| CYP3A4/5 substrates | Decreases substrate metabolism and increased risk of substrate toxicity | Use with caution and consider dose reductions of CYP3A4/5 substrates. MAOIs are contraindicated |
| Cholestyramine | Decreased absorption of metronidazole | Separate administration by 2 h |
| Disulfiram | Increased CNS toxicity and disulfiram reactions | Contraindicated |
| Warfarin | Increase in warfarin concentration resulting in increase in INR and risk of bleeding | Consider reducing the dose of warfarin; monitor INR and bleeding |

### Adverse Reactions: Metronidazole

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Headaches, nausea | Diarrhea, dizziness, neuropathy, abnormal taste | Severe hypersensitivity, seizures, ototoxicity, clinically insignificant dark urine, Stevens-Johnson syndrome, neutropenia/thrombocytopenia |

**Efficacy Monitoring Parameters.** Resolution of clinical signs of infection (fever, cultures) within 2-3 d.

**Toxicity Monitoring Parameters.** Seek medical attention if severe diarrhea, dark urine, yellowing of skin or eyes, unusual bruising or bleeding, blistering skin rash, or shortness of breath. Monitor CBC for prolonged/repeated courses of therapy.

**Key Patient Counseling Points.** Avoid alcohol while taking this medicine and for 3 d after, may cause severe disulfiram-like reaction. Complete full course of therapy. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner. Extended-release tablets should be taken on an empty stomach (1 h before or 2 h after meals). Immediate-release tablets and capsules may be administered with food to minimize stomach upset.

**Clinical Pearls.** May resume normal activities after 24 h of antibiotics and afebrile. Drug of choice for mild-moderate *C. difficile* infection.

# MINOCYCLINE: Minocin, Various

**Class:** Tetracycline Antibiotic

**Dosage Forms.** **Oral Tablet:** 50 mg, 75 mg, 100 mg; **Oral Tablet, Extended Release:** 45 mg, 55 mg, 65 mg, 80 mg, 90 mg, 105 mg, 115 mg, 135 mg; **Oral Capsule:** 50 mg, 75 mg, 100 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Acne vulgaris: Extended-release, 1 mg/kg/d po daily × 12 wk
2. Allergy to penicillin—bacterial infectious disease: Adults, initial, 200 mg po, followed by 100 mg po q12h; Children >8 y of age, 4 mg/kg po, followed by 2 mg/kg/dose q12h (*max* dose 400 mg)

**Off-Label Uses.**

1. Leprosy: 100 mg po daily

**MOA.** Tetracyclines are broad-spectrum bacteriostatic compounds that inhibit protein synthesis at the 30S ribosomal subunit. Activity includes gram-positive, gram-negative, aerobic, and anaerobic bacteria, as well as spirochetes, mycoplasmas, rickettsiae, chlamydiae, and some protozoa. Many bacteria have developed plasmid-mediated resistance. Most Enterobacteriaceae and *P. aeruginosa* are resistant.

50 mg 100 mg

Watson generic pictured

**Drug Characteristics: Minocycline**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 90%; can be taken without regard to food |
| **Dose Adjustment Renal** | No specific recommendations, but consider dose reduction or extending the interval. Do not exceed 200 mg daily. | **Distribution** | Aqueous humor, CSF, gingival fluids, sinus, saliva, tears |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatically metabolized, extent unknown |
| **Pregnancy Category** | D | **Elimination** | Renal elimination is 10-20% with a half-life of 11-22 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

**Medication Safety Issues: Minocycline**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | ER formulations | No | Indocin, Lincocin, Minizide, niacin, Dyazide, Dynapen | No |

### Drug Interactions: Minocycline

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Acitretin | Risk of increased intracranial pressure; mechanism unknown | Concurrent use contraindicated |
| Aluminum, calcium, and magnesium containing antacids, iron | Decreased absorption via binding | Separate use by 1-2 h |
| Ethinyl estradiol and other estrogen-based birth control products | Alters intestinal f ora that, in turn, reduces the enterohepatic circulation of estrogen metabolites; decreased efficacy of birth control | Use an alternative form of birth control |
| Digoxin | Tetracyclines alter bacterial f ora resulting in decreased metabolism of digoxin | Monitor and consider dose adjustments of digoxin |
| Isotretinoin and vitamin A | Additive risk of intracranial hypertension | Avoid concurrent use |
| Penicillin | Bacteriostatic drugs, such as the tetracyclines, may interfere with the bactericidal effect of penicillin | Avoid concurrent use |

### Adverse Reactions: Minocycline

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Dizziness and vertigo, tooth discoloration in children <8 y of age, headache | Nausea, vomiting, diarrhea, fatigue | Hypersensitivity, hepatotoxicity, renal toxicity, *C. diff cile* colitis, increased intracranial pressure, decreased growth in children |

**Efficacy Monitoring Parameters.** Resolution of signs and symptoms of infection, or decreased acne.

**Toxicity Monitoring Parameters.** Seek medical attention if extreme headache, bloody diarrhea, tooth darkening, or yellowing of the eyes/skin occurs. LFTs, SCr in patients receiving long-term treatment.

**Key Patient Counseling Points.** May take with food that does not contain calcium (dairy). Complete full course of therapy. Symptoms should improve within 2-3 d if treating infection; if they worsen, seek follow-up with health-care practitioner. Acne should improve within 1-2 wk. Wear sunscreen. Avoid driving or using hazardous machines until side effects are known (dizziness). Warn patients (both male and female) to avoid pregnancy.

**Clinical Pearls.** Dosing is not interchangeable with extended-release and immediate-release products. Dizziness occurs more frequently in women than men. Less hepatotoxicity than is usually seen with doxycycline. May resume normal activities after 24 h of antibiotics and afebrile. Not for use in children <8 y of age due to bone and tooth discoloration.

# MIRTAZAPINE: Remeron, Various

**Class:** Antidepressant, $\alpha_2$-Antagonist

**Dosage Forms. Oral Tablet:** 7.5 mg, 15 mg, 30 mg, 45 mg; **Oral Disintegrating Tablet:** 15 mg, 30 mg, 45 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Depression: 15 mg po daily hs, may titrate to 45 mg po daily hs

15 mg

30 mg

Teva generic pictured

45 mg

Sandoz generic pictured

**Off-Label Uses.** None

**MOA.** Mirtazapine is an antidepressant that antagonizes presynaptic $\alpha_2$-adrenergic auto- and heteroreceptors that are responsible for controlling the release of norepinephrine and serotonin (5-HT). It is also a potent antagonist of postsynaptic 5-$HT_2$ and 5-$HT_3$ receptors. The net outcome of these effects is increased noradrenergic activity and enhanced 5-HT activity, especially at 5-$HT_{1A}$ receptors. This unique mechanism of action preserves antidepressant efficacy but minimizes many of the adverse effects common to heterocyclic antidepressants and SSRIs.

## Drug Characteristics: Mirtazapine

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Increase dose slowly as needed and tolerated | **Absorption** | F = 50%; minimal effect of food on absorption |
| **Dose Adjustment Renal** | CrCl <40 mL/min, increase dose slowly as needed and tolerated | **Distribution** | Vd = 4.5 L/kg; 85% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, CYP3A4/5, 2D6 and 1A2 substrate |
| **Pregnancy Category** | C | **Elimination** | Renal elimination (metabolites) is 75% and 15% in feces, with a half-life of 20-40 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to mirtazapine; concurrent MAOI, linezolid, IV methylene blue use | **Black Box Warnings** | Suicidality; not for use in children |

## Medication Safety Issues: Mirtazapine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| SolTab | No | Disintegrating tablet | No | Premarin, ramelteon, Rozerem, Zemuron | No |

### Drug Interactions: Mirtazapine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP2D6, CYP3A4/5, and CYP1A2 inducers | Increased metabolism of mirtazapine and decreased efficacy | Avoid concomitant use if possible or consider dose increases of mirtazapine |
| CYP2D6, CYP3A4/5, and CYP1A2 inhibitors | Decreased metabolism of mirtazapine and increased toxicity | Avoid concomitant use if possible or consider dose decreases of mirtazapine |
| Fluoxetine, f uvoxamine, linezolid, MAOIs, olanzapine, tramadol, venlafaxine | Increased risk of serotonin syndrome | Avoid concomitant use |

### Adverse Reactions: Mirtazapine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Constipation, increased appetite, somnolence, xerostomia, increased serum cholesterol | Asthenia, dizziness, increased liver enzymes, increased serum triglycerides, weight gain, edema, f u-like symptoms, abnormal thinking | Neutropenia, suicidal thoughts |

**Efficacy Monitoring Parameters.** Improvement in symptoms of depression (suicidal thoughts or intent, change in appetite, lack of energy, change in sleep patterns, etc).

**Toxicity Monitoring Parameters.** Worsening of depression, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases; monitor CBC, lipid panel, body weight, and LFTs.

**Key Patient Counseling Points.** Orally disintegrating tablet blister pack should be opened with dry hands and placed on tongue; no water is needed; tablet should be used immediately after removal from package; once removed, it cannot be stored. Avoid activities requiring mental alertness until drug effects are realized. Report worsening depression, suicidal ideation, or unusual changes in behavior. Do not drink alcohol while taking this drug. Take in the evening prior to sleep.

**Clinical Pearls.** Safety and effectiveness in pediatric patients have not been established. Use with caution in elderly patients who may be more susceptible to adverse effects. Medication guide required at dispensing. QT prolongation/torsades de pointes has been reported.

# MODAFINIL: Provigil, Various

**Class:** CNS Stimulant. C-IV

**Dosage Forms. Oral Tablet:** 100 mg, 200 mg

Cephalon pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Narcolepsy: 200 mg po daily in the morning, *max* 400 mg/d
2. Obstructive sleep apnea, improve excessive sleepiness; adjunct: 200 mg po daily in the morning, *max* 400 mg/d
3. Shift work-sleep disorder: 200 mg po daily 1 h before start of work shift, *max* 400 mg/d

**Off-Label Uses.**

1. Attention-deficit hyperactivity disorder: 200 mg po daily

**MOA.** The mechanism of action of modafinil is uncertain. Modafinil is a wakefulness-promoting agent acting as a CNS stimulant. It is chemically and pharmacologically unrelated to other CNS stimulants, such as methylphenidate, amphetamine, or pemoline.

**Drug Characteristics: Modafinil**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Severe hepatic impairment, 100 mg po daily | **Absorption** | Rapid absorption, food slows absorption but does not affect extent |
| **Dose Adjustment Renal** | CrCl <20 mL/min, initial dose 100-200 mg/d | **Distribution** | Vd = 0.9 L/kg; 60% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, CYP3A4/5 substrate. Strong CYP2C19 inhibitor |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 80% (10% unchanged) and 1% in feces, with a half-life of 7.5-15 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | Use with caution in CYP2C19 poor metabolizers |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

**Medication Safety Issues: Modafinil**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Plaquenil | No |

### Drug Interactions: Modafinil

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inducers | Increased modafinil metabolism and decreased modafinil efficacy | Avoid concurrent use or monitor efficacy and consider modafinil dose increases |
| CYP3A4/5 inhibitors | Decreased modafinil metabolism increases risk of modafinil toxicity | Avoid concurrent use or monitor toxicity and consider modafinil dose decreases |
| CYP2C19 substrates | Decreased metabolism of substrates, increased risk of substrate toxicity | Avoid concurrent use if possible or consider dose reductions of substrates |
| Combination contraceptives | Decreased contraceptive bioavailability and reduced effectiveness | Use alternative non-hormonal contraceptive method of birth control; monitor closely for signs of breakthrough bleeding and/or pregnancy |

### Adverse Reactions: Modafinil

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Anxiety, headache, insomnia, nausea | Chest pain, dizziness, feeling nervous, hypertension, loss of appetite, palpitations, rash, tachycardia, xerostomia | Cardiac dysrhythmia, Stevens-Johnson syndrome |

**Efficacy Monitoring Parameters.** Degree of sleepiness, improvement of mental, and behavioral symptoms.

**Toxicity Monitoring Parameters.** Palpitations, near syncope, or syncope; may be indicative of a cardiac condition; BP and HR. Weight.

**Key Patient Counseling Points.** This drug may decrease effectiveness of hormonal or IUD contraception. Recommend additional form of birth control during therapy and 1 mo after last dose. Avoid activities requiring mental alertness or coordination until drug effects are realized. If using drug for daytime wakefulness, take in the morning; if using to maintain wakefulness during shift work, take drug 1 h prior to working. Do not drink alcohol while taking this drug. Practice good sleep hygiene. Does not replace need for CPAP machines in patients with obstructive sleep apnea.

**Clinical Pearls.** Safety and effectiveness in children <16 y old have not been established. HR and BP should be evaluated at baseline, during routine follow-up within 1-3 mo, and at follow-up visits every 6-12 mo. Increases in BP and HR have been reported with the use of certain ADHD drugs. Dispense with medication safety guide.

# MOMETASONE NASAL: Nasonex, Various

**Class:** Intranasal Corticosteroid

**Dosage Forms. Nasal Spray:** 50 mcg/actuation

**Common FDA Label Indication, Dosing, and Titration.**

1. Seasonal and perennial allergic rhinitis: Children 2-11 y of age, 1 spray/nostril daily (100 mcg/d); Children ≥12 y of age and Adults, 2 sprays/nostril daily (200 mcg/d)
2. Nasal polyp: 2 sprays/nostril (50 mcg/spray) bid (400 mcg/d), reduce dose to 2 sprays/nostril daily if possible

**Off-Label Uses.** None

**MOA.** Mometasone has anti-inflammatory, antipruritic, and vasoconstrictive properties. Corticosteroids are thought to act by the induction of phospholipase A2 inhibitory proteins, lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor, arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A2.

Schering Corporation pictured

**Drug Characteristics: Mometasone Nasal**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Minimal (<2%) absorption after nasal administration |
| **Dose Adjustment Renal** | Not required | **Distribution** | Not absorbed |
| **Dialyzable** | Not dialyzable | **Metabolism** | Not absorbed |
| **Pregnancy Category** | C | **Elimination** | Not absorbed |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

**Medication Safety Issues: Mometasone Nasal**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | No |

**Drug Interactions:** **Mometasone Nasal.** None known

**Adverse Reactions: Mometasone Nasal**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Nasal irritation and burning, headache, pharyngitis | Epistaxis, cough | Severe hypersensitivity, glaucoma, pneumonia, secondary hypocortisolism; osteoporosis |

**Efficacy Monitoring Parameters.** Control of rhinitis signs and symptoms.

**Toxicity Monitoring Parameters.** While only small amounts of mometasone reach systemic circulation, BMD and growth and development in children should be monitored. Routine ophthalmologic examinations should be performed. Monitor for signs and symptoms of adrenal suppression or infection.

**Key Patient Counseling Points.** Advise patients on the proper administration technique for this product. Nasal spray needs to be primed before using and if not used for 1 wk. Instruct patients to monitor for signs of toxicity, especially adrenal insufficiency.

**Clinical Pearls.** Oral inhalation and topical dosage forms of mometasone are also available for treatment of other allergic disorders. While oral antihistamines (either over the counter or prescription) remain the mainstay for treatment of rhinitis, nasal steroids are a recommended option if symptoms are severe, unresolved with oral antihistamines, or if oral antihistamines cause undesirable adverse effects. May begin treatment for seasonal allergic rhinitis 2-4 wk before the expected start of allergy season at the dose approved for the treatment of allergic rhinitis.

# MONTELUKAST: Singulair, Various

**Class:** Leukotriene Receptor Antagonist

**Dosage Forms. Oral Tablet:** 10 mg; **Oral Chewable Tablet:** 4 mg, 5 mg; **Oral Granules:** 4 mg/packet

Merck 10 mg pictured

**Common FDA Label Indication, Dosing, and Titrations.**

1. Asthma: Children 12 mo to 5 y of age, 4 mg po daily; Children 6-14 y of age, 5 mg po daily; Children ≥15 y of age and Adults, 10 mg po daily
2. Exercise-induced asthma: Children 6-14 y of age, 5 mg po 2 h before exercise; Children ≥15 y of age and Adults, 10 mg po 2 h before exercise, *max* 1 dose/24 h
3. Seasonal allergic rhinitis: Children 2 to 5 y of age, 4 mg po daily; Children 6-14 y of age, 5 mg po daily; Children ≥15 y of age and Adults, 10 mg po daily

**Off-Label Uses.**

1. Atopic dermatitis: 10 mg po daily

**MOA.** Leukotrienes are products of arachidonic acid metabolism and are released from various cells, including mast cells and eosinophils, and bind to leukotriene receptors. Montelukast binds with leukotriene receptors to inhibit physiologic actions of leukotriene.

**Drug Characteristics: Montelukast**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 63-73%, food decreases bioavailability |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 8-11 L; >99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, CYP3A4/5 and CYP2C9 substrate |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is <1% with a half-life of 3-6 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

**Medication Safety Issues: Montelukast**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Oralair, SINEquan | No |

### Drug Interactions: Montelukast

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP2C9 and CYP3A4/5 inducers | Increased metabolism of montelukast decreases montelukast efficacy | Monitor for efficacy of montelukast; consider dose increases |
| CYP2C9 and CYP3A4/5 inhibitors | Decreased metabolism of montelukast increases the risk of montelukast toxicity | Monitor for toxicity of montelukast; consider dose reductions |
| Prednisone | Severe peripheral edema | Use with caution; monitor for edema |

### Adverse Reactions: Montelukast

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Headache | Dizziness, fatigue, rash, increased LFTs, dyspepsia | Allergic granulomatosis angiitis, cholestatic hepatitis, aggressive behavior, altered behavior, suicidal thoughts |

**Efficacy Monitoring Parameters.** Resolution of clinical signs of asthma (improved pulmonary function tests) or symptoms of rhinitis.

**Toxicity Monitoring Parameters.** Seek medical attention if change in behavior/mood, including suicidal thinking or suicide or neuropsychiatric symptoms (eg, agitation, aggression, anxiousness, etc,) occurs; monitor blood chemistry and LFT monitoring.

**Key Patient Counseling Points.** Not indicated for acute asthma attacks. Report increased use or frequency of short-acting inhaled bronchodilators and advise patients not to discontinue or decrease the dose of other asthma medications unless instructed by a health-care professional. Patients with asthma or allergic rhinitis should take dose in the evening.

**Clinical Pearls.** Current treatment guidelines published by the National Heart, Lung, and Blood Institute (NHLBI) emphasize the use of inhaled corticosteroids as first-line therapy for long-term control of persistent asthma symptoms in both children and adults. Leukotriene receptor antagonists are alternative agents, but not preferred, for the treatment of mild persistent asthma in children ≥5 y of age, and in adults. Consult guidelines for more information on asthma management.

# MORPHINE ER: MS Contin, Avinza, Kadian, Various

**Class:** Opioid Analgesic. C-II

**Dosage Forms. Oral Tablet:** 15 mg 30 mg; **Oral Tablet, Extended Release:** 15 mg, 30 mg, 60 mg, 100 mg, 200 mg; **Oral Capsule, Extended Release, 24 h:** Avinza: 30 mg, 45 mg, 60 mg, 75 mg, 90 mg, 120 mg; Kadian: 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 80 mg, 100 mg, 200 mg; **Oral Solution:** 10 mg/5 mL, 20 mg/5 mL, 20 mg/1 mL, 100 mg/5 mL; **Rectal Suppository:** 5 mg, 10 mg, 20 mg, 30 mg

15 mg

Endo generic pictured

30 mg

Mallinckrodt generic pictured

60 mg

Endo generic pictured

**Common FDA Label Indication and Dosing.**

1. Pain, chronic, moderate to severe: 10-20 mg po q12h, titrate to response; use immediate-release formulation to determine patient's morphine requirement and titrate to response. Avinza is given once daily; Kadian may be given once daily or q12h. MS Contin is given q8-12h.

**Off-Label Uses.** None

**MOA.** Morphine is a pure mu agonist. Mu receptors are responsible for analgesia, respiratory depression, miosis, decreased GI motility, and euphoria. In the CNS, it promotes analgesia and respiratory depression by decreasing brain stem respiratory centers' response to carbon dioxide tension and electrical stimulation. It also decreases gastric, biliary, and pancreatic secretion, induces peripheral vasodilation, and promotes opioid-induced hypotension due to histamine release.

**Drug Characteristics: Morphine ER**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Severe impairment, extend dosing interval or start with lower doses | **Absorption** | F = <40%, food slows rate, but not extent of absorption |
| **Dose Adjustment Renal** | CrCl 10-50 mL/min, reduce dose by 25%; CrCl <10 mL/min, reduce dose by 50% | **Distribution** | Vd = 1-6 L/kg; 20-36% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic by glucuronidation |
| **Pregnancy Category** | C | **Elimination** | Renal elimination (metabolites) is 90% with a half-life of 15 h |
| **Lactation** | Compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to opioids, acute or severe asthma, paralytic ileus, respiratory depression, GI obstruction | **Black Box Warnings** | Abuse/misuse/diversion; ethanol; extended release products; concentrated oral solutions; overdose; respiratory depression |

### Medication Safety Issues: Morphine ER

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | AVINza | ER formulations | Yes | Evista, INVanza, OxyCONTIN, hydromorphone, methadone, magnesium sulfate | No |

### Drug Interactions: Morphine ER

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Barbiturates, benzodiazepines, centrally acting muscle relaxants, opioids, phenothiazines | Additive CNS depression | Monitor and consider dose adjustments |
| Buprenorphine, opioid agonists/antagonists, opioid antagonists | Precipitation of withdrawal symptoms | Avoid concurrent use with opioids |
| MAOIs | Additive respiratory depression, increased serotonin syndrome | Contraindicated |

### Adverse Reactions: Morphine ER

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Constipation, nausea, vomiting, hypotension, dizziness, sedation, edema, pruritus, headaches, depression, xerostomia | Dyspnea | Cardiac arrest, physical dependence, tolerance, respiratory depression |

**Efficacy Monitoring Parameters.** Relief of pain.

**Toxicity Monitoring Parameters.** Excessive drowsiness, decreased breathing, severe constipation, chest pain, dizziness, vital signs.

**Key Patient Counseling Points.** Use a stool softener and stimulant or laxative for preventing constipation. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol and other CNS depressants. Extended-release products must not be crushed or chewed. Crushing or chewing will release the total dose of morphine at once and increase risk of respiratory depression. ER capsule can be opened and sprinkled on soft food, but must be swallowed whole and not chewed.

**Clinical Pearls.** Tolerance and physical dependence may occur with chronic use; avoid abrupt discontinuation. Extended-release products are not for use in children. Fatal respiratory depression has occurred; highest risk at initiation and with dosage increases. Do not administer Avinza with alcoholic beverages or ethanol-containing products, which may disrupt extended-release characteristic of product. Highly concentrated oral solutions are available. Check doses carefully when using highly concentrated oral solutions. The 100 mg/5 mL (20 mg/mL) concentration is indicated for use in opioid-tolerant patients only. Now in an REMS program.

# MOXIFLOXACIN: Avelox

**Class:** Fluoroquinolone Antibiotic

**Dosage Forms.** **Oral Tablet:** 400 mg

Bayer 400 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Acute infective exacerbation of chronic obstructive pulmonary disease: 400 mg po daily × 5 d
2. Bacterial sinusitis, acute: 400 mg po daily × 10 d
3. Community-acquired pneumonia: 400 mg po daily × 7-14 d
4. Infection of skin and/or subcutaneous tissue: 400 mg po daily × 7-21 d

**Off-Label Uses.**

1. Tuberculosis: 400 mg po daily × 6 mo

**MOA.** Moxifloxacin is a fluoroquinolone that inhibits bacterial topoisomerase II and IV. It has a broad spectrum of activity, including gram-positive and gram-negative organisms, *Chlamydia*, and anaerobes. It is effective for respiratory tract infections caused by *S. pneumoniae*, *H. influenzae*, and others.

**Drug Characteristics: Moxifoxacin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 90%, no food effect, take without regard to meals |
| **Dose Adjustment Renal** | Not required | **Distribution** | Abdominal tissue, bronchial mucosa CSF, sinus, sputum |
| **Dialyzable** | Not dialyzable | **Metabolism** | 52% hepatic via glucuronide and sulfate conjugation |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 20% with a half-life of 12 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | Myasthenia gravis; tendinitis and tendon rupture |

**Medication Safety Issues: Moxifoxacin**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Avonex | No |

### Drug Interactions: Moxif oxacin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Antidiabetic agents | Hypoglycemic or hyperglycemic episodes have been reported when f uoroquinolones were used with antidiabetic agents; mechanism unknown | Caution with concurrent use; monitor plasma glucose and consider dose adjustments of antidiabetic agent |
| Aluminum, calcium and calcium-fortified foods, didanosine, iron | Decreased absorption of f uoroquinolones caused by chelation | Moxif oxacin should be taken 4 h before or 8 h after agents that decrease moxif oxacin absorption |
| Class III antiarrhythmic agents or other agents that effect the QTc interval | Additive potential for QTc prolongation | Contraindicated |
| Corticosteroids | Increased risk of tendon rupture | Counsel patients to discontinue moxif oxacin and seek medical attention if tendon pain or rupture |
| NSAIDs | Increased risk of seizures via inhibition of GABA resulting in CNS stimulation | Avoid NSAIDs if possible |

### Adverse Reactions: Moxif oxacin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Nausea, dizziness, diarrhea, headache | Stevens-Johnson syndrome, renal failure, severe hypersensitivity, anemia, neutropenia, thrombocytopenia, seizure, cardiac arrhythmias, liver failure, tendon rupture, psychosis, exacerbation of myasthenia gravis |

**Efficacy Monitoring Parameters.** Resolution of signs and symptoms of infection. WBC.

**Toxicity Monitoring Parameters.** Seek medical attention if decreased urination, yellowing of eyes/skin, blistering skin rash or extreme fatigue, unusual bruising or bleeding, shortness of breath or chest pain, tendon pain, unusual thoughts, or numbness or tingling in the arms or legs. Baseline renal function tests.

**Key Patient Counseling Points.** Seek medical attention if rash develops. Complete full course of therapy. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner. If tendon pain develops, discontinue use and seek medical attention. Patients >65 y of age and on concurrent steroids are at increased risk. You may take this medicine with or without food. Do not take this medicine with milk, yogurt, or other dairy products or calcium-fortified products (some juices and breads). If using antacids, sucralfate, or mineral supplements and multivitamins with calcium, iron, or zinc, take moxifloxacin at least 4 h before or 8 h after these medicines. Wear sunscreen.

**Clinical Pearls.** Moxifloxacin is not approved for children <18 y of age. Oral and IV dosing is interchangeable. May be used for patients with β-lactam allergy or if initial therapy fails.

# MOXIFLOXACIN OPHTHALMIC: Vigamox

**Class:** Fluoroquinolone Antibiotic, Ophthalmic

**Dosage Forms. Ophthalmic Solution:** 0.5%

**Common FDA Label Indication and Dosing.**

1. Bacterial conjunctivitis: Adults and Children >1 y of age, 1 drop to affected eye(s) tid × 7 d

**Off-Label Uses.** None

**MOA.** Moxifloxacin is a fluoroquinolone that inhibits bacterial topoisomerase II and IV. It has a broad spectrum of activity, including gram-positive and gram-negative organisms, and anaerobes.

Alcon pictured

**Drug Characteristics: Moxifoxacin Ophthalmic**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Not absorbed after ocular administration |
| **Dose Adjustment Renal** | Not required | **Distribution** | Not absorbed |
| **Dialyzable** | Not dialyzable | **Metabolism** | Not absorbed |
| **Pregnancy Category** | C | **Elimination** | Not absorbed |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

**Medication Safety Issues: Moxifoxacin Ophthalmic**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Fisamox | No |

**Drug Interactions: Moxifloxacin Ophthalmic.** None known

**Adverse Reactions: Moxifoxacin Ophthalmic**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (>1%) |
|---|---|---|
| | Conjunctivitis, dry eyes, eye pain, subconjunctival hemorrhage, tearing and burning of the eyes, reduced visual acuity | Fungal or bacterial ocular superinfection |

**Efficacy Monitoring Parameters.** Resolution of signs and symptoms of infection.

**Toxicity Monitoring Parameters.** Seek medical attention if severe eye pain, itching, redness, or burning.

**Key Patient Counseling Points.** Symptoms should improve within 2-3 d, but complete full course of therapy. If symptoms worsen, seek follow-up with health-care practitioner. Wash hands with soap and water before and after use. Lie down or tilt your head back. With your index finger, pull down the lower lid of your eye to form a pocket. Hold the dropper close to your eye, but not touching, with the other hand. Drop the correct number of drops into the pocket made between your lower lid and eyeball. Gently close your eyes. Place your index finger over the inner corner of your eye for 1 min. Do not rinse or wipe the dropper or allow it to touch anything, including your eye. Contact lenses should not be worn during therapy.

**Clinical Pearls.** Bacterial conjunctivitis is very contagious and spreads by direct contact.

# MUPIROCIN: Bactroban, Various

**Class:** Topical Antibacterial

**Dosage Forms.** **Topical Ointment:** 2%; **Topical Cream:** 2%; **Nasal Ointment:** 2%

**Common FDA Label Indication and Dosing.**

1. Impetigo: Apply topically tid × 3-5 d, reevaluate if no response
2. Secondary skin infections: Apply topically tid × 10 d, reevaluate if no response in 3-5 d
3. Eradication of nasal colonization of MRSA during institutional outbreaks: Apply one-half of single use tube to each nostril bid × 5 d

**Off-Label Uses.**

1. Surgical prophylaxis in MRSA carriers: Apply one-half of single tube to each nostril bid × 5 d

**MOA.** Mupirocin is an antibacterial agent active against a wide range of gram-positive bacteria including methicillin-resistant *S. aureus*. It is also active against certain gram-negative bacteria. Mupirocin inhibits bacterial protein synthesis by reversibly and specifically binding to bacterial isoleucyl transfer-RNA synthetase. Because of this unique mode of action, mupirocin demonstrates no in vitro cross-resistance with other classes of antimicrobial agents.

Teva generic 2% ointment pictured

**Drug Characteristics: Mupirocin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Minimal absorption after application to intact skin |
| **Dose Adjustment Renal** | Not required | **Distribution** | Not absorbed |
| **Dialyzable** | Not dialyzable | **Metabolism** | Not absorbed |
| **Pregnancy Category** | B | **Elimination** | Not absorbed |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

**Medication Safety Issues: Mupirocin**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| AT Nasal | No | No | No | Bacitracin, baclofen, Bactrim | No |

**Drug Interactions: Mupirocin.** None known

**Adverse Reactions: Mupirocin**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Headache, pruritus, burning at site of application, stinging sensation, rhinitis | *C. diff cile* diarrhea |

**Efficacy Monitoring Parameters.** Resolution of clinical signs of infection within 3-5 d. Eradication of nasal colonization.
**Toxicity Monitoring Parameters.** Seek medical attention if local adverse effects are severe.
**Key Patient Counseling Points.** Instruct patients on proper application technique. Avoid drug exposure to open wounds, burns, or eyes.
**Clinical Pearls.** The area treated may be covered with gauze dressing if desired.

# NAPROXEN: Naprosyn, Various



**Class:** NSAID

**Dosage Forms.** **Oral Tablet:** 250 mg, 275 mg, 375 mg, 500 mg; **Oral Tablet, Extended Release:** 375 mg, 500 mg, 750 mg; **Oral Tablet, Enteric Coated, Delayed Release:** 375 mg, 500 mg; **Oral Capsule:** 220 mg; **Oral Suspension:** 125 mg/5 mL

Teva generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Osteoarthritis: 250-500 mg po bid, extended-release 750-1000 mg po once daily
2. Rheumatoid arthritis: 250-500 mg po bid, extended-release 750-1000 mg po once daily
3. Gout, acute: 250 mg po tid
4. Fever: Adults and Children >12 y of age, 200-400 mg po q8-12h prn, to a *max* of 600 mg daily
5. Pain: Adults, 500 mg po q12h or 25 mg po q6-8h

**Off-Label Uses.**

1. Migraine: Initial, 750 mg po; may administer an additional 250-500 mg prn, *max* of 1250 mg/24 h

**MOA.** Nonselective inhibitor of COX-1 and COX-2.

**Drug Characteristics: Naproxen**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required, use at lowest effective dose, reduced dose may be considered | **Absorption** | F = 95%, food has minimal effect on absorption |
| **Dose Adjustment Renal** | Avoid if CrCl <30 mL/min | **Distribution** | Vd = 0.16 L/kg; >99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic not via CYP450 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 95% with a half-life of 12-17 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to naproxen, other NSAIDs, aspirin or sulfonamides; asthma or allergic-type reaction following aspirin or other NSAID administration, CABG surgery, treatment of perioperative pain | **Black Box Warnings** | Cardiovascular and GI risk; CABG |

**Medication Safety Issues: Naproxen**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| DS, DR, EC | No | Do not crush or chew extended-release formulation | No | Natacyn, Anaspaz, Nebcin, Avapro, Naprelan | Avoid chronic use unless other alternatives are not effective and patient can take gastroprotective agent |

### Drug Interactions: Naproxen

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Aspirin, low-molecular-weight heparins, SSRIs, NSAIDs, pentoxifylline | Additive GI toxicity and increased risk of bleeding | Concurrent ketorolac, contraindicated; others, monitor for GI toxicity |
| Antihypertensive agents: ACE-Is, ARBs, beta-blockers, loop and thiazide diuretics | Decreased diuretic and antihypertensive efficacy via decreased renal prostaglandin production | Monitor and consider alternative therapy |
| Cyclosporine, tacrolimus | Increased risk of cyclosporine, tacrolimus toxicity, unknown mechanism | Monitor cyclosporine and tacrolimus levels and consider dose adjustments |
| Pemetrexed | Decreased renal clearance and increased toxicity of pemetrexed | Avoid concurrent use in patients with renal dysfunction |
| Sulfonylureas | Increased risk of hypoglycemia via inhibition of sulfonylurea metabolism | Monitor FBG and adjust as necessary |
| Warfarin, rivaroxaban, apixaban, dabigatran | Increased risk of bleeding | Monitor for GI toxicity/bleeding |

### Adverse Reactions: Naproxen

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Edema, itching, rash, GI distress, dizziness, tinnitus, ototoxicity | Stevens-Johnson syndrome, GI bleeding, thrombosis, elevated LFTs, acute renal failure, congestive heart failure, aplastic anemia |

**Efficacy Monitoring Parameters.** Decreased pain and improved range of motion.

**Toxicity Monitoring Parameters.** Severe skin rash, black tarry stools, chest pain, yellowing of eyes or skin, change in urination; monitor CBC, LFTs, SCr, fecal occult blood tests, BP (if patient has hypertension) if chronic use.

**Key Patient Counseling Points.** Take with food or milk to decrease GI upset.

**Clinical Pearls.** Elderly patients are at increased risk of GI ulceration. Patients with underlying cardiac dysfunction are at increased risk of cardiovascular effects. Use lowest dose for shortest period of time to minimize toxicity. Naproxen is also available OTC as a 220-mg tablet. If taken as OTC for fever, do not take longer than 10 d unless directed by physician. Medication guide required at dispensing.

# NEBIVOLOL: Bystolic



**Class:** β-Adrenergic Blocker, Cardioselective, $B_1$ Selective

**Dosage Forms. Oral Tablet:** 2.5 mg, 5 mg, 10 mg, 20 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Hypertension: 5 mg po daily; may titrate to *max* 40 mg po daily

**Off-Label Uses.**

1. Heart failure: 1.25 mg po daily, may titrate to 10 mg po daily

**MOA.** Nebivolol is a long-acting cardioselective $\beta_1$-adrenoceptor antagonist without intrinsic sympathomimetic activities. The mechanism of action of the antihypertensive response of nebivolol is not fully understood. Possible mechanisms include decreased heart rate, decreased myocardial contractility and vasodilation, and decreased peripheral vascular resistance.

Forest Laboratories 5 mg pictured

**Drug Characteristics: Nebivolol**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Moderate hepatic dysfunction, initial dose 2.5 mg po daily, titrate carefully<br>Severe impairment, avoid | **Absorption** | F = 12% (extensive metabolizers), F = 96% (poor metabolizers); no effect of food on absorption |
| **Dose Adjustment Renal** | CrCl <30 mL/min, initial dose 2.5 mg po daily, titrate carefully | **Distribution** | Vd = 695-2755 L; 98% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, via CYP2D6 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 38% (extensive metabolizers) to 67% (poor metabolizers) with a half-life of 12-19 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to nebivolol; severe bradycardia, 2nd- or 3rd-degree AV block, sick sinus syndrome; decompensated heart failure, cardiogenic shock; severe hepatic impairment | **Black Box Warnings** | None |

**Medication Safety Issues: Nebivolol**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | No |

### Drug Interactions: Nebivolol

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| NSAIDs | Decreased antihypertensive effect of nebivolol | Avoid concurrent use or monitor BP |
| Amiodarone, dronedarone | Increased risk of bradycardia, heart block, sinus arrest | Avoid concurrent use in patients with sick sinus syndrome or AV block |
| Antidiabetic drugs | Decreased glycemic control | Monitor blood glucose levels |
| Calcium channel blockers | Increased risk of hypotension and/or bradycardia and AV block (non-dihydropyridine) | Monitor BP and HR, may need to avoid with non-dihydropyridines |
| Digoxin | Increased risk of AV block | Monitor HR, ECG, and serum digoxin concentrations |
| Alpha-blockers, fentanyl | Increased risk of hypotension | Monitor BP |
| CYP2D6 inhibitors | Decreased nebivolol metabolism increases risk of nebivolol toxicity | Monitor and consider dose decreases of nebivolol |

### Adverse Reactions: Nebivolol

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Bradyarrhythmias, bronchospasm, disorder of glucose regulation, dizziness, dyspnea, headache, hypotension, nausea, diarrhea, somnolence | Heart block, withdrawal symptoms (angina, myocardial infarction, ventricular arrhythmias) |

**Efficacy Monitoring Parameters.** Decreased BP and HR.

**Toxicity Monitoring Parameters.** Decreased HR, bronchospasm, blood glucose levels in diabetic patients.

**Key Patient Counseling Points.** Report signs/symptoms of hypotension, worsening heart failure, or bronchospastic disease. Do not drink alcohol. May cause dizziness. Avoid activities that could be dangerous if not alert. Diabetic patients should carefully monitor blood sugar levels as beta-blockers may mask symptoms of hypoglycemia. Do not discontinue drug abruptly, as this may cause rebound angina or, in some cases, myocardial infarction.

**Clinical Pearls.** Safety and efficacy not established in children. Patients should avoid concomitant use of calcium channel blockers, as concomitant use may significantly affect HR or heart rhythm.

# NIACIN: Niaspan, Slo-Niacin, Various

Abbott Laboratories pictured

**Class:** Antihyperlipidemic

**Dosage Forms.** **Oral Capsule, Extended Release:** 250 mg, 500 mg; **Oral Tablet:** 50 mg, 100 mg, 250 mg, 500 mg; **Oral Tablet, Extended Release:** 250 mg, 500 mg, 750 mg, 1000 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Coronary arteriosclerosis, hypercholesterolemia: Extended release, 500 mg po daily, may titrate to 2000 mg/d po
2. Dyslipidemia: Adults, immediate release, 100-1000 mg po tid, may titrate to 3000 mg/d po; extended release, 500-2000 mg po daily hs, may titrate to 2000 mg/d po; Children, 100-250 mg/d in 3 divided doses with meals, may titrate to 10 mg/kg/d
3. Myocardial infarction, secondary prophylaxis: Extended release, 500-2000 mg po daily hs, may titrate to 2000 mg/d po

**Off-Label Uses.**

1. Pellagra: 50-100 mg po tid-qid, may titrate to 500 mg/d po

**MOA.** Not well defined. May involve partial inhibition of release of free fatty acids from adipose tissue, and increased lipoprotein lipase activity, which may increase the rate of chylomicron triglyceride removal from plasma. Niacin decreases the rate of hepatic synthesis of VLDL and LDL.

**Drug Characteristics: Niacin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Contraindicated in patients with significant or unexplained hepatic dysfunction | **Absorption** | F = 60%, fatty meals decrease absorption |
| **Dose Adjustment Renal** | Not required, use caution | **Distribution** | Unknown |
| **Dialyzable** | Unknown | **Metabolism** | Hepatic not via CYP450 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 60-88% with a half-life of 20-45 min |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to niacin, active liver disease, PUD, arterial hemorrhage | **Black Box Warnings** | None |

### Medication Safety Issues: Niacin

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| Slo | No | Long-acting formulations | No | Minocin | No |

### Drug Interactions: Niacin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Statins, colchicine | Increased risk of myopathy or rhabdomyolysis | Avoid concurrent use, or monitor for myopathy and consider dose reductions |
| Cholestyramine, colestipol | Decreased absorption of niacin | Separate administration by 1 h before or 4 h after |

### Adverse Reactions: Niacin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Flushing | Atrial fibrillation, pruritus, rash, nausea, vomiting, reduced platelet count, elevated LFTs, myalgia | Hypophosphatemia, hepatotoxicity, rhabdomyolysis |

**Efficacy Monitoring Parameters.** Reduction in total cholesterol, LDL, and triglycerides levels; increase in HDL.

**Toxicity Monitoring Parameters.** Signs/symptoms of rhabdomyolysis (myalgias, dark urine, arthralgias, fatigue), yellowing of eyes or skin, severe abdominal pain, monitor LFT, CBC; serum creatine kinase if muscle pain occurs, FBG or $HbA_{1c}$, uric acid

**Key Patient Counseling Points.** Start with a low dose and titrate based on tolerability (primarily flushing). Avoid alcohol and warm beverages with niacin to reduce flushing. If discontinued for several days, may need to restart on a lower dose and retitrate. Aspirin or NSAID 30 min prior to niacin may reduce flushing. Take at bedtime with a low-fat snack to help with flushing.

**Clinical Pearls.** Also known as vitamin $B_3$. Statins are first-line therapy for hyperlipidemia. Niacin may be added for high-risk patients not able to achieve lipid goals with statin therapy.

# NIFEDIPINE: Adalat CC, Procardia XL, Various



**Class:** Calcium Channel Blocker

**Dosage Forms.** **Oral Tablet, Extended Release:** 30 mg, 60 mg, 90 mg; **Oral Capsule:** 10 mg, 20 mg

Teva generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Hypertension: Adults, 30 mg po daily, may titrate to 90 mg/d po (Adalat CC) or 120 mg/d po (Procardia XL); Children, 0.25 mg/kg po daily in 1 or 2 divided doses, may titrate to 3 mg/kg/d po (*max* of 180 mg/d)
2. Stable chronic angina: 30-60 mg po daily, may titrate to 120 mg/d po
3. Variant angina: 30-60 mg po daily, may titrate to 120 mg/d po

**Off-Label Uses.**

1. Raynaud phenomenon: 30-60 mg po daily

**MOA.** Nifedipine is a calcium ion influx inhibitor that selectively inhibits the transmembrane influx of calcium ions into cardiac muscle and smooth muscle. Nifedipine does not alter serum calcium concentrations.

## Drug Characteristics: Nifedipine

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Clearance is reduced in patients with cirrhosis, use with caution | **Absorption** | Complete absorption, food delays absorption of Adalat CC |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 1.4-202 L/kg; 92-98% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic, CYP3A4/5 substrate |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 70-80% with a half-life of ~7 h (Adalat CC) |
| **Lactation** | Compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to nifedipine, cardiogenic shock, concurrent CYP3A4/5 inducers | **Black Box Warnings** | None |

## Medication Safety Issues: Nifedipine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| CC, XL | NIFEdipine | Extended-release tablets | No | niCARdipine, niMODipine, nisoldipine, Cartia XT | Avoid immediate release. Potential for hypotension; risk of precipitating myocardial ischemia |

### Drug Interactions: Nifedipine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| NSAIDs | Decreased antihypertensive effect of nifedipine | Avoid concurrent use or monitor BP |
| Amiodarone | Increased amiodarone concentrations and toxicity which may result in bradycardia, AV block, or sinus arrest | Caution is advised, may avoid concurrent use |
| Beta-blockers | Increased hypotension, bradycardia | Avoid concurrent use or monitor BP and HR |
| Clopidogrel | Decreased antiplatelet activity of clopidogrel | Avoid concurrent use |
| CYP3A4/5 inducers | Increased nifedipine metabolism reduces nifedipine effectiveness | Avoid concurrent use or consider dose increases of nifedipine |
| CYP3A4/5 inhibitors | Decreased nifedipine metabolism increases risk of nifedipine toxicity | Avoid concurrent use or consider dose decreases of nifedipine |
| Tacrolimus | Increased risk of tacrolimus toxicity | Monitor plasma concentrations |
| Quinidine | Decreased efficacy of quinidine, increased risk of nifedipine toxicity | Monitor quinidine plasma concentrations, monitor BP |

### Adverse Reactions: Nifedipine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Flushing, headache, peripheral edema, dizziness | Constipation, fatigue, gastroesophageal ref ux, hypotension, myalgia, myocardial infarction, nausea, palpitations, pruritus, rash, sleep disturbances, gingival hyperplasia, | Aplastic anemia, thrombocytopenia, angina, tachycardia |

**Efficacy Monitoring Parameters.** BP, reduction in chest pain, decreased number of angina attacks, reduction in use of nitroglycerin to relieve chest pain.

**Toxicity Monitoring Parameters.** Signs/symptoms of peripheral edema, angina, tachycardia, heart failure.

**Key Patient Counseling Points.** Take Adalat CC on an empty stomach. Report signs/symptoms of hypotension, exacerbation of angina, peripheral edema, fatigue, or hypotension. Do not drink alcohol. Avoid sudden discontinuation of drug as this may cause rebound hypertension. May cause dizziness; avoid driving or using hazardous machinery until effects are known. Avoid grapefruit juice.

**Clinical Pearls.** With Adalat CC, two 30-mg tablets may be interchanged for one 60-mg tablet, but using three 30-mg tablets results in 29% higher peak plasma concentrations than a single 90-mg tablet; not considered interchangeable.

# NITAZOXANIDE: Alinia



**Class:** Antiprotozoal

**Dosage Forms. Oral Tablet:** 500 mg; **Oral Suspension:** 100 mg/5 mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Diarrhea caused by *C. parvum* or *G. lamblia*: Adults and Children ≥12 y of age, 500 mg po q12h × 3 d; Children 1-3 y of age, 100 mg po q12h × 3 d; Children 4-11 y of age, 200 mg po q12h × 3 d

**Off-Label Uses.**

1. *C. difficile*–associated diarrhea: 500 mg po q12h × 10 d

**MOA.** Interference with the pyruvate ferredoxin oxidoreductase (PFOR) enzyme-dependent electron transfer reaction, which is essential to anaerobic metabolism of protozoans.

Romark 500 mg pictured

**Drug Characteristics: Nitazoxanide**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Use with caution | **Absorption** | F <5%, food enhances absorption by 50% |
| **Dose Adjustment Renal** | Use with caution | **Distribution** | 98-99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Metabolized to 1 active metabolite by plasma esterases |
| **Pregnancy Category** | B | **Elimination** | 33% renal, 67% fecal |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to nitazoxanide | **Black Box Warnings** | None |

**Medication Safety Issues: Nitazoxanide**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | No |

**Drug Interactions: Nitazoxanide.** None known

**Adverse Reactions: Nitazoxanide**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Nausea, vomiting, diarrhea, headache, abdominal pain | Elevated LFTs |

**Efficacy Monitoring Parameters.** Resolution of signs and symptoms of infection, improvement in diarrhea.

**Toxicity Monitoring Parameters.** Consider LFTs and CBC prior to therapy.

**Key Patient Counseling Points.** Complete full course of therapy; take with food. Store suspension at room temperature (expiration = 1 wk).

**Clinical Pearls.** Suspension bioavailability is 70% of tablet, not interchangeable. Preferred agent for treating *Cryptosporidium* diarrhea in immunocompetent adults; has not been proven to be superior to placebo in HIV-infected individuals. Equivalent efficacy to metronidazole for *C. difficile* and *Giardia*, however, based on cost metronidazole remains the treatment of choice.

# NITROFURANTOIN: Macrodantin, Macrobid, Various



**Class:** Nitrofuran Antibiotic

**Dosage Forms. Oral Capsule:** 25 mg, 50 mg, 100 mg;

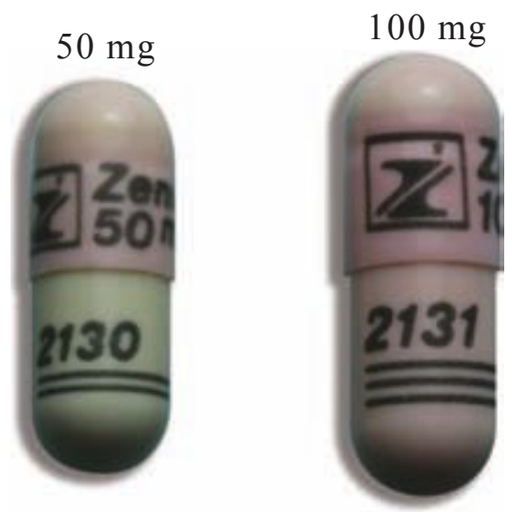
**Oral Suspension:** 25 mg/ 5mL; **Oral Capsule, Extended Release:** 100 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Urinary tract infection treatment: Adults and Children >12 y of age, Macrobid 100 mg po bid × 7 d; Furadantin, Macrodantin, 50-100 mg po q6h × 7 d; Children ≥1 mo of age, 5-7 mg/kg/d in divided doses q6h po × 7 d (*max* 400 mg/d)
2. Urinary tract infection prophylaxis: Adults, Furadantin, Macrodantin, 50-100 mg po daily hs; Children ≥1 mo of age, 1 mg/kg/d po in divided doses every 12-24 h (*max* dose 100 mg/d)

**Off-Label Uses.** None

**MOA.** Nitrofurantoin is a synthetic nitrofuran that inactivates bacterial ribosomes and is bactericidal in urine at therapeutic doses. It is active against most bacteria that cause UTIs except nearly all strains of *Pseudomonas* are resistant.



Teva generic pictured

**Drug Characteristics: Nitrofurantoin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 94%, food increases absorption |
| **Dose Adjustment Renal** | Contraindicated if CrCl <60 mL/min | **Distribution** | 90% protein bound |
| **Dialyzable** | Yes, hemodialysis only | **Metabolism** | Metabolism in all tissues to inactive metabolite |
| **Pregnancy Category** | B, contraindicated in pregnancy at term | **Elimination** | Renal elimination is 40% with a half-life of 1 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | Those with G6PD deficiency are more likely to develop hemolytic anemia |
| **Contraindications** | Hypersensitivity to nitrofurantoin, use in neonates or during delivery (risk of hemolytic anemia), anuria or oliguria | **Black Box Warnings** | None |

### Medication Safety Issues: Nitrofurantoin

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Do not open capsules | No | Nitro-Bid, nitroglycerine, microK, Neurontin, nitroglycerin | Avoid for long-term suppression; avoid in patients with CrCl <60 mL/min |

### Drug Interactions: Nitrofurantoin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Fluconazole | Increased risk of hepatic and pulmonary toxicity, unknown mechanism | Avoid concurrent use, or increase monitoring of toxicity |
| Norfloxacin | Antagonism of the antibacterial effect of norfloxacin | Avoid concurrent use |

### Adverse Reactions: Nitrofurantoin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Nausea, headache, discoloration of urine | Diarrhea | Severe hypersensitivity, hepatic failure, hemolytic anemia, interstitial lung disease |

**Efficacy Monitoring Parameters.** Resolution of clinical signs of infection within 2-3 d.

**Toxicity Monitoring Parameters.** Severe diarrhea, yellowing of skin or eye, unusual bruising or bleeding, blistering skin rash, or shortness of breath.

**Key Patient Counseling Points.** May make urine brown; this is not harmful and is a breakdown product of the drug. Complete full course of therapy. For the suspension, shake well and store at room temperature, use within 30 d. Avoid mixing suspension with food or beverages, but food can be taken afterward. Symptoms should improve within 2-3 d; if they worsen, seek follow-up care.

**Clinical Pearls.** Nitrofurantoin does not reach effective levels in tissue and is only indicated for UTIs (not pyelonephritis). May resume normal activities after 24 h of antibiotics if afebrile. The drug is used primarily to prevent recurrent UTIs but is also effective in the treatment of uncomplicated UTIs.

# NITROGLYCERIN: Minitran, Nitro-Dur, Nitrostat, Various



**Class:** Nitrate, Antianginal

**Dosage Forms.** **Oral Capsule, Extended Release:** 2.5 mg, 6.5 mg, 9 mg; **Sublingual Tablet:** 0.3 mg, 0.4 mg, 0.6 mg; **Patch:** 0.1 mg/h, 0.2 mg/h, 0.3 mg/h, 0.4 mg/h, 0.6 mg/h, 0.8 mg/h; **Sublingual Spray:** 0.4 mg/actuation; **Ointment:** 2%

**Common FDA Label Indication, Dosing, and Titration.**

1. Angina, prophylaxis: Extended release, 2.5-6.5 mg po tid-qid; Sublingual, 1 tab or 1-2 sprays 5-10 min before activity, which may induce angina; Transdermal, 0.2-0.4 mg/h worn topically 12-14 h per day, may titrate to 0.8 mg/h worn topically
2. Angina, acute: Sublingual, 1 tab or 1-2 sprays at first sign of angina, repeat every 5 min if needed for total of 3 tabs or doses in 15 min

**Off-Label Uses.** None

**MOA.** Nitroglycerin is believed to be converted to nitric oxide (NO) by vascular endothelium. NO activates guanylate cyclase, increasing cyclic GMP that in turn decreases intracellular calcium, resulting in direct relaxation of vascular smooth muscle. In myocardial ischemia, nitrates dilate large epicardial vessels, enhance collateral size and flow, and reduce coronary vasoconstriction.

Pfizer 0.4 mg pictured

**Drug Characteristics: Nitroglycerin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 38-75%, food has no effect on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 3 L/kg; 60% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic not via CYP |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 22% with a half-life of 2-3 min |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to nitrates, concurrent use with erectile dysfunction meds, symptomatic hypotension, severe anemia or increased intracranial pressure | **Black Box Warnings** | None |

### Medication Safety Issues: Nitroglycerin

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| BID, DUR, TIME | No | Extended-release capsules | No | Macrobid, NicoDerm, nitrofurantoin, nitroprusside, Nizoral, Nilstat, nystatin | No |

### Drug Interactions: Nitroglycerin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Phosphodiesterase inhibitors | Excessive hypotension | Concurrent use contraindicated |

### Adverse Reactions: Nitroglycerin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Headache | Bradycardia, drug tolerance, flushing, hypotension, light-headedness, nausea, orthostatic hypotension, tachycardia, vomiting | Increased intracranial pressure, severe hypotension, syncope, methemoglobinemia |

**Efficacy Monitoring Parameters.** Decreased use of sublingual nitroglycerin to treat anginal episodes, reduction in angina episodes, reduction in anginal pain.

**Toxicity Monitoring Parameters.** Signs/symptoms of hypotension, problematic headaches, or decreasing efficacy (drug tolerance). BP and HR.

**Key Patient Counseling Points.** Sit prior to using sublingual tablets, lingual aerosol, or spray. Tablet should be dissolved under tongue or in buccal pouch at 1st sign of angina; do not swallow. Spray should be sprayed onto or under tongue; do not inhale; do not spit out or rinse mouth after use. Rise slowly from a sitting position in order to prevent light-headedness. Allow a 10- to 12-h/d drug-free interval to avoid development of nitrate tolerance for both patches and extended-release capsules. Avoid concurrent use of alcohol, CNS depressants, antihypertensives, or other drugs that cause hypotension. Do not use with phosphodiesterase inhibitors, which may result in hypotension. The ointment may stain clothing.

**Clinical Pearls.** Safety and efficacy not established in children. Patch contains aluminum; remove before MRI.

# NORTRIPTYLINE: Pamelor, Various



**Class:** Tricyclic Antidepressant

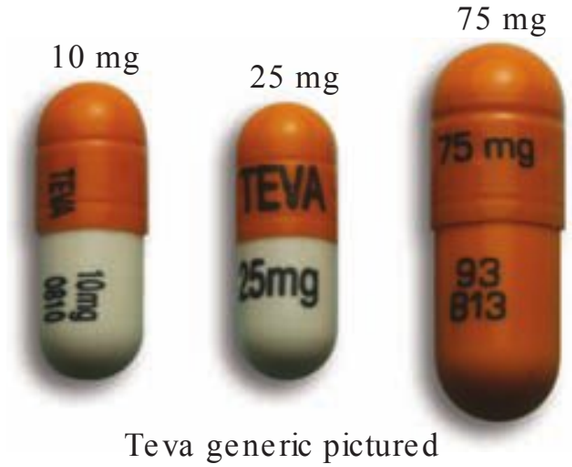
**Dosage Forms. Oral Tablet:** 10 mg, 25 mg, 50 mg, 75 mg; **Oral Solution:** 10 mg/5 mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Depression: Adults, 25 mg po tid-qid, may titrate to 150 mg/d po; Adolescents, 30-50 mg/d po in single or divided doses

**Off-Label Uses.** None

**MOA.** Nortriptyline is the demethylated metabolite of amitriptyline, a heterocyclic antidepressant that blocks presynaptic reuptake of norepinephrine with subsequent downregulation of adrenergic receptors. Heterocyclic antidepressants have less effect on serotonergic activity than on other neurotransmitters.




Teva generic pictured

## Drug Characteristics: Nortriptyline

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 60%, food has no effect on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 15-27 L/kg; 86-95% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, CYP2D6 substrate |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 2% with a half-life of 15-39 h |
| **Lactation** | Compatible | **Pharmacogenetics** | Caution with CYP2D6 poor metabolizers; at risk for drug interactions and greater toxicity |
| **Contraindications** | Hypersensitivity to nortriptyline or other TCAs; concurrent MAOI; use during acute recovery period after MI, patient using linezolid or IV methylene blue | **Black Box Warnings** | Suicidality |

## Medication Safety Issues: Nortriptyline

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Amitriptyline, Demerol, Bentyl, desipramine, Norpramin, Tambocor | No |

### Drug Interactions: Nortriptyline

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Amphetamines | Increased risk of hypertension, cardiac effects, and CNS stimulation | Use caution with concomitant therapy |
| Linezolid, MAOIs, methylene blue, SSRIs | Increased risk of serotonin syndrome | Concomitant use with MAOIs contraindicated, others with caution |
| Antiarrhythmics, and drugs that cause QT prolongation | Increased risk of cardiotoxicity (QT prolongation, torsades de pointes, cardiac arrest) | Avoid concurrent use |
| CYP2D6 inhibitors | Decreased metabolism of nortriptyline increases risk of nortriptyline toxicity | Avoid concurrent use |

### Adverse Reactions: Nortriptyline

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Constipation | Blurred vision, confusion, constipation, dizziness, headache, sexual dysfunction, somnolence, urinary retention, weight gain, xerostomia | Cardiac dysrhythmia, heart block, hepatotoxicity, seizures, suicidal thoughts |

**Efficacy Monitoring Parameters.** Improvement in symptoms of depression (suicidal thoughts or intent, change in appetite, lack of energy, change in sleep patterns, etc).

**Toxicity Monitoring Parameters.** Worsening of depression, suicidality, or unusual changes in behavior; monitor ECG and LFTs, BP, weight. Signs and symptoms of serotonin syndrome.

**Key Patient Counseling Points.** Avoid activities requiring mental alertness or coordination until drug effects are realized, as drug may cause somnolence and dizziness. Report worsening depression, suicidal ideation, unusual changes in behavior, or unusual bleeding. Avoid abrupt discontinuation, may precipitate withdrawal symptoms. Do not drink alcohol while taking this drug.

**Clinical Pearls.** Symptomatic improvement may not be seen for several weeks. Medication guide required at dispensing.

# NYSTATIN SYSTEMIC: Bio-Statin, Various



**Class:** Polyene Antifungal

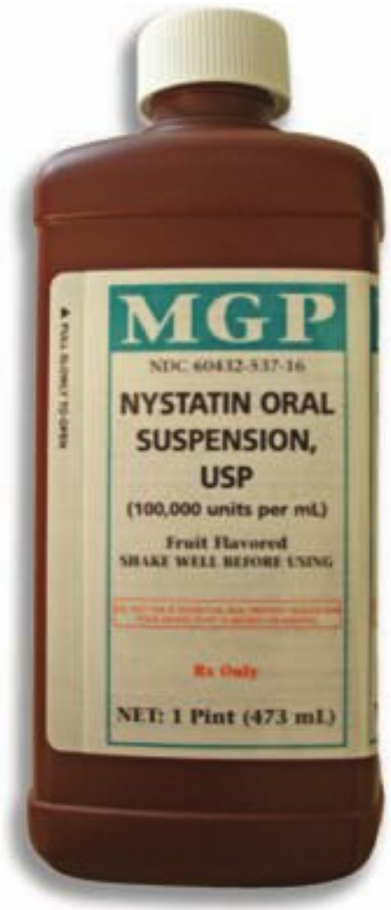
**Dosage Forms. Oral Suspension:** 100,000 units/mL; **Oral Tablet:** 500,000 units; **Oral Capsule:** 500,000 units, 1,000,000 units

**Common FDA Label Indication, Dosing, and Titration.**

1. GI candidiasis, nonesophageal: 500,000-1,000,000 units po tid
2. Oropharyngeal candidiasis: 400,000-600,000 units po qid (retained in mouth as long as possible prior to swallowing)

**Off-Label Uses.** None

**MOA.** Nystatin binds to the sterols in fungal cell walls, damaging the fungal cell wall membrane and altering its permeability.




MGP generic pictured

**Drug Characteristics: Nystatin Systemic**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Minimal absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Minimal absorption |
| **Dialyzable** | Unknown | **Metabolism** | Minimal absorption |
| **Pregnancy Category** | C | **Elimination** | Unknown |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to nystatin | **Black Box Warnings** | None |

**Medication Safety Issues: Nystatin Systemic**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | HMG-CoA agents (“statins”) | No |

**Drug Interactions: Nystatin Systemic.** None known

**Adverse Reactions: Nystatin Systemic**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | GI distress, nausea, vomiting constipation | Rash |

**Efficacy Monitoring Parameters.** Resolution of clinical symptoms.
**Toxicity Monitoring Parameters.** Seek medical attention if severe mucosal irritation or rash occurs.
**Key Patient Counseling Points.** Store the oral liquid or tablets at room temperature. Shake suspension well before using.
**Clinical Pearls.** As effective as clotrimazole in treating topical *Candida* infections. Nystatin is not absorbed and will not treat systemic infections.

# NYSTATIN TOPICAL: Mycostatin, Nyamyc, Nystop, Various

Fougera generic ointment pictured

**Class:** Polyene Antifungal

**Dosage Forms.** **Topical Cream:** 100,000 units/g; **Topical Ointment:** 100,000 units/g; **Topical Powder:** 100,000 units/g

**Common FDA Label Indication, Dosing, and Titration.**

1. Candidiasis of skin (cutaneous and mucocutaneous infections): Apply liberally to affected areas topically bid until healing complete

**Off-Label Uses.** None

**MOA.** Nystatin binds to the sterols in fungal cell walls, damaging the fungal cell wall membrane and altering its permeability.

## Drug Characteristics: Nystatin Topical

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Not absorbed |
| **Dose Adjustment Renal** | Not required | **Distribution** | Not absorbed |
| **Dialyzable** | Unknown | **Metabolism** | Not absorbed |
| **Pregnancy Category** | C | **Elimination** | Unknown |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to nystatin | **Black Box Warnings** | None |

## Medication Safety Issues: Nystatin Topical

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| AF | No | No | No | HMG-CoA agents ("statins"), Nitrostat | No |

**Drug Interactions:** **Nystatin Topical**. None known

## Adverse Reactions: Nystatin Topical

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Dry skin, skin irritation | Rash, hypersensitivity reaction, Stevens-Johnson syndrome |

**Efficacy Monitoring Parameters.** Resolution of clinical symptoms.

**Toxicity Monitoring Parameters.** Severe skin irritation or rash.

**Key Patient Counseling Points.** Apply to affected area of skin. Skin should be intact. Do not get it in eyes, nose, or mouth. Avoid occlusive dressings, tight-fitting diapers, and plastic pants if using on diaper area of children.

**Clinical Pearls.** As effective as clotrimazole in treating topical *Candida* infections. Vaginal tablet for vaginal *Candida* infections is still available but infrequently used. Miconazole and terconazole are both more effective than nystatin and are available OTC for vaginal candidiasis.

# OLANZAPINE: Zyprexa, Various



**Class:** Thienobenzodiazepine, Antipsychotic

**Dosage Forms. Oral Tablet:** 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg; **Oral Disintegrating Tablet:** 5 mg, 10 mg, 15 mg, 20 mg

Lilly pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Bipolar disorder, acute mixed or manic episodes: Adults, 10-15 mg/d po, may titrate in 5 mg/d increments; Children 13-17 y of age, 2.5-5 mg/d po, may titrate in 2.5-5 mg/d increments
2. Schizophrenia: Adults, 5-10 mg/d po, may titrate in 5 mg/d increments at 1-wk intervals to 10-20 mg/d po; Children 13-17 y of age, 2.5-5 mg/d po, may titrate in 2.5-5 mg increments
3. Depression, treatment resistant, in combination with fluoxetine: Adults, 2.5-20 mg po daily

**Off-Label Uses.** None

**MOA.** Olanzapine is an atypical antipsychotic agent that is a potent serotonin-5-$HT_2$ and dopamine-$D_2$ antagonist. Antipsychotic effect is most likely related to blockade of postsynaptic dopaminergic receptors in the mesolimbic and prefrontal cortexes of the brain, although other neurotransmitter systems also are involved.

**Drug Characteristics: Olanzapine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required, except when used with fluoxetine (limit initial olanzapine dose to 2.5-5 mg daily) | **Absorption** | Well absorbed, food has no effect on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 1000 L; 93% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic via glucuronidation, CYP1A2 substrate |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 57% with a half-life of 21-54 h |
| **Lactation** | Weigh risks and benef ts | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to olanzapine | **Black Box Warnings** | Mortality in elderly patients with dementia-related psychosis; coma and excessive sedation with injectable formulation |

**Medication Safety Issues: Olanzapine**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | ZyPREXA, OLANZapine | Disintegrating tablet | No | CeleXA, ZyrTEC, olsalazine, QUEtiapine, Reprexain, Zestril, Zelapar, zolpidem | Avoid use for behavioral problems of dementia unless nonpharmacologic options have failed and patient is threat to self or others |

## Drug Interactions: Olanzapine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Tramadol | Additive serotonergic effects | Avoid concurrent use or monitor for adverse effects |
| Haloperidol | Increased risk of parkinsonism | Monitor for signs of parkinsonism; adjust haloperidol dose |
| Metoclopramide | Increased risk of extrapyramidal symptoms | Concurrent use contraindicated |
| CYP1A2 inducers | Increased olanzapine metabolism reduces olanzapine effectiveness | Consider dose increases of olanzapine |
| CYP1A2 inhibitors | Decreased olanzapine metabolism increases risk of olanzapine toxicity | Consider dose decreases of olanzapine |
| QTc-prolonging agents | May increase the QTc interval | Avoid combining olanzapine with other agents that prolong the QTc interval |

## Adverse Reactions: Olanzapine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Akathisia, asthenia, dizziness, hypercholesterolemia, hyperglycemia, increased appetite, increased prolactin levels, increased triglycerides, somnolence, tremor, weight gain, xerostomia | Constipation, orthostatic hypotension, peripheral edema, personality disorder | Neuroleptic malignant syndrome, pancreatitis, sudden cardiac death, suicidal thoughts, tardive dyskinesia |

**Efficacy Monitoring Parameters.** Improvement in schizophrenia, bipolar disorder, agitation, or treatment-resistant depression.

**Toxicity Monitoring Parameters.** FBG/$HbA_{1c}$ prior to treatment and periodically in patients with DM. CBC, lipid profiles at baseline and periodically thereafter. Check body weight and BMI regularly during treatment. LFTs and electrolytes. Symptoms of neuroleptic malignant syndrome and involuntary movements/parkinsonian signs.

**Key Patient Counseling Points.** Avoid activities requiring mental alertness or coordination until drug effects are realized. Drug may impair heat regulation. Rise from a sitting/lying-down position slowly. Report symptoms of tardive dyskinesia or neuroleptic malignant syndrome. Diabetic patients should monitor for hyperglycemia and report difficulties with glycemic control. Avoid alcohol while taking this drug.

**Clinical Pearls.** *Max* dose is 20 mg/d. Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death compared to placebo. Although the causes of death in clinical trials were varied, most of the deaths were cardiovascular or infectious in nature. Also available as an extended-release IM injection, which is used after establishing tolerance with oral olanzapine.

# OLMESARTAN: Benicar

Daichi-Sankyo 40 mg pictured

**Class:** Angiotensin II Receptor Antagonist

**Dosage Forms.** **Oral Tablet:** 5 mg, 20 mg, 40 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Hypertension: Adults, 20 mg po daily, may titrate to 40 mg po daily; Children 6-16 y of age weighing 20-34 kg, 10 mg po daily, may titrate to 20 mg po daily; Children 6-16 y of age weighing >35 kg, 20 mg po daily, may titrate to 40 mg po daily

**Off-Label Uses.** None

**MOA.** Olmesartan is a selective, reversible, competitive antagonist of the angiotensin II receptor (AT1).

**Drug Characteristics: Olmesartan**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 26%, food has no effect on absorption |
| **Dose Adjustment Renal** | Not required, use with caution with CrCl <20 mL/min | **Distribution** | Vd = 17 L; 99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Intestinal wall; not via CYP |
| **Pregnancy Category** | D | **Elimination** | Renal elimination is 35-50% with a half-life of 3 h |
| **Lactation** | Weigh risks and benef ts | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to olmesartan or other ARB, pregnancy, concurrent use with aliskiren in patients with DM | **Black Box Warnings** | Pregnancy |

**Medication Safety Issues: Olmesartan**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Mevacor | No |

### Drug Interactions: Olmesartan

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Potassium-sparing diuretics | Increased risk of hypotension, hyperkalemia | Avoid concurrent use or monitor BP and serum potassium levels |
| ACE-Is | Increased risk of hypotension, hyperkalemia, nephrotoxicity | Avoid concurrent use or monitor BP, SCr, and potassium levels |
| Eplerenone | Increased risk of hyperkalemia | Avoid concurrent use or monitor serum potassium levels |
| Potassium supplements | Increased risk of hyperkalemia and cardiac arrhythmias | Avoid concurrent use or monitor serum potassium levels |
| NSAIDs | Decreased antihypertensive and natriuretic effect of olmesartan, increased risk of nephrotoxicity | Avoid concurrent use or monitor BP and SCr level |
| Diuretics | Increased risk of postural hypotension due to hypovolemia | Monitor BP |
| Aliskiren | Increased risk of hyperkalemia, hypotension, nephrotoxicity | Avoid use in with GFR <60 mL/min; monitor K, SCr, and BP |

### Adverse Reactions: Olmesartan

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Back pain, dizziness, headache, hyperkalemia, hypotension | Angioedema, birth defects, hepatotoxicity, rhabdomyolysis, acute renal failure |

**Efficacy Monitoring Parameters.** Decreased BP.

**Toxicity Monitoring Parameters.** Report signs/symptoms of hypotension. Baseline and periodic potassium, SCr, prior to initiating therapy and periodically thereafter.

**Key Patient Counseling Points.** Avoid pregnancy. Use potassium supplements or salt substitutes only under medical supervision. May cause dizziness that may worsen if dehydrated. Seek care if angioedema, excessive fluid loss, hyperkalemia, reduction in urination, or jaundice occurs. May cause orthostatic hypotension.

**Clinical Pearls.** ARBs can cause injury or death to the developing fetus; therapy should be stopped as soon as possible if pregnancy is detected.

# OLOPATADINE: Patanol, Pataday



**Class:** Ophthalmic Antihistamine

**Dosage Forms. Ophthalmic Solution:** 0.1%, 0.2%

**Common FDA Label Indication, Dosing, and Titration.**

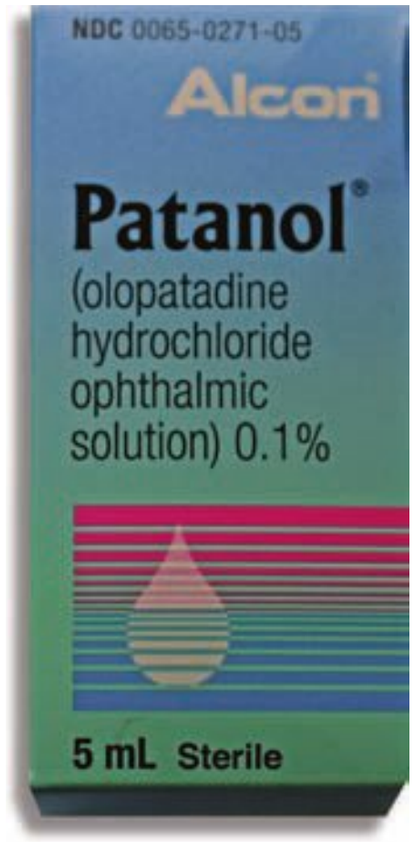
1. Allergic conjunctivitis: 1 drop of 0.1% solution in affected eye bid or 1 drop of 0.2% solution in affected eyes daily

**Off-Label Uses.** None

**MOA.** Olopatadine hydrochloride is a relatively selective histamine $H_1$-antagonist that exerts its effect by inhibiting the release of histamine from mast cells. It also blocks the type 1 immediate hypersensitivity reactions, including prevention of histamine-mediated effects on human conjunctival epithelial cells. It has no activity on dopamine, α-adrenergic, and muscarinic type 1 and type 2 receptors.

**Drug Characteristics: Olopatadine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Not measurable after ocular instillation |
| **Dose Adjustment Renal** | Not required | **Distribution** | Not measurable after ocular instillation |
| **Dialyzable** | Not dialyzable | **Metabolism** | Not absorbed |
| **Pregnancy Category** | C | **Elimination** | Not absorbed |
| **Lactation** | Weigh risks and benef ts | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to olopatadine | **Black Box Warnings** | None |




Alcon 0.1% solution pictured

**Medication Safety Issues: Olopatadine**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Platinol | No |

**Drug Interactions: Olopatadine.** None known

**Adverse Reactions: Olopatadine**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Taste sense altered, unpleasant taste in mouth, burning sensation in eye, keratitis, xerophthalmia, pharyngitis, cold syndrome, headache, nausea | Hypersensitivity reaction |

**Efficacy Monitoring Parameters.** Reduction in ocular redness, itching, and irritation.

**Toxicity Monitoring Parameters.** Signs of hypersensitivity.

**Key Patient Counseling Points.** Wash hands. For administration, lie down or tilt head back. With index finger, pull down the lower lid of eye to form a pocket. Hold the dropper close to eye with the other hand. Drop the correct number of drops into the pocket made between lower lid and eyeball. Gently close eyes. Place index finger over the inner corner of your eye for 1 min. Do not rinse or wipe the dropper or allow it to touch anything, including eye. Put the cap on the bottle right away. Twice-daily dosing should be at least 6-8 h apart. Remove contact lens prior to administration and wait at least 10 min before reinserting. Do not use contact lenses if eyes are red.

**Clinical Pearls.** Not for use to treat contact lens-related irritation. Efficacy and safety established for patients ≥3 y of age. Also available in nasal formulation for seasonal allergic rhinitis.

# OMEGA-3-ACID ETHYL ESTERS: Lovaza, Various



**Class:** Antihyperlipidemic, Omega-3 Fatty Acids

**Dosage Forms.** **Oral Capsule, Liquid Filled:** 1 g

**Common FDA Label Indication, Dosing, and Titration.**

1. Hypertriglyceridemia, adjunct to diet in adults with triglyceride levels 500 mg/dL or higher: 4 g po daily or divided into 2 doses

**Off-Label Uses.**

1. Coronary arteriosclerosis, hypertriglyceridemia: 4 g po daily or divided into 2 doses
2. Familial combined hyperlipidemia: 4 g po daily or divided into 2 doses
3. Heart failure: 4 g po daily or divided into 2 doses
4. Hyperlipidemia, hypertriglyceridemia, triglyceride levels <500 mg/dL: 4 g po daily or divided into 2 doses

GlaxoSmithKline 1 g pictured

**MOA.** Potential mechanisms of action include inhibition of acyl-CoA:1,2-diacylglycerol acyltransferase, increased mitochondrial and peroxisomal β-oxidation in the liver, decreased lipogenesis in the liver, and increased plasma lipoprotein lipase activity. Lovaza may reduce the synthesis of triglycerides in the liver because eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are poor substrates for the enzymes responsible for TG synthesis, and EPA and DHA inhibit esterification of other fatty acids.

**Drug Characteristics: Omega-3-Acid Ethyl Esters**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Unknown |
| **Dose Adjustment Renal** | Not required | **Distribution** | Unknown |
| **Dialyzable** | Unknown | **Metabolism** | Oxidized in the liver similar to fatty acids derived from dietary sources; EPA: minor via CYP450 |
| **Pregnancy Category** | C | **Elimination** | Half-life: EPA: ~37-89 h, DHA: ~46 h |
| **Lactation** | Weigh risks and benef ts | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to omega-3–acid ethyl esters, f sh, or shellf sh | **Black Box Warnings** | None |

**Medication Safety Issues: Omega-3-Acid Ethyl Esters**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Liquid capsules | No | LORazepam | No |

**Drug Interactions: Omega-3-Acid Ethyl Esters.** None known

**Adverse Reactions: Omega-3–Acid Ethyl Esters**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Indigestion, taste alterations, rash, burping, diarrhea, arthralgia | Anaphylaxis, elevated LFTs |

**Efficacy Monitoring Parameters.** Reduction in triglyceride levels.

**Toxicity Monitoring Parameters.** LDL, LFTs.

**Key Patient Counseling Points.** Swallow the whole capsule; take with food. Seek medical attention if severe rash, chest pain, heart palpitations, or shortness of breath.

**Clinical Pearls.** Omega-3–acid ethyl esters are available OTC as fish oil and contain lower amounts of DHA and EPA than the prescription version. OTC products have varying amounts of DHA and EPA. Each Lovaza capsule contains ~375 mg of DHA and 465 mg of EPA. Treatment of hypertriglyceridemia with omega-3–acid ethyl esters has shown to be equivalent to gemfibrozil in efficacy. Omega-3–acid ethyl esters have not been shown to decrease cardiovascular mortality.

# OMEPRAZOLE: Prilosec, Various



**Class:** Proton Pump Inhibitor

**Dosage Forms. Oral Capsule, Delayed Release:** 10 mg, 20 mg, 40 mg; **Oral Tablet, Delayed Release:** 20 mg; **Oral Suspension:** 2 mg/mL; **Oral Packet:** 2.5 mg, 10 mg

20 mg

40 mg

Kremers Urban generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Duodenal ulcer disease: 20 mg po daily × up to 4 wk
2. Gastric ulcer disease: 40 mg po daily × up to 8 wk
3. *H. pylori* GI infection: 20 mg po bid × 10-14 d in combination with amoxicillin 1000 mg and clarithromycin 500 mg po bid
4. Erosive esophagitis, GERD: Adults and Children ≥1 y of age and ≥20 kg, 20 mg po daily; Children ≥1 y of age, 5-10 kg, 5 mg po daily; Children ≥1 y of age, 10-20 kg, 10 mg po daily

**Off-Label Uses.**

1. Drug-induced GI disturbance, indigestion: 20-40 mg po daily

**MOA.** Omeprazole is a PPI that, when protonated in the secretory canaliculi of the parietal cells, covalently binds to $H^+/K^+$-ATPase (proton pump), which is the final pathway for acid secretion. Produces a profound and prolonged antisecretory effect and inhibits basal, nocturnal, and pentagastrin- and food-stimulated gastric acid secretion.

**Drug Characteristics: Omeprazole**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Consider dose adjustment in hepatic failure | **Absorption** | F = 30-40%, food delays but does not reduce absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 0.34-0.37 L/kg; 95% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, CYP2C19 substrate |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 77% with a half-life of 30-60 min |
| **Lactation** | Weigh risks and benef ts | **Pharmacogenetics** | CYP2C19 poor metabolizers have greater gastric acid suppression |
| **Contraindications** | Hypersensitivity to omeprazole or esomeprazole | **Black Box Warnings** | None |

### Medication Safety Issues: Omeprazole

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| OTC | PriLOSEC | ER capsules and tablets | No | Plendil, Prevacid, PROzac | No |

### Drug Interactions: Omeprazole

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Clopidogrel | Competitive inhibition of clopidogrel metabolism to active form, reducing clopidogrel effectiveness | Avoid concurrent use |
| CYP2C19 inhibitors | Decreased omeprazole metabolism increases risk of omeprazole toxicity | Consider dose decreases of omeprazole |
| CYP2C19 inducers | Increased omeprazole metabolism reduces omeprazole effectiveness | Consider dose increases of omeprazole |
| pH-dependent drugs | Lower gastric pH reduces absorption | Avoid concurrent use |
| Warfarin | Increased anticoagulant effect | Monitor INR and adjust warfarin dose accordingly |

### Adverse Reactions: Omeprazole

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Abdominal pain, diarrhea, headache | Toxic epidermal necrolysis, *C. diff cle* diarrhea, pancreatitis, hepatotoxicity, hip fracture, rhabdomyolysis, acute interstitial nephritis |

**Efficacy Monitoring Parameters.** Resolution of GI discomfort, resolution of ulcers shown on endoscopy; for treatment of *H. pylori*, negative urea breath test.

**Toxicity Monitoring Parameters.** Severe headache or blistering skin rash. Seek medical attention for signs of liver failure, elevated LFTs.

**Key Patient Counseling Points.** Should be taken 1 h before meals.

**Clinical Pearls.** Multiple *H. pylori* regimens exist that include different combinations of PPIs and antibiotics; patients should complete full regimen if prescribed for *H. pylori* management. Many PPI and $H_2$ antagonists available OTC; warn patients not to take multiple products concurrently to avoid additive risk of adverse effects. Increased risk of fractures, especially in elderly. Use lowest effective dose for those at risk for osteoporosis. Medication guide required at dispensing.

# ONDANSETRON: Zofran, Various



**Class:** Antiemetic

**Dosage Forms.** **Oral Tablet:** 4 mg, 8 mg, 24 mg; **Oral Dispersible Tablet:** 4 mg, 8 mg; **Oral Solution:** 4 mg/5 mL; **Oral Film:** 4 mg, 8 mg

Sandoz generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Chemotherapy-induced nausea and vomiting, highly emetogenic chemotherapy: 24 mg po 30 min prior to the start of chemotherapy
2. Chemotherapy-induced nausea and vomiting, moderately emetogenic chemotherapy: Adults and Children >12 y of age, 8 mg po 30 min prior to chemotherapy and repeated in 8 h, then 8 mg po q12h for 1-2 d post chemotherapy; Children 4-11 y of age, 4 mg po 30 min prior to chemotherapy, repeated 4 and 8 h after the 1st dose, then q8h for 1-2 d postchemotherapy
3. Prevention of postoperative nausea and vomiting: 16 mg po 1 h before anesthesia induction
4. Radiation-induced nausea and vomiting: 8 mg po 1-2 h prior to radiotherapy and q8h after 1st dose of radiation on each day of radiotherapy

**Off-Label Uses.**

1. Severe hyperemesis associated with pregnancy: 8 mg po q12h

**MOA.** Ondansetron is a selective 5-$HT_3$ receptor antagonist. Serotonin receptors of the 5-$HT_3$ type are present both peripherally and centrally in the chemoreceptor trigger zone. Cytotoxic chemotherapy releases serotonin from the enterochromaffin cells of the small intestine, initiating the vomiting reflex.

**Drug Characteristics: Ondansetron**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Severe hepatic dysfunction, *max* daily dose 8 mg | **Absorption** | F = 56%, food has minimal effect on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 2.5 L/kg |
| **Dialyzable** | Unknown | **Metabolism** | Hepatic, CYP3A4/5 substrate |
| **Pregnancy Category** | B | **Elimination** | Renal 5%, with a half-life of 4.6 h |
| **Lactation** | Weigh risks and benef ts | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to ondansetron, concurrent apomorphine or drugs that increase QT interval | **Black Box Warnings** | None |

### Medication Safety Issues: Ondansetron

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| ODT | No | Film and disintegrating tablet | No | Zantac, Zosyn | No |

### Drug Interactions: Ondansetron

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Apomorphine | Additive hypotension | Contraindicated |
| Agents that increase QT interval | Increased risk of QT prolongation (torsades de pointes, cardiac arrest) | Contraindicated |
| Cyclophosphamide | Ondansetron decreases the systemic exposure of cyclophosphamide | Avoid concurrent use |

### Adverse Reactions: Ondansetron

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Constipation, diarrhea, headache | Xerostomia, increased LFTs, dizziness, fever | Arrhythmias, anaphylaxis, serotonin syndrome |

**Efficacy Monitoring Parameters.** Reduction in nausea and vomiting.

**Toxicity Monitoring Parameters.** Heart palpitations, shortness of breath, severe rash.

**Key Patient Counseling Points.** Dry hands before handling disintegrating tablet. Do not open the blister pack that contains the tablet until you are ready to take it. Do not push the oral disintegrating tablet through the foil. Place tablet in mouth, allow to melt, swallow, or drink water.

**Clinical Pearls.** Tablets, disintegrating tablets, and solution are bioequivalent and are dosed interchangeably. 5-$HT_3$ receptor antagonists are often combined with dexamethasone and aprepitant for the prevention of chemotherapy-induced nausea/vomiting. Also available in injectable formulation.

Kariva by Teva pictured

**Class:** Oral Contraceptive

**Product Contents: Oral Contraceptive—Biphasic**

| Phase 1 Content | Phase 2 Content | Example Brand Names |
|---|---|---|
| Ethinyl estradiol 20 mcg; desogestrel 0.15 mg (21 d) | Ethinyl estradiol 10 mcg (5 d) | Kariva, Azurette, Mircette |
| Ethinyl estradiol 20 mcg; levonorgestrel 0.1 mg (84 d) | Ethinyl estradiol 10 mcg (7 d) | LoSeasonique, Amethia Lo |
| Ethinyl estradiol 30 mcg; levonorgestrel 0.15 mg (84 d) | Ethinyl estradiol 10 mcg (7 d) | Seasonique, Amethia |
| Ethinyl estradiol 35 mcg; norethindrone 0.5 mg (10 d) | Ethinyl estradiol 35 mcg; norethindrone 1 mg (11 d) | Necon 10/11 |
| Ethinyl estradiol 10 mcg; norethindrone 1 mg (24 d) | Ethinyl estradiol 10 mcg (2 d) | Lo Loestrin Fe |

**Dosage Forms.** **Oral Tablet:** Biphasic products contain 2 sets of tablets, each phase containing a combination of varying doses of estrogen/progestin agents, or an estrogen agent alone; products are either in 28-d or in 90-d cycles; may also include inert tablets containing either plain lactose or iron supplements, generally as 75-mg ferrous fumarate

**Common FDA Label Indication, Dosing, and Titration.**

1. Contraception: 1 tablet po daily beginning either on the 1st Sunday after menstruation begins ("Sunday start") or on the 1st day of menstruation ("day 1 start"); tablets are taken sequentially, following the arrows marked on the dispenser

**Off-Label Uses.** None

**MOA.** See Preface C Card: General Content Related to All Oral Contraceptives.

## Drug Characteristics: Oral Contraceptive—Biphasic[a]

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 40% for ethinyl estradiol; food has no effect on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 45 L/kg for ethinyl estradiol; highly protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, CYP3A4/5 substrate |
| **Pregnancy Category** | X | **Elimination** | Renal elimination with a half-life of 24 h for ethinyl estradiol |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to ethinyl estradiol or progestin component; history of thromboembolic disorders, endometrial cancer, uncontrolled hypertension, known or suspected pregnancy; smoking 15 or more cigarettes per day | **Black Box Warnings** | Cigarette smokers >35 y old |

[a]See Preface C Card: General Content Related to All Oral Contraceptives for ADME data on progestins.

## Medication Safety Issues: Oral Contraceptive—Biphasic

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Multiple product names | Avoid oral estrogen and topical patch |

**Drug Interactions and Adverse Reactions: Oral Contraceptive—Biphasic.** See Preface C Card: General Content Related to All Oral Contraceptives.

**Efficacy Monitoring Parameters.** Lack of pregnancy.

**Toxicity Monitoring Parameters.** Annual physical examination including cervical cytology (Pap smear) and breast exam.

**Key Patient Counseling Points.** See Preface C Card: General Content Related to All Oral Contraceptives.

**Clinical Pearls.** Patients should not smoke during therapy, as this increases the risk of serious cardiovascular side effects. Noncontraceptive benefits (non-FDA approved) of oral contraceptive use include treatment of dysmenorrhea; acne; menstrual migraine; pelvic pain due to endometriosis; and decreased risk of endometrial, ovarian, and colorectal cancer. Multiphasic products have a lower total steroid dose than monophasic products and may have lower adverse effect rates, but treatment is usually initiated with monophasic products. Multiple non-oral hormonal contraceptive products also available.

# ORAL CONTRACEPTIVE—MONOPHASIC: Various

**Class:** Oral Contraceptive

**Product Contents: Oral Contraceptive—Monophasic**

| Estrogen Component | Progestin Component | Example Brand Names |
|---|---|---|
| Ethinyl estradiol 50 mcg | Norgestrel 0.5 mg | Ogestrel 0.5/50 |
| Ethinyl estradiol 35 mcg | Norethindrone 1 mg | Ortho-Novum 1/35, Norinyl 1 + 35 |
| Ethinyl estradiol 35 mcg | Norethindrone 0.5 mg | Brevicon, Modicon |
| Ethinyl estradiol 35 mcg | Norethindrone 0.4 mg | Ovcon-35, Balziva |
| Ethinyl estradiol 35 mcg | Norethindrone 0.25 mg | MonoNessa, Ortho-Cyclen |
| Ethinyl estradiol 30 mcg | Drospirenone 3 mg | Ocella, Yasmin |
| Ethinyl estradiol 30 mcg | Norethindrone 1.5 mg | Loestrin 21 1.5/30 |
| Ethinyl estradiol 30 mcg | Norgestrel 0.3 mg | Low-Ogestrel, Lo/Ovral |
| Ethinyl estradiol 30 mcg | Desogestrel 0.15 mg | Apri, Ortho-Cept |
| Ethinyl estradiol 30 mcg | Levonorgestrel 0.15 mg | Levora, Nordette-28 |
| Ethinyl estradiol 20 mcg | Drospirenone 3 mg | Yaz, Loryna |
| Ethinyl estradiol 20 mcg | Levonorgestrel 0.1 mg | Aviane, Lutera |
| Ethinyl estradiol 20 mcg | Norethindrone 1 mg | Loestrin 21 1/20 |

Apri by Barr pictured

**Dosage Forms.** **Oral Tablet:** Monophasic products include tablets that each contains the same dose of an estrogen and progestin agent; products are either in 21-d or in 28-d cycles; may also include inert tablets containing either plain lactose or iron supplements, generally as 75-mg ferrous fumarate.

**Common FDA Label Indication, Dosing, and Titration.**

1. Contraception: 1 tablet po daily beginning either on the 1st Sunday after menstruation begins ("Sunday start") or on the 1st day of menstruation ("day 1 start"); tablets are taken sequentially, following the arrows marked on the dispenser

**Off-Label Uses.** None

**MOA.** See Preface C Card: General Content Related to All Oral Contraceptives.

## Drug Characteristics: Oral Contraceptive—Monophasic[a]

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 40% for ethinyl estradiol; food has no effect on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 45 L/kg for ethinyl estradiol; highly protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, CYP3A4/5 substrate |
| **Pregnancy Category** | X | **Elimination** | Renal elimination with a half-life of 24 h for ethinyl estradiol |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to ethinyl estradiol or progestin component; history of thromboembolic disorders, endometrial cancer, uncontrolled hypertension, known or suspected pregnancy; smoking 15 or more cigarettes per day | **Black Box Warnings** | Cigarette smokers >35 y old |

[a]See Preface C Card: General Content Related to All Oral Contraceptives for ADME data on progestins.

## Medication Safety Issues: Oral Contraceptive—Monophasic

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Multiple product names | Avoid oral estrogen and topical patch |

**Drug Interactions and Adverse Reactions: Oral Contraceptive—Monophasic.** See Preface C Card: General Content Related to All Oral Contraceptives.

**Efficacy Monitoring Parameters.** Lack of pregnancy.

**Toxicity Monitoring Parameters.** Annual physical examination including cervical cytology (Pap smear) and breast exam.

**Key Patient Counseling Points.** See Preface C Card: General Content Related to All Oral Contraceptives.

**Clinical Pearls.** Patients should not smoke during therapy, as this increases the risk of serious cardiovascular side effects. Noncontraceptive benefits (non-FDA approved) of oral contraceptive use include treatment of dysmenorrhea; acne; menstrual migraine; pelvic pain due to endometriosis; and decreased risk of endometrial, ovarian, and colorectal cancer. Multiphasic products have a lower total steroid dose than monophasic products and may have lower adverse effect rates, but treatment is usually initiated with monophasic products. Multiple non-oral hormonal contraceptive products also available.

# ORAL CONTRACEPTIVE—TRIPHASIC: Various



**Class:** Oral Contraceptive

**Product Contents: Oral Contraceptive—Triphasic**

| Phase 1 | Phase 2 | Phase 3 | Example Brand Names |
|---|---|---|---|
| Ethinyl estradiol 35 mcg; norethindrone 0.5 mg (7 d) | Ethinyl estradiol 35 mcg; norethindrone 1 mg (9 d) | Ethinyl estradiol 35 mcg; norethindrone 0.5 mg (5 d) | Tri-Norinyl, Aranelle |
| Ethinyl estradiol 35 mcg; norethindrone 0.5 mg (7 d) | Ethinyl estradiol 35 mcg; norethindrone 0.75 mg (7 d) | Ethinyl estradiol 35 mcg; norethindrone 1 mg (7 d) | Ortho-Novum 7/7/7, Necon 7/7/7 |
| Ethinyl estradiol 35 mcg; norgestimate 0.18 mg (7 d) | Ethinyl estradiol 35 mcg; norgestimate 0.215 mg (7 d) | Ethinyl estradiol 35 mcg; norgestimate 0.25 mg (7 d) | Ortho Tri-Cyclen, Tri-Sprintec, TriNessa |
| Ethinyl estradiol 25 mcg; norgestimate 0.18 mg (7 d) | Ethinyl estradiol 25 mcg; norgestimate 0.215 mg (7 d) | Ethinyl estradiol 25 mcg; norgestimate 0.25 mg (7 d) | Ortho Tri-Cyclen Lo |
| Ethinyl estradiol 20 mcg; norethindrone 1 mg (5 d) | Ethinyl estradiol 30 mcg; norethindrone 1 mg (7 d) | Ethinyl estradiol 35 mcg; norethindrone 1 mg (9 d) | Estrostep Fe, Tri-Legest |

Tri-Sprintec by Barr pictured

**Dosage Forms.** **Oral Tablet:** Triphasic products contain 3 sets of tablets, each phase containing a combination of varying doses of estrogen/progestin agents; products are either in 21-d or in 28-d cycles; may also include inert tablets containing either plain lactose or iron supplements, generally as 75-mg ferrous fumarate.

**Common FDA Label Indication, Dosing, and Titration.**

1. Contraception: 1 tablet po daily beginning either on the 1st Sunday after menstruation begins ("Sunday start") or on the 1st day of menstruation ("day 1 start"); tablets are taken sequentially, following the arrows marked on the dispenser
2. Acne vulgaris, moderate: In females at least 15 y of age who have achieved menarche and are unresponsive to topical antiacne medications, same dosing as for contraception (Ortho Tri-Cyclen and Estrostep Fe are the only products with this FDA-approved indication)

**Off-Label Uses.** None

**MOA.** See Preface C Card: General Content Related to All Oral Contraceptives.

## Drug Characteristics: Oral Contraceptive—Triphasic[a]

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 40% for ethinyl estradiol; food has no effect on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 45 L/kg for ethinyl estradiol; highly protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, CYP3A4/5 substrate |
| **Pregnancy Category** | X | **Elimination** | Renal elimination with a half-life of 24 h for ethinyl estradiol |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to ethinyl estradiol or progestin component; history of thromboembolic disorders, endometrial cancer, uncontrolled hypertension, known or suspected pregnancy; smoking 15 or more cigarettes per day | **Black Box Warnings** | Cigarette smokers >35 y old |

[a]See Preface C Card: General Content Related to All Oral Contraceptives for ADME data on progestins.

## Medication Safety Issues: Oral Contraceptive—Triphasic

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Multiple product names | Avoid oral estrogen and topical patch |

**Drug Interactions and Adverse Reactions: Oral Contraceptive—Triphasic.** See Preface C Card: General Content Related to All Oral Contraceptives.

**Efficacy Monitoring Parameters.** Lack of pregnancy.

**Toxicity Monitoring Parameters.** Annual physical examination including cervical cytology (Pap smear) and breast exam.

**Key Patient Counseling Points.** See Preface C Card: General Content Related to All Oral Contraceptives.

**Clinical Pearls.** Patients should not smoke during therapy, as this increases the risk of serious cardiovascular side effects. Noncontraceptive benefits (non-FDA approved) of oral contraceptive use include treatment of dysmenorrhea; acne; menstrual migraine; pelvic pain due to endometriosis; and decreased risk of endometrial, ovarian and colorectal cancer. Multiphasic products have a lower total steroid dose than monophasic products and may have lower adverse effect rates, but treatment is usually initiated with monophasic products. Multiple non-oral hormonal contraceptive products also available.

# OSELTAMIVIR: Tamiflu



**Class:** Neuraminidase Inhibitor, Antiviral

**Dosage Forms. Oral Capsule:** 30 mg, 45 mg, 75 mg; **Oral Suspension:** 6 mg/mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Influenza virus types A and B, treatment: Children >1 y of age and <15 kg, 30 mg po bid × 5 d; Children >1 y of age and 15-23 kg, 45 mg po bid × 5 d; Children >1 y of age and 23-40 kg, 60 mg po bid × 5 d; Adults and Children >1 y of age and >40 kg, 75 mg po bid × 5 d
2. Influenza virus types A and B, prophylaxis: Same dose as for treatment; may dose for 6 wk during a community outbreak

**Off-Label Uses.**

1. Influenza virus types A and B, prophylaxis: Children >2 wk and <3 mo of age, 3 mg/kg/d for up to 6 wk during community outbreak

**MOA.** Oseltamivir is an inhibitor of influenza virus neuraminidase affecting release of viral particles.

30 mg

45 mg

75 mg

Roche pictured

**Drug Characteristics: Oseltamivir**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 75%, food has minimal effect on absorption |
| **Dose Adjustment Renal** | CrCl = 10-30 mL/min, reduce dose to 30 mg po daily for prophylaxis and 75 mg po daily × 5 d for treatment | **Distribution** | Vd = 23-26 L; 42% protein bound |
| **Dialyzable** | Yes | **Metabolism** | Oseltamivir phosphate is a prodrug that is extensively metabolized to oseltamivir carboxylate by ester hydrolysis |
| **Pregnancy Category** | C | **Elimination** | Renal elimination 99%, with a half-life of 1-3 h |
| **Lactation** | Weigh risks and benef ts | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to oseltamivir | **Black Box Warnings** | None |

### Medication Safety Issues: Oseltamivir

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Thera-Flu | No |

### Drug Interactions: Oseltamivir

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Influenza vaccine (live) | Interferes with vaccine effectiveness | Vaccinate 2 wk before or 48 h after administration of oseltamivir |

### Adverse Reactions: Oseltamivir

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Nausea, vomiting | Diarrhea, elevated LFTs | Arrhythmias, anaphylaxis, Stevens-Johnson syndrome, seizures, delirium |

**Efficacy Monitoring Parameters.** Prevention or resolution of influenza infection symptoms.

**Toxicity Monitoring Parameters.** Seek care if heart palpitations, shortness of breath, severe rash, swelling, confusion, or anxiety occurs.

**Key Patient Counseling Points.** Complete full course of therapy. Symptoms should improve within 2-3 d; if they worsen, seek care. Suspension is available in a 6-mg/mL concentration and is packaged with an oral syringe calibrated in milliliters up to a total of 10 mL. Instructions to the patient should be provided based on these units of measure (ie, mL). When providing oseltamivir suspension for children <1 y of age, use a lower calibrated (ie, <10 mL) oral syringe to ensure accurate dosing. If suspension unavailable, open capsules and compound a 6-mg/mL suspension.

**Clinical Pearls.** Candidates for prophylaxis include close contacts of a confirmed or suspected case during their infectious period who are at high risk for influenza complications, health-care workers and emergency medical personnel, and pregnant women; treatment must start within 48 h of exposure. Capsules may be opened and administered in liquid or via nasogastric tube. Severely ill patients may require longer treatment.

# OXCARBAZEPINE: Trileptal, Various



**Class:** Dibenzazepine Carboxamide, Anticonvulsant

**Dosage Forms. Oral Tablet:** 150 mg, 300 mg, 600 mg; **Oral Tablet, Extended Release:** 150 mg, 300 mg, 600 mg; **Oral Suspension:** 300 mg/5 mL

Sun Pharma generic 300 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Partial seizure: Adults, 300 mg po bid, may titrate to 1200 mg/d po; Children 4-16 y of age, 8-10 mg/kg/d po in 2 divided doses, may titrate to 600 mg/d po

**Off-Label Uses.**

1. Trigeminal neuralgia: 300 mg po bid-qid, may titrate to 2400 mg po daily

**MOA.** Oxcarbazepine is a 10-keto analogue of carbamazepine that exerts its anticonvulsant effect through an active 10-monohydroxy metabolite (MHD). Its mechanism of action is not known but likely involves blockade of voltage-dependent sodium channels and inhibition of repetitive neuronal firing.

**Drug Characteristics: Oxcarbazepine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 100%, food has no effect on absorption |
| **Dose Adjustment Renal** | CrCl <30 mL/min, initiate at 300 mg/d and increase slowly | **Distribution** | Vd = 49 L; 40-60% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic metabolism, CYP3A4/5 substrate; inducer of CYP3A4/5 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is >95% with a half-life of 8-13 h |
| **Lactation** | Weigh risks and benef ts | **Pharmacogenetics** | None |
| **Contraindications** | Hypersensitivity to oxcarbazepine | **Black Box Warnings** | None |

**Medication Safety Issues: Oxcarbazepine**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| XR | OXcarbazepine | Extended-release tablets | No | CarBAMazepine | No |

### Drug Interactions: Oxcarbazepine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inducers | Increased oxcarbazepine metabolism reduces oxcarbazepine effectiveness | Consider dose increases of oxcarbazepine |
| CYP3A4/5 inhibitors | Decreased oxcarbazepine metabolism increases oxcarbazepine toxicity | Monitor and consider dose decreases of oxcarbazepine |
| CYP3A4/5 substrates | Oxcarbazepine increases metabolism of substrates drugs, lowers plasma concentration, and decreases substrate drug activity | Avoid concurrent use or monitor substrate drug and increase dose |
| Carbamazepine, phenobarbital, valproic acid, verapamil | Decreased oxcarbazepine concentrations | Monitor eff cacy of oxcarbazepine |
| Oral contraceptives | Decreased contraceptive eff cacy | Use an alternative form of birth control |

### Adverse Reactions: Oxcarbazepine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Somnolence, headache, diplopia, dizziness | Abnormal vision, anorexia, ataxia, constipation, diarrhea, drowsiness, fatigue, hyponatremia, nausea, rash, tremor, vomiting, weight gain | Anaphylaxis, angioedema, Stevens-Johnson syndrome, suicidal thoughts |

**Efficacy Monitoring Parameters.** Reduction in seizure frequency.

**Toxicity Monitoring Parameters.** Serum sodium during maintenance treatment, emergence or worsening of depression, suicidal behavior or ideation, or unusual changes in behavior.

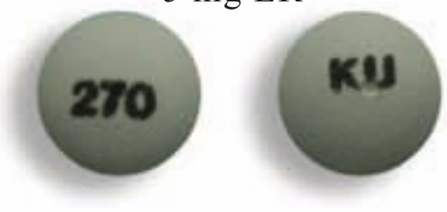
**Key Patient Counseling Points.** Suspension should be shaken well and dose prepared immediately using oral dosing syringe. Suspension can be mixed in a small glass of water just prior to administration or may be swallowed directly from the syringe. Avoid activities requiring mental alertness or coordination until drug effects are realized. Advise patient to report signs/symptoms of serious dermatologic reactions, myelosuppression, or hepatotoxicity. Take with food, but not alcohol, grapefruit, or grapefruit juice. Avoid abrupt discontinuation to avoid risk of seizure.

**Clinical Pearls.** Safety and efficacy not established in pediatric patients <4 y of age. With adjunctive therapy, children 2-4 y of age may require up to twice the oxcarbazepine dose per body weight compared to adults, and children 4-12 y of age may require a 50% higher oxcarbazepine dose per body weight compared to adults. Medication guide required at dispensing.

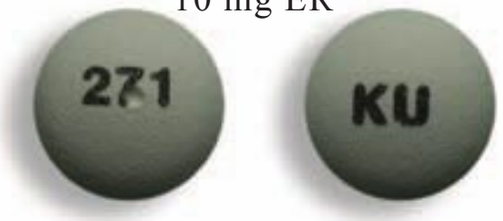
# OXYBUTYNIN: Ditropan, Various



5 mg ER




10 mg ER




Kremers Urban generic ER pictured

5 mg
immediate release

Qualitest generic pictured

**Class:** Urinary Antispasmodic

**Dosage Forms.** **Oral Tablet:** 5 mg; **Oral Tablet, Extended Release:** 5 mg, 10 mg, 15 mg; **Oral Syrup:** 5 mg/5 mL; **Transdermal Gel**: 3%, 10%; **Transdermal Patch:** 3.9 mg/24 h

**Common FDA Label Indication, Dosing, and Titration.**

1. Overactive or neurogenic bladder: Oral, 5-10 mg/d po, may titrate to 30 mg/d po; Gel, 100 mg/g applied once daily; Patch, 1 patch applied twice weekly

**Off-Label Uses.** None

**MOA.** Oxybutynin is a competitive muscarinic receptor antagonist. Muscarinic receptors play an important role in several major cholinergically mediated functions, including contractions of the urinary bladder smooth muscle and stimulation of salivary secretion.

**Drug Characteristics: Oxybutynin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 6%, food has no effect on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 193 L |
| **Dialyzable** | Unknown | **Metabolism** | Hepatic, CYP3A4/5 substrate |
| **Pregnancy Category** | B | **Elimination** | Renal with a half-life of 2-3 h |
| **Lactation** | Weigh risks and benef ts | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to oxybutynin, gastric retention, glaucoma, urinary retention | **Black Box Warnings** | None |

### Medication Safety Issues: Oxybutynin

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| XL | No | Extended-release formulation | No | OxyCONTIN, Diprivan | No |

### Drug Interactions: Oxybutynin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inhibitors | Decreased oxybutynin metabolism increases risk of oxybutynin toxicity | Consider dose decreases of oxybutynin |
| CYP3A4/5 inducers | Increased oxybutynin metabolism decreases oxybutynin efficacy | Consider dose increases of oxybutynin |
| Anticholinergic agents | Additive anticholinergic adverse effects can occur | Avoid concurrent use or monitor carefully for adverse effects |

### Adverse Reactions: Oxybutynin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Constipation, xerostomia, blurred vision | Abdominal pain, dizziness, indigestion, urinary retention, arthralgias, hyperglycemia | Prolonged QTc interval, seizures, tachycardia |

**Efficacy Monitoring Parameters.** Resolution of clinical signs of incontinence, urinary frequency, urinary urgency.

**Toxicity Monitoring Parameters.** Seek medical attention if anticholinergic effects (dry mouth, constipation, cognitive impairment, vision changes) are severe; monitor FBG, HR.

**Key Patient Counseling Points.** This drug may cause anticholinergic effects, including constipation, urinary retention, blurred vision, dyspepsia, or xerostomia. Heat prostration (due to decreased sweating) can occur when used in a hot environment.

**Clinical Pearls.** Patients should be advised to exercise caution in decisions to engage in potentially dangerous activities until the drug's effects have been determined. May note decline in cognitive function, especially in elderly. The transdermal patch is available OTC.

# OXYCODONE: Oxycontin, Various



**Class:** Opioid Analgesic. C-II

**Dosage Forms.** **Oral Tablet, Immediate Release**: 5 mg, 10 mg, 15 mg, 20 mg, 25 mg; **Oral Tablet, Extended Release:** 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 60 mg, 80 mg; **Oral Capsule:** 5 mg; **Oral Concentrate**: 100 mg/5 mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Pain, chronic, moderate to severe: Extended release, 10-20 mg po q12h prn pain, may titrate to response; immediate release, 5-15 mg po q4-6h prn pain

**Off-Label Uses.** None

**MOA.** Oxycodone is pure mu agonist. Mu receptors are responsible for analgesia, respiratory depression, miosis, decreased GI motility, and euphoria. In the CNS, it promotes analgesia and respiratory depression by decreasing the brain stem respiratory centers' response to carbon dioxide tension and electrical stimulation. It also decreases gastric, biliary, and pancreatic secretion, induces peripheral vasodilation, and promotes opioid-induced hypotension due to histamine release.

Purdue Pharma pictured

**Drug Characteristics: Oxycodone**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Moderate impairment, reduce dose by 33%; severe impairment, reduce dose by 50% | **Absorption** | F = 60-87%; absorption enhanced by food |
| **Dose Adjustment Renal** | CrCl <60 mL/min, reduce starting dose | **Distribution** | Vd = 2.6 L/kg; 45% protein bound |
| **Dialyzable** | Unknown | **Metabolism** | Hepatic, CYP3A4/5 substrate |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 20% with a half-life of 5 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to oxycodone or other opioids, asthma, paralytic ileus, respiratory depression, hypercarbia | **Black Box Warnings** | Abuse potential; do not crush ER tablet |

### Medication Safety Issues: Oxycodone

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | OxyCODONE | Do not crush or chew ER or abuse deterrent formulation | Yes | HYDROcodone, MS Contin, oxybutynin | No |

### Drug Interactions: Oxycodone

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Barbiturates, benzodiazepines, centrally acting muscle relaxants, opioids, phenothiazines | Additive CNS depression | Monitor and consider dose adjustments |
| Opioid agonists/antagonists, opioid antagonists | Precipitation of withdrawal symptoms | Avoid concurrent use with opioids |
| CYP3A4/5 inducers | Increased oxycodone metabolism decreases efficacy | Use with caution, consider increasing dose of oxycodone |
| CYP3A4/5 inhibitors | Decreased oxycodone metabolism increases risk of toxicity | Use with caution, consider decreasing dose of oxycodone |

### Adverse Reactions: Oxycodone

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Constipation, GI distress, sedation, sweating, pruritus | Asthenia, dyspnea, hypotension, euphoria | Cardiac arrest, physical dependence, tolerance, severe hypersensitivity |

**Efficacy Monitoring Parameters.** Relief of pain.

**Toxicity Monitoring Parameters.** Excessive drowsiness, severe skin rash, decreased breathing, severe constipation, chest pain, dizziness. Monitor vital signs, specifically respiratory rate and BP.

**Key Patient Counseling Points.** Use a stool softener and/or laxative for preventing constipation. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol and other CNS depressants.

**Clinical Pearls.** Tolerance and physical dependence may occur with chronic use; avoid abrupt discontinuation. Extended-release products must not be crushed or chewed. Crushing or chewing will release the total dose of oxycodone at once and increase risk of respiratory depression. Extended-release products are not for use in children. Advise patients to keep in safe place, and dispose of properly when no longer needed. Now in REMS program prescribers are required to receive appropriate training. Medication guide required when dispensing.

# PANTOPRAZOLE: Protonix, Various

**Class:** Proton Pump Inhibitor

**Dosage Forms.** **Oral Tablet, Delayed Release:** 20 mg, 40 mg; **Oral Packet:** 40 mg

Teva generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Erosive esophagitis, GERD: Children ≥5 y of age and 15-40 kg, 20 mg po daily × up to 8 wk; Adults and Children ≥5 y of age and >40 kg, 40 mg po daily
2. Gastric hypersecretion: 40 mg po bid, may titrate to 240 mg/d po
3. Zollinger-Ellison syndrome: 40 mg po bid, may titrate to 240 mg/d po

**Off-Label Uses.**

1. *H. pylori* GI tract infection: 40 mg po bid × 10-14 d in combination with amoxicillin 1000 mg and clarithromycin 500 mg po bid
2. Duodenal ulcer disease: 40-80 mg po daily × up to 4-8 wk

**MOA.** Pantoprazole is a PPI that, when protonated in the secretory canaliculi of the parietal cells, covalently binds to $H^+/K^+$-ATPase (proton pump), which is the final pathway for acid secretion. Produces a profound and prolonged antisecretory effect and inhibits basal, nocturnal, pentagastrin-stimulated, and food-stimulated gastric acid secretion.

**Drug Characteristics: Pantoprazole**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 77%, food has no effect on absorption of delayed release tablet |
| **Dose Adjustment Renal** | Not required | **Distribution** | 98% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, substrate for CYP2C19 |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 71% with a half-life of 1 h (10 h in CYP2C19-deficient patients) |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | Poor CYP2C19 metabolizers; if known, consider lower dose |
| **Contraindications** | Hypersensitivity to pantoprazole | **Black Box Warnings** | None |

**Medication Safety Issues: Pantoprazole**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Delayed-release tablet, oral packet | No | ARIPiprazole | No |

### Drug Interactions: Pantoprazole

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP2C19 inducers | Increased pantoprazole metabolism reduces pantoprazole effectiveness | Consider dose increases of pantoprazole |
| CYP2C19 inhibitors | Decreased pantoprazole metabolism increases risk of pantoprazole toxicity | Consider dose decreases of pantoprazole |
| Clopidogrel | Competitive inhibition of clopidogrel metabolism to active form, reducing clopidogrel effectiveness | Avoid concurrent use |
| Methotrexate | Pantoprazole blocks the active secretion of methotrexate, increasing methotrexate levels | Use with caution; monitor for signs of methotrexate toxicity |
| pH dependent drugs | Lower gastric pH reduces absorption | Monitor for lack of effectiveness of interacting drug and adjust dose as necessary |

### Adverse Reactions: Pantoprazole

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Abdominal pain, diarrhea, f atulence, headache | Toxic epidermal necrolysis, Stevens-Johnson syndrome, thrombocytopenia, hip fracture, rhabdomyolysis, acute interstitial nephritis |

**Efficacy Monitoring Parameters.** Resolution of GI discomfort, resolution of ulcers shown on endoscopy; for treatment of *H. pylori*, negative urea breath test.

**Toxicity Monitoring Parameters.** Seek medical care for severe headache or blistering skin rash.

**Key Patient Counseling Points.** Can be taken with or without food but best if taken before meals to reduce acid production caused by food.

**Clinical Pearls.** When the intravenous route is used, converted to oral route as soon as possible to avoid cost and risks of intravenous therapy. Multiple *H. pylori* regimens exist that include different combinations of PPIs and antibiotics; counsel patient to complete full regimen if prescribed for *H. pylori* management. Other PPI and $H_2$ antagonists are available OTC; do not take multiple products concurrently to avoid additive risk of adverse effects. Also available as IV formulation. Packet formulation is delayed release; sprinkle into apple sauce or apple juice only, swallow immediately.

# PAROXETINE: Paxil, Paxil CR, Various

**Class:** SSRI Antidepressant

**Dosage Forms. Oral Tablet:** 10 mg, 20 mg, 30 mg, 40 mg; **Oral Tablet, Controlled Release:** 12.5 mg, 25 mg, 37.5 mg; **Oral Solution, Oral Syrup:** 10 mg/5 mL; **Oral Suspension:** 10 mg/5 mL; **Oral Capsule:** 7.5 mg

Aurobindo generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Depression: Adults, immediate release, 20 mg po daily, may titrate to 50 mg po daily; Adults, controlled release, 25 mg po daily, may titrate to 62.5 mg po daily; Children ≥8 y of age, 10-20 mg po daily
2. Generalized anxiety disorder: Adults, 20 mg po daily
3. Social anxiety disorder: Adults, 20 mg po daily; Children ≥8 y of age, 10 mg po daily
4. OCD: Adults, 20 mg po daily, titrate to 60 mg po daily; Children ≥8 y of age, 10 mg po daily, may titrate to 30 mg daily
5. Panic disorder: Immediate release, 10 mg po daily, may titrate to 60 mg po daily; controlled release, 12.5 mg po daily, may titrate to 75 mg po daily
6. Posttraumatic stress disorder (PTSD): Adults, 20 mg po daily, may titrate to 50 mg po daily
7. Premenstrual dysphoric disorder (PMDD): 12.5 mg po daily or × 14 d prior to expected start of menses, may titrate to 25 mg po daily
8. Vasomotor symptoms of menopause: 7.5 mg po daily at bedtime

**Off-Label Uses.** None

**MOA.** Paroxetine is a highly selective and potent inhibitor of serotonin reuptake (SSRI).

**Drug Characteristics: Paroxetine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | *Max* dose 40 mg immediate release, or 50 mg controlled release | **Absorption** | F = 100%, food increases Cmax and AUC |
| **Dose Adjustment Renal** | *Max* dose 40 mg immediate release, or 50 mg controlled release | **Distribution** | 93-95% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, CYP2D6 substrate |
| **Pregnancy Category** | D | **Elimination** | Renal elimination is 64% with a half-life of 15-22 h |
| **Lactation** | Avoid | **Pharmacogenetics** | Use with caution in CYP2D6 poor metabolizers |
| **Contraindications** | Hypersensitivity to paroxetine; concomitant use of thioridazine or MAOIs | **Black Box Warnings** | Suicidality |

### Medication Safety Issues: Paroxetine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| CR | PARoxetine | CR or film-coated product | No | Doxil, Plavix, PROzac, FLUoxetine | No |

### Drug Interactions: Paroxetine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP2D6 inhibitors | Decreased paroxetine metabolism increases risk of paroxetine toxicity | Consider dose decreases of paroxetine |
| Antiplatelet drugs, NSAIDs | Increased risk of bleeding | Monitor for bleeding |
| Triptans, dextroamphetamine, tramadol, linezolid, MAOIs | Increased risk of serotonin syndrome | Monitor closely for symptoms of serotonin syndrome; linezolid, MAOIs contraindicated |
| Clozapine | Increased clozapine concentrations | Monitor for adverse effects |
| Agents that increase QT interval | Increased risk of QT prolongation (torsades de pointes, cardiac arrest) | Avoid concurrent use or monitor carefully |

### Adverse Reactions: Paroxetine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Abnormal ejaculation, asthenia, constipation, diarrhea, headache, insomnia, nausea, somnolence | Anxiety, asthenia, bleeding, dizziness, diaphoresis, feeling nervous, impotence, insomnia, loss of appetite, rash, reduced libido, tremor, vomiting, xerostomia | Serotonin syndrome, suicidal thoughts |

**Efficacy Monitoring Parameters.** Improvement in symptoms of depression, panic disorder, OCD, premenstrual syndrome, vasomotor symptoms.

**Toxicity Monitoring Parameters.** Worsening of depression, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases; signs/symptoms of abnormal bleeding.

**Key Patient Counseling Points.** Do not chew or crush controlled-release tablet or film-coated tablet (Pexeva). Shake suspension well before using. Avoid activities requiring mental alertness or coordination until drug effects are realized. Symptomatic improvement may not be seen for several weeks. Avoid abrupt discontinuation. Do not drink alcohol. Use caution with NSAIDs or aspirin while taking this drug.

**Clinical Pearls.** If intolerable withdrawal symptoms occur following a decrease in dose or therapy discontinuation, may need to resume the previous dose and taper at a more gradual rate.

# PENICILLIN: Various

**Class:** Antibiotic

**Dosage Forms.** **Oral Tablet:** 250 mg, 500 mg; **Oral Solution:** 125 mg/5 mL, 250 mg/5 mL

Sandoz generic 500 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Bacterial endocarditis, prophylaxis in patients with congenital heart disease or rheumatic/acquired valvular heart disease: Adults, 2 g po 1 h prior to procedure and then 1 g po 6 h later; Children <60 lb, 1 g po 1 h prior to procedure and then 500 mg po 6 h later
2. Otitis media, mild-moderate, pneumococcal: Adults, 250-500 mg po q6h until afebrile for at least 2 d; Children <12 y of age, 25-50 mg/kg/d po in 3-4 divided doses, *max* 3 g/d
3. Streptococcal pharyngitis: Adults, 500 mg po bid × 10 d; Children <60 lb, 250 mg po bid × 10 d

**Off-Label Uses.**

1. Pneumococcal infectious disease, prophylaxis in patients with sickle cell disease or asplenia: Children 2 mo to 5 y of age, 125 mg po bid; Children ≥5 y of age, 250 mg po bid; discontinue at age 5 y for children who received pneumococcal vaccination and who have not experienced invasive pneumococcal disease

**MOA.** Penicillins are active against most gram-positive organisms and some gram-negative organisms, notably *Neisseria* spp., by interfering with late stages of bacterial cell wall synthesis; resistance is caused primarily by bacterial production of β-lactamases; some organisms have altered penicillin-binding protein targets (eg, *Enterococci* spp. and *S. pneumoniae*); others have impermeable outer cell wall layers.

**Drug Characteristics: Penicillin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 25%, food delays but does not reduce absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Pericardium, pleural fluid, and inner ear |
| **Dialyzable** | Unknown | **Metabolism** | Not metabolized |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 20-40% with a half-life of 30 min |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to penicillins | **Black Box Warnings** | None |

### Medication Safety Issues: Penicillin

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Penicillin G | No |

### Drug Interactions: Penicillin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Probenecid | Increases serum concentration of penicillin | Avoid concurrent use |
| Tetracyclines | Decreased effectiveness of penicillins | Avoid concurrent use |

### Adverse Reactions: Penicillin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Diarrhea, nausea | Skin rash | Severe hypersensitivity, renal failure, hepatic failure, hemolytic anemia |

**Efficacy Monitoring Parameters.** Resolution of clinical signs of infection.

**Toxicity Monitoring Parameters.** Seek care for severe diarrhea, dark urine, yellowing of skin or eyes, unusual bruising or bleeding, blistering skin rash, or shortness of breath. Assess SCr and CBC if prolonged therapy.

**Key Patient Counseling Points.** Complete full course of therapy. Symptoms should improve within 2-3 d; if they worsen, seek medical care. Take on an empty stomach.

**Clinical Pearls.** There is cross-hypersensitivity between penicillin and cephalosporins (<10%); use with caution in cephalosporin allergy if severe penicillin reaction. May resume normal activities after 24 h of antibiotics if afebrile. First antibiotic, produced in 1943, referred to as the "magic bullet." Aminopenicillins have replaced use of penicillin for many indications, including endocarditis and otitis media.

# PENTOSAN: Elmiron

**Class:** Urinary Analgesic

**Dosage Forms: Oral Capsule:** 100 mg

Janssen 100 mg pictured



**Common FDA Label Indication, Dosing, and Titration.**

1. Pain relief from interstitial nephritis: 100 mg po tid

**Off-Label Uses.** None

**MOA.** Pentosan is a low-molecular-weight heparin-like compound. The mechanism of action of pentosan in relieving pain associated with interstitial cystitis is not known, but it has been found to adhere to the mucosal membrane of the bladder wall and may act as a buffer to control cell permeability, which prevents irritating solutes in urine from reaching the cells.

**Drug Characteristics: Pentosan**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 6% |
| **Dose Adjustment Renal** | Not required | **Distribution** | Uroepithelium of genitourinary tract |
| **Dialyzable** | Not known | **Metabolism** | Metabolized in liver and spleen via desulfation |
| **Pregnancy Category** | B | **Elimination** | Majority of dose eliminated unchanged in feces with half-life of 20-27 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | None | **Black Box Warnings** | None |

**Medication Safety Issues: Pentosan**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Imuran, pentostatin | No |

**Drug Interactions: Pentosan**

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Antiplatelet agents, NSAIDs, and anticoagulants | Additive risk of bleeding | Use with caution and monitor carefully |

**Adverse Reactions: Pentosan**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Alopecia, rash, diarrhea, nausea, dizziness, headache, ecchymosis, epistaxis, gum bleeding | Rectal hemorrhage, thrombocytopenia |

**Efficacy Monitoring Parameters.** Resolution of signs and symptoms of interstitial nephritis, including nocturia, urinary pain, urinary frequency, or urinary urgency.

**Toxicity Monitoring Parameters.** Monitor for bleeding complications.

**Key Patient Counseling Points.** Take 1 h before or 2 h after meals. Use caution and monitor for bleeding if using concomitant NSAIDs or aspirin-containing products.

**Clinical Pearls.** Patients should be evaluated after 3 mo, and if treatment has not provided benefit, a 2nd 3-mo trial may be attempted (provided no adverse effects have occurred). If the patient does not respond after 6 mo, the product is not likely to provide benefit.

# PERTUSSIS VACCINE, ACELLULAR: Daptacel, Adacel, Boostrix



**Class:** Vaccine

**Dosage Forms. Suspension for Intramuscular Injection:** For Adults, available in combination with tetanus and diphtheria toxoids (Tdap); for Children, available in combination with diphtheria and tetanus toxoids (DTaP), and in combination with other pediatric vaccines

Infanrix, GlaxoSmithKline pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Prevention of pertussis: Children, all infants at age 2, 4, 6, and 12-15 mo, and a 5th dose at age 4-6 y, as primary series of DTaP; Tdap at age 11-12 y; single dose of Tdap for all adults at next opportunity

**Off-Label Uses.**

1. Prevention of pertussis during pregnancy and in early infancy: Pregnant females, preferably during 27-36 wk gestation of each pregnancy, Tdap.

**Drug Characteristics: Pertussis Vaccine, Acellular**

| | | | |
|---|---|---|---|
| **Pregnancy Category** | C | **ADME** | None known |
| **Lactation** | Caution advised; weigh risk and benefit | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to pertussis vaccine or a component of the vaccine; Encephalopathy without known cause within 7 d of a pertussis containing vaccine | **Black Box Warnings** | None |

**Medication Safety Issues: Pertussis Vaccine, Acellular**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names |
|---|---|---|---|---|
| No | No | No | No | Adacel, Daptacel |

**Drug Interactions: Pertussis Vaccine, Acellular**

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Moderate- to high-dose corticosteroids | Immunosuppression reduces vaccine efficacy | Delay pertussis vaccine administration until corticosteroid therapy has been discontinued if possible |
| Immunosuppressing agents | Immunosuppression reduces vaccine efficacy | Delay pertussis vaccine administration until immunosuppressive therapy has been discontinued if possible |

**Adverse Reactions: Pertussis Vaccine, Acellular**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Injection site reactions, including erythema and soreness. Fever, headache, fatigue, swelling of limb | GI symptoms | Anaphylaxis, swelling or severe arm pain, Guillain-Barré syndrome |

**Efficacy Monitoring Parameters.** Prevention of pertussis.

**Toxicity Monitoring Parameters.** Monitor for syncope, fever after administration.

**Key Patient Counseling Points.** Return to provider for each dose in the series.

**Clinical Pearls.** Use the same brand of vaccine to complete the entire series, if possible. Adacel not for use in children <11 y of age. Daptacel not for use in children <6 wk or >6 y of age. Use caution to avoid mistaking Tdap and DTaP products.

# PHENAZOPYRIDINE: Pyridium, Various



**Class:** Urinary Tract Analgesic

**Dosage Forms. Oral Tablet:** 95 mg, 97.2 mg, 100 mg, 200 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Dysuria (pain, burning, and other discomforts of the lower urinary tract caused by infection, trauma, surgery, endoscopic procedures, or the passage of catheters): 100-200 mg po tid after meals; should not be used for >2 d when administered in conjunction with an antibiotic

**Off-Label Uses.** None

**MOA.** Phenazopyridine is excreted in the urine where it exerts a topical analgesic effect on the mucosa of the urinary tract. This action helps relieve pain, burning, urgency, and frequency. The precise mechanism of action is not known.

Breckenridge generic
100 mg pictured

**Drug Characteristics: Phenazopyridine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Not known |
| **Dose Adjustment Renal** | CrCl <50 mL/min, avoid | **Distribution** | Not known |
| **Dialyzable** | Unknown | **Metabolism** | Some hepatic metabolism |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 66% |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to phenazopyridine, renal failure | **Black Box Warnings** | None |

**Medication Safety Issues: Phenazopyridine**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Phenoxybenzamine, pyridoxine | No |

**Drug Interactions: Phenazopyridine.** None known

**Adverse Reactions: Phenazopyridine**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Headache, rash, pruritus, GI upset | Anaphylaxis, methemoglobinemia, hemolytic anemia, hepatotoxicity, nephrotoxicity |

**Efficacy Monitoring Parameters.** Resolution of clinical symptoms of dysuria (painful urination).

**Toxicity Monitoring Parameters.** Signs of hemolytic anemia, hepatotoxicity, or nephrotoxicity.

**Key Patient Counseling Points.** Drug may discolor urine and sclera to red or orange, causing staining of undergarments and contact lenses. Patient should take drug with food to minimize gastric irritation.

**Clinical Pearls.** When used in the treatment of a urinary tract infection, phenazopyridine should not exceed 2 d because there is a lack of evidence that the combined administration of phenazopyridine and an antibacterial provides greater benefit than administration of the antibacterial alone after 2 d. Many OTC products containing phenazopyridine are also available.

# PHENOBARBITAL: Luminal, Various

**Class:** Long-Acting Barbiturate. C-IV

**Dosage Forms. Oral Tablet:** 15 mg, 16.2 mg, 30 mg, 32.4 mg, 60 mg, 64.8 mg, 97.2 mg, 100 mg; **Oral Elixir, Oral Solution:** 20 mg/5 mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Epilepsy: Adults, 50-100 mg po bid-tid; Children, 15-50 mg po bid-tid (tablet) or 3-6 mg/kg/d po (solution)
2. Daytime sedation: Adults, 30-120 mg po divided into 2-3 doses, may titrate to 400 mg/d; Children, 6 mg/kg/d po divided into 3 doses

Excellium generic pictured

**Off-Label Uses.**

1. Sleep: Adults, 100-320 mg po as single dose.

**MOA.** Phenobarbital produces different degrees of depression within the CNS, from sedation to general anesthesia. It has been demonstrated to depress monosynaptic responses in the CNS only transiently, but synaptic recovery is delayed and a decrease in postsynaptic resistance is observed at some synapses.

**Drug Characteristics: Phenobarbital**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Dosage reduction recommended | **Absorption** | F = 80-100%, food has no effect on absorption |
| **Dose Adjustment Renal** | CrCl <10 mL/min, extend dosing interval to q12-16h | **Distribution** | Vd = 0.5-1 L/kg; 20-60% protein bound |
| **Dialyzable** | Yes | **Metabolism** | Hepatic, CYP2C19 substrate; strong inducer of CYP1A2, 2A6, 2B6, 2C8, 2C9, and 3A4/5 |
| **Pregnancy Category** | D | **Elimination** | Renal elimination is 21% with a half-life of 1.5-4.9 d |
| **Lactation** | Compatible, monitor infant for side effects | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to barbiturates; marked liver function impairment; respiratory disease with evidence of dyspnea or obstruction; history of sedative or hypnotic addiction; personal or family history of acute intermittent porphyria | **Black Box Warnings** | None |

**Medication Safety Issues: Phenobarbital**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | PHENobarbital | No | No | PENTobarbital, Phenergan | Avoid |

### Drug Interactions: Phenobarbital

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Substrates of CYP1A2, 2A6, 2B6, 2C8, 2C9, and 3A4/5 | Increases metabolism of substrates, reducing effectiveness | Consider increasing dose of substrates |
| CYP2C19 inducers | Increased phenobarbital metabolism reduces phenobarbital effectiveness | Consider dose increases of phenobarbital |
| CYP2C19 inhibitors | Decreased phenobarbital metabolism increases risk of phenobarbital toxicity | Consider dose decreases of phenobarbital |
| Barbiturates, benzodiazepines, opioids | Additive CNS respiratory depression | Avoid concomitant use |
| Phenytoin | Increased or decreased phenytoin concentrations | Monitor phenytoin levels |
| Valproic acid | Increased risk of phenobarbital toxicity or decreased valproic acid efficacy | Monitor phenobarbital and valproic acid levels |

### Adverse Reactions: Phenobarbital

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Apnea, ataxia, confusion, dizziness, hypotension, hypoventilation, rash, somnolence, syncope | Barbiturate withdrawal, bradyarrhythmia, megaloblastic anemia |

**Efficacy Monitoring Parameters.** Control of seizures, achieving adequate sleep; phenobarbital serum levels: therapeutic 10-40 mcg/mL; toxic >40 mcg/mL.

**Toxicity Monitoring Parameters.** SCr, LFTs, and CBC annually.

**Key Patient Counseling Points.** Avoid activities requiring mental alertness or coordination until drug effects are realized, as drug may cause dizziness, light-headedness, or somnolence. Advise patient against sudden discontinuation of drug. Do not drink alcohol or use other CNS depressant drugs while taking phenobarbital. Many drug interactions; check with pharmacist when starting new medications or OTC products.

**Clinical Pearls.** Efficacy for inducing and maintaining sleep begins to decline after ~2 wk; should not be used long term. Avoid use in children and elderly who are at higher risk of toxicity. Avoid abrupt withdrawal to decrease risk of seizures.

# PHENTERMINE: Adipex-P, Various

**Class:** Centrally Acting Appetite Suppressant, C-IV

**Dosage Forms. Oral Capsule:** 15 mg, 30 mg, 37.5 mg; **Oral Tablet:** 37.5 mg; **Oral Dispersible Tablet:** 15 mg, 30 mg, 37.5 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Simple obesity (BMI ≥30 kg/m$^2$ or >27 kg/m$^2$ with risk factors), short-term, adjunct treatment: 15-37.5 mg (capsules) or 37.5 mg (tablets) po daily either before breakfast or 1-2 h after breakfast; may titrate to response

Mutual Pharmaceutical generic 37.5 mg pictured



**Off-Label Uses.** None

**MOA.** Phentermine is a sympathomimetic amine with pharmacologic activity similar to amphetamines. Actions include CNS stimulation and elevation of BP. Weight loss is due to anorectic effect, primarily one of appetite suppression, but may also have other CNS or metabolic effects.

**Drug Characteristics: Phentermine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Not known |
| **Dose Adjustment Renal** | Not required | **Distribution** | Not known |
| **Dialyzable** | Unknown | **Metabolism** | Not metabolized |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 80% with a half-life of 20 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to phentermine or other sympathomimetic amines, use in agitated states, cardiovascular disease, history of drug abuse, glaucoma, moderate to severe hypertension, hyperthyroidism | **Black Box Warnings** | None |

**Medication Safety Issues: Phentermine**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Dispersible tablet | No | Phenytoin, Phentolamine | No |

### Drug Interactions: Phentermine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Fenfluramine, dexfenfluramine, TCAs | Unknown; combined use associated with primary pulmonary hypertension, valvular disorders, and death | Avoid concurrent use |
| MAOIs | Increases hypertensive effects of phentermine | Avoid phentermine within 14 d of MAOI discontinuation; do not use MAOIs within 5 wk of phentermine discontinuation |

### Adverse Reactions: Phentermine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Increased BP, palpitations, tachyarrhythmia, urticaria, constipation, diarrhea, xerostomia, dizziness, excitement, headache, insomnia, tremor, dysphoric mood, euphoria, restlessness | Heart valve disorder, psychotic disorder, primary pulmonary hypertension |

**Efficacy Monitoring Parameters.** Weight loss.

**Toxicity Monitoring Parameters.** Signs and symptoms of heart valve disorders and primary pulmonary hypertension, ECG, BP.

**Key Patient Counseling Points.** Phentermine may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly.

**Clinical Pearls.** Phentermine is indicated only as short-term monotherapy for the management of exogenous obesity. The safety and efficacy of combination therapy with phentermine and any other drug products for weight loss, including SSRIs, have not been established. Primary pulmonary hypertension and valvular heart disease have been reported to occur in patients receiving a combination of phentermine with fenfluramine or dexfenfluramine and should be avoided. Tolerance to the anorectic effect usually develops within a few weeks. When this occurs, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued. Should be used in conjunction with a comprehensive weight management program.

# PHENYTOIN: Dilantin, Various



**Class:** Hydantoin Anticonvulsant

**Dosage Forms. Oral Capsule:** 30 mg, 100 mg, 200 mg, 300 mg; **Oral Chewable Tablet**: 50 mg; **Oral Suspension:** 125 mg/5 mL

Taro generic 100 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Seizure, generalized tonic-clonic, complex partial, or following neurosurgery, treatment, and prophylaxis: Adults, 100 mg po tid, may titrate to 200 mg po tid; Children, 5 mg/kg/d po divided into 2-3 doses, may titrate to 300 mg/d

**Off-Label Uses.** None

**MOA.** Phenytoin is a hydantoin that suppresses the spread of seizure activity mainly by inhibiting synaptic post-tetanic potentiation and blocking the propagation of electric discharge. Phenytoin might decrease sodium transport and block calcium channels at the cellular level to produce these actions.

**Drug Characteristics: Phenytoin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Monitor and consider dose adjustments | **Absorption** | F = 70-100%, food increases absorption |
| **Dose Adjustment Renal** | Monitor and consider dose adjustments | **Distribution** | Vd = 0.75 L/kg; 88-93% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic, CYP2C19 and CYP2C9 substrate; strong inducer of CYP2B6, 2C19, 2C8, 2C9, and 3A4/5 |
| **Pregnancy Category** | D | **Elimination** | Fecal elimination with a half-life of 7-42 h |
| **Lactation** | Compatible | **Pharmacogenetics** | Patient with HLA-B*1502 at increased risk of Stevens-Johnson syndrome |
| **Contraindications** | Hypersensitivity to phenytoin, sinus bradycardia, AV block | **Black Box Warnings** | Hypotension and arrhythmias with IV administration |

**Medication Safety Issues: Phenytoin**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | ER capsules | Yes | PHENobarbital, Dilaudid, diltiazem | No |

## Drug Interactions: Phenytoin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP2C19, CYP2C9 inducers | Increased phenytoin metabolism reduces phenytoin effectiveness | Consider dose increases of phenytoin |
| CYP2C19, CYP2C9 inhibitors | Decreased phenytoin metabolism increases risk of phenytoin toxicity | Consider dose decreases of phenytoin |
| Substrates of CYP2B6, 2C19, 2C8, 2C9 and 3A4/5 | Metabolism of substrates increased, reducing effectiveness of substrates | Consider increasing dose of substrate if necessary |
| Acetaminophen | Decreased acetaminophen efficacy and increased risk of hepatotoxicity | Avoid large and/or chronic acetaminophen doses; monitor for hepatotoxicity. |
| Carbamazepine, valproic acid | Altered phenytoin carbamazepine or valproic acid concentrations | Monitor concentrations; adjust doses as necessary |

## Adverse Reactions: Phenytoin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Gingival hyperplasia | Ataxia, confusion, constipation, decreased coordination, dizziness, feeling nervous, headache, hypertrichosis, impaired cognition, insomnia, intentional tremor, nausea, nystagmus, osteomalacia, peripheral neuropathy, rash, slurred speech, spasmodic movement, vomiting | Hepatotoxicity, pancytopenia, systemic lupus erythematosus, Stevens-Johnson syndrome, suicidal behavior, withdrawal seizures |

**Efficacy Monitoring Parameters.** Reduction in the frequency and severity of seizures; phenytoin serum level range 10-20 mcg/mL (obtain after at least 5-7 half-lives after treatment initiation or dosage change).

**Toxicity Monitoring Parameters.** Emergence or worsening of depression, suicidal behavior or ideation, or unusual changes in behavior; monitor CBC and LFTs.

**Key Patient Counseling Points.** Do not crush extended-release capsules. Avoid activities requiring mental alertness or coordination until drug effects are realized. Report signs/symptoms of pancytopenia, hepatotoxicity, systemic lupus erythematosus, or severe skin reaction. Do not drink alcohol while taking this drug. Many drug interactions; check with health-care provider when starting new medications or OTC products.

**Clinical Pearls.** Highly protein bound, so albumin levels should be taken into account when measuring phenytoin concentration; dose adjustment based on free phenytoin concentration. Injectable formulation available, but not for use IM (causes “purple glove syndrome” related to tissue necrosis). Medication guide required at dispensing.

# PIOGLITAZONE: Actos, Various



**Class:** Thiazolidinedione Antidiabetic

**Dosage Forms. Oral Tablet:** 15 mg, 30 mg, 45 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Diabetes mellitus, type 2: 15-30 mg po daily; may titrate to *max* of 45 mg po daily as monotherapy, or in combination with sulfonylurea or metformin

**Off-Label Uses.** None

**MOA.** Pioglitazone is a thiazolidinedione antihyperglycemic and a potent peroxisome proliferator-activated receptor-γ (PPAR-γ) agonist used to improve insulin sensitivity in patients with type 2 diabetes. Insulin-dependent glucose disposal in skeletal muscle is improved and hepatic glucose production is decreased; both actions contribute to pioglitazone's glucose-lowering effects.

Takeda 30 mg pictured

**Drug Characteristics: Pioglitazone**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Avoid if LFTs elevated | **Absorption** | F = 50%, food delays but does not reduce absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 0.63 L/kg; 99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, CYP2C8 substrate; moderate inhibitor of CYP2C8 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 15-30% with a half-life of 16-24 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to pioglitazone, NYHA III/IV heart failure | **Black Box Warnings** | Heart failure risk |

**Medication Safety Issues: Pioglitazone**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | Yes | Actidose, Actonel | No |

### Drug Interactions: Pioglitazone

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP2C8 inducers | Increased pioglitazone metabolism reduces pioglitazone effectiveness | Consider dose increases of pioglitazone |
| CYP2C8 inhibitors | Decreased pioglitazone metabolism increases risk of pioglitazone toxicity | Consider dose decreases of pioglitazone |
| Substrates of CYP2C8 | Metabolism of substrates decreased, increasing risk of toxicity | Monitor for toxicity and consider decreasing dose of substrate if necessary |
| Corticosteroids | May diminish or increase hypoglycemic effect of pioglitazone | Monitor and consider pioglitazone dose adjustment if chronic steroid use |
| NSAIDs, SSRIs | Altered glucose metabolism and increased risk of hypoglycemia and hyperglycemia | Monitor blood glucose and consider dose adjustments |
| MAOIs | Stimulation of insulin secretion, hypoglycemic effects | Monitor blood glucose and consider dose adjustments |

### Adverse Reactions: Pioglitazone

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Edema, weight gain | Myalgia, bone fractures, sinusitis, headache | Heart failure, anemia, hepatotoxicity, diabetic macular edema, hypoglycemia when used in combination with insulin or sulfonylureas |

**Efficacy Monitoring Parameters.** Pre-prandial blood glucose between 70 and 130 mg/dL, $HbA_{1c}$ <7% (goal $HbA_{1c}$ may be 6.5-8% based on patient-specific characteristics).

**Toxicity Monitoring Parameters.** Weight for assessment of edema, Hgb, LFTs; symptoms of hypoglycemia include, nausea, sweating, and loss of consciousness; seek care for bone pain, yellowing of skin or eyes, eye pain, or shortness of breath; eye exams.

**Key Patient Counseling Points.** Monitor blood glucose in frequent intervals (2-4 times per d). May take without regard to food. May require several weeks for max effect.

**Clinical Pearls.** Pioglitazone causes edema, which may exacerbate underlying heart failure; contraindicated with NYHA III/IV heart failure. Stimulates ovulation. Premenopausal anovulatory individuals may resume ovulation. Increased risk of pregnancy in premenopausal female diabetics; use effective birth control. Not for use in children. Medication guide required at dispensing.

# PNEUMOCOCCAL VACCINE: Prevnar13, Pneumovax23



**Class:** Vaccine, Inactivated, Bacterial

**Dosage Forms.** **Suspension for Intramuscular Injection:** 0.5 mL (13 valent conjugate vaccine, PCV13, Prevnar13); **Solution for Intramuscular or Subcutaneous Injection:** 0.5 mL (23 valent polysaccharide vaccine, PPSV23, Pneumovax23)

Wyeth pictured

## Common FDA Label Indication, Dosing, and Titration.

1. Prevention of invasive pneumococcal disease: Adults ≥50 y of age, single dose IM once (either product); Children, single dose at 2, 4, 6, and 12-15 mo of age as primary series (conjugate product), multiple approved schedules for "catching up" in children who do not start their vaccine series on time

## Off-Label Uses.

1. Prevention of invasive pneumococcal disease, immunosuppressed individuals ≥6 y of age: If vaccine naive, single-dose PCV13 IM once, followed by single dose PPSV23 IM once in 8 wk; if previously vaccinated with PPSV23, single-dose PCV13 IM at least 12 mo after last PPSV23
2. Prevention of invasive pneumococcal disease, individuals ≥65 y of age: If vaccine naive, single-dose PCV13 IM once, followed by single dose PPSV23 IM once in 6-12 mo; if previously vaccinated with PPSV23, single-dose PCV13 IM at least 12 mo after last PPSV23
3. Prevention of invasive pneumococcal disease in individuals at high risk for invasive pneumococcal disease, including asplenia, chronic heart disease, chronic lung disease, diabetes, cerebrospinal fluid leak, cochlear implant, alcoholism, chronic liver disease (including asthma if ≥19 y of age), cigarette smoker ≥19 y of age, hemoglobinopathy, immunocompromised (congenital or acquired, HIV infection, leukemia, lymphoma, generalized malignancy, iatrogenic immunosuppression, solid-organ transplant, multiple myeloma): single-dose PPSV23 IM once
4. Prevention of invasive pneumococcal disease in individuals at high risk for invasive pneumococcal disease, including asplenia, hemoglobinopathy, immunocompromised: Single dose PPSV23 IM once and repeat single dose IM once.

Merck pictured

## Drug Characteristics: Pneumococcal Vaccine

| | | | |
|---|---|---|---|
| **Pregnancy Category** | PCV13, B<br>PPSV23, C | **ADME** | Not known |
| **Lactation** | Infant risk is minimal | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to pneumococcal vaccine or a component of the vaccine | **Black Box Warnings** | None |

### Medication Safety Issues: Pneumococcal Vaccine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Prevnar13, Pneumovax23 | No |

### Drug Interactions: Pneumococcal Vaccine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Moderate- to high-dose corticosteroids | Immunosuppression reduces vaccine efficacy | Delay vaccination until corticosteroid therapy has been discontinued, if possible |
| Immunosuppressing agents | Diminished immune response to vaccine due to immunosuppression | Delay pneumococcal vaccine administration until immunosuppressive therapy has been discontinued, if possible |
| Herpes zoster vaccine | Immunologic interference | Concomitant administration with PPSV23 lowers antibody concentrations to zoster vaccine; clinical consequences are unknown and no change in efficacy observed if administered simultaneously; separate vaccines by 4 wk if follow-up assured |

### Adverse Reactions: Pneumococcal Vaccine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Injection site reactions, including erythema and soreness. Rash, decreased appetite, arthralgia, myalgia, decreased sleep, somnolence, headache, asthenia | Diarrhea, vomiting, fever | Thrombocytopenia, anaphylaxis |

**Efficacy Monitoring Parameters.** Prevention of invasive pneumococcal disease, including bacterial meningitis.

**Toxicity Monitoring Parameters.** Monitor for syncope, fever after administration.

**Key Patient Counseling Points.** May administer antipyretics to reduce fever after vaccine administration.

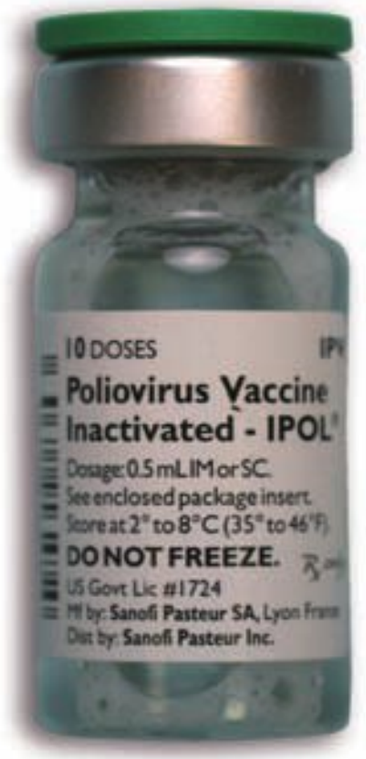
**Clinical Pearls.** PCV13 used for routine immunization of infants and young children, for immunosuppressed individuals ≥6 y of age and those ≥65 y of age. PPSV23 should not be used in children <2 y of age. PPSV23 used for individuals with chronic diseases, including immunosuppressive diseases.

# POLIOVIRUS VACCINE, INACTIVATED: Ipol



**Class:** Vaccine, Inactivated, Viral

**Dosage Forms. Solution for Intramuscular or Subcutaneous Injection:** 0.5 mL; also available in combination with other pediatric vaccines



Sanofi Pasteur pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Prevention of poliomyelitis: Children, one 0.5-mL dose IM or sq at 2, 4, and 6-18 mo of age, and a booster at 4-6 y of age as primary series

**Off-Label Uses.**

1. Prevention of poliomyelitis, in adults previously vaccinated but who are at risk for polio exposure: One 0.5-mL dose IM or sq
2. Prevention of poliomyelitis, in adults previously incompletely vaccinated but who are at risk for polio exposure: One 0.5-mL dose IM or sq
3. Prevention of poliomyelitis, in adults previously unvaccinated but who are at risk for polio exposure: Two 0.5-mL doses IM or sq at 1-2 mo intervals followed by a 3rd dose 6-12 mo later

**Drug Characteristics: Poliovirus Vaccine, Inactivated**

| | | | |
|---|---|---|---|
| **Pregnancy Category** | C | **ADME** | None known |
| **Lactation** | Infant risk is minimal | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to Hib vaccine or a component of the vaccine (2-phenoxyethanol, calf serum, formaldehyde, neomycin, polymixin, streptomycin) | **Black Box Warnings** | None |

**Medication Safety Issues: Poliovirus Vaccine, Inactivated**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | PPD | No |

### Drug Interactions: Poliovirus Vaccine, Inactivated

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Moderate- to high-dose corticosteroids | Immunosuppression reduces vaccine efficacy | Delay vaccination until corticosteroid therapy has been discontinued, if possible |
| Immunosuppressing agents | Diminished immune response to vaccine due to immunosuppression | Delay vaccination until immunosuppressive therapy has been discontinued, if possible |

### Adverse Reactions: Poliovirus Vaccine, Inactivated

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Injection site reactions, including erythema and soreness, loss of appetite, fatigue, irritability | Vomiting, fever | Anaphylaxis, febrile seizure, Guillain-Barré syndrome |

**Efficacy Monitoring Parameters.** Prevention of poliomyelitis.

**Toxicity Monitoring Parameters.** Monitor for syncope, fever after administration.

**Key Patient Counseling Points.** Return to provider for each dose in the series.

**Clinical Pearls.** Adults, even those without evidence of previous immunization, rarely need poliovirus vaccine. A single dose is needed only if exposure likely, such as travel to an endemic area (eg, Pakistan, Nigeria). The United States has been polio-free since 1979.

# POLYETHYLENE GLYCOL: Golytely, Various



**Class:** Hyperosmotic Laxative

**Dosage Forms. Powder for Oral Solution:** 119-420 g

**Common FDA Label Indication, Dosing, and Titration.**

1. Colonoscopy or barium enema preparation: Adults, 17 g of powder dissolved in 240 mL of reconstituted solution po q10min until diarrhea is clear or 4 L are consumed or 20-30 mL/min via nasogastric tube until rectal effluent is clear or 4 L are administered
2. Constipation: Adults, 17g of powder dissolved in 240 mL of reconstituted solution once daily; Children, 0.5-1.5 g/kg po daily

**Off-Label Uses.**

1. Whole bowel irrigation after toxic ingestions, 240 mL of reconstituted solution q10min until diarrhea is clear or 4 L are consumed or 20-30 mL/min via nasogastric tube until rectal effluent is clear or 4 L are administered

**MOA.** Polyethylene glycol (PEG) electrolyte lavage solution is a hyperosmotic solution that includes various electrolytes (sodium sulfate, sodium bicarbonate, sodium chloride, potassium chloride).

Kremer Urban generic pictured

**Drug Characteristics: Polyethylene Glycol**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Not absorbed |
| **Dose Adjustment Renal** | Not required | **Distribution** | Not absorbed |
| **Dialyzable** | Not dialyzable | **Metabolism** | Not absorbed |
| **Pregnancy Category** | C | **Elimination** | Not absorbed |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Bowel perforation, gastric retention, GI obstruction, ileus, toxic colitis | **Black Box Warnings** | None |

**Medication Safety Issues: Polyethylene Glycol**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| C G | GoLYTELY, NuLYTRLY | No | No | NuLYTELY | No |

### Drug Interactions: Polyethylene Glycol

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Potassium supplements | Additive hyperkalemia | Monitor serum potassium and SCr |
| Potassium-sparing diuretics | Additive hyperkalemia | Monitor serum potassium and SCr |
| ACE-Is | Additive hyperkalemia | Monitor serum potassium and SCr |

### Adverse Reactions: Polyethylene Glycol

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Anal irritation, bloating symptom, epigastric fullness, nausea, stomach cramps, vomiting | Urticaria | Anaphylaxis, dehydration, seizures |

**Efficacy Monitoring Parameters.** Bowel movements should begin within 60 min of initiating administration and dosing should continue until rectal effluent is clear if utilized as bowel preparation for imaging study.

**Toxicity Monitoring Parameters.** Seek medical attention if urticaria, rhinorrhea, or dermatitis occurs.

**Key Patient Counseling Points.** This preparation may cause nausea, anal irritation, or vomiting. If severe bloating, abdominal distension, or abdominal pain occurs, patient should slow the consumption of solution, and once symptoms have resolved, the patient may resume administration. If utilized as bowel preparation for imaging study, advise patient to avoid solid foods for 3-4 h before beginning this treatment.

**Clinical Pearls.** Encourage patients to drink each portion rapidly, as this method is preferred over drinking small amounts continuously. The solution tastes better chilled, but ice should not be added to the solution. Since oral medications are flushed from their system by this treatment and may not be absorbed, patients should receive guidance from the prescriber of PEG solution regarding whether and when to take oral doses of other medications. Risk of drug interactions resulting in hyperkalemia offset by diarrheal loss of potassium, clinical relevance uncertain.

# POTASSIUM CHLORIDE: Klor-con, Various

Upsher-Smith pictured

**Class:** Electrolyte, Potassium

**Dosage Forms. Oral Capsule, Extended Release:** 8 mEq, 10 mEq; **Powder for Oral Solution:** 20 mEq, 25 mEq; **Oral Solution:** 20 mEq/15 mL; **Oral Tablet, Extended Release:** 8 mEq, 10 mEq, 15 mEq, 20 mEq

**Common FDA Label Indication, Dosing, and Titration.**

1. Hypokalemia: Adults, 20-100 mEq/d po divided 1-5 times daily after meals; Children, 3-8 mEq/d po divided 1-5 times daily after meals
2. Hypokalemia, prophylaxis: 20 mEq/d po daily

**Off-Label Uses.** None

**MOA.** Potassium is an electrolyte required for maintenance of the excitatory properties of neuromuscular tissues, and the resting membrane potential of cells is related to potassium concentrations, varying directly with the ratio of intracellular to extracellular potassium level.

**Drug Characteristics: Potassium Chloride**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Well absorbed |
| **Dose Adjustment Renal** | Contraindicated | **Distribution** | 98% of total body potassium is located intracellularly |
| **Dialyzable** | Yes | **Metabolism** | Not metabolized |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 85-95% |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to potassium, acute renal failure, structural, pathological, or pharmacologic cause delay in tablet passage through the GI tract, hyperkalemia, Addison disease, acute dehydration | **Black Box Warnings** | None |

### Medication Safety Issues: Potassium Chloride

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| 10, M10, M20, K | No | Do not crush extended-release products | Yes (IV) | HCl, Macrobid, Micronase | No |

### Drug Interactions: Potassium Chloride

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Anticholinergics | Decreased GI motility and increased risk of erosions caused by potassium | Contraindicated |
| Potassium-sparing diuretics | Increased risk of hyperkalemia | Monitor potassium levels and consider alternative therapies |
| ACE-Is, ARBs | ACE-Is and ARBs may lower aldosterone levels, which may result in potassium retention | Monitor potassium levels |

### Adverse Reactions: Potassium Chloride

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Nausea, indigestion, flatulence | Vomiting | ECG changes with hypokalemia or hyperkalemia, esophagitis |

**Efficacy Monitoring Parameters.** Monitor serum potassium and adjust dose to maintain serum potassium in the normal range 3.5-5 mEq/L.

**Toxicity Monitoring Parameters.** SCr, ECG if hypokalemic or hyperkalemic.

**Key Patient Counseling Points.** Take with food. Take the powder, granule, or oral liquid only after mixing in 4 oz of water or juice. Crush or break only specifically designed extended-release formulations. Capsules may be opened, sprinkled on apple sauce, and ingested immediately.

**Clinical Pearls.** The total potassium content in a 70-kg male is approximately 3500 mEq. Some drugs (insulin, β-agonists) decrease potassium levels by causing an intracellular shift of potassium. If replacement does not normalize potassium level, check magnesium levels and calcium levels and replace as necessary.

# POTASSIUM IODIDE: SSKI, ThyroShield, Various

**Class:** Antithyroid Agent

**Dosage Forms. Oral Solution:** 65 mg/mL (SSKI), 1 g/mL (ThyroShield)

**Common FDA Label Indication, Dosing, and Titration.**

1. Prevention of thyroid dysfunction due to radiation exposure: Children, birth to 1 mo of age, 16.25 mg po daily; Children 1 mo to 3 y of age, 32.5 mg po daily; Children 3-12 y of age, 65 mg po daily; Children >12 y of age but <150 lb, 65 mg po daily; Children >12 y of age and ≥150 lb and Adults, 130 mg po daily

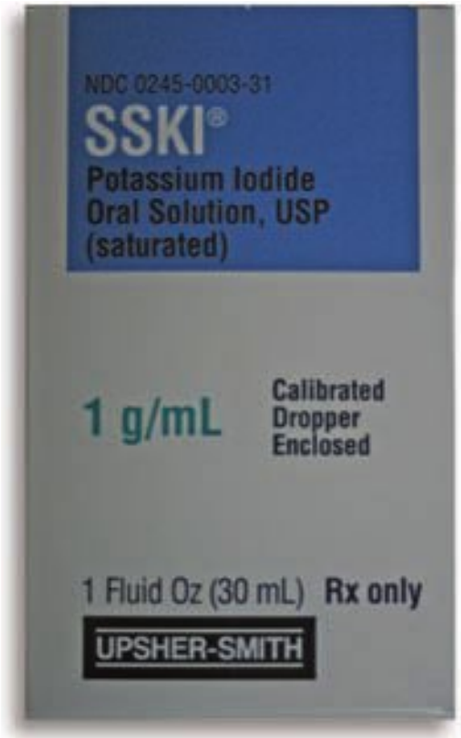
**Off-Label Uses.**

1. Induction or involution of thyroid: 60-250 mg po tid × 10 d preoperatively to reduce vascularity of the gland prior to thyroidectomy
2. Graves disease (short-term reduction in thyroid hormone production prior to ablation or surgery): 50 mg po q8h

**MOA.** Iodine is needed for the production of thyroid hormones. In patients with disorders causing hyperthyroidism, iodide is administered to inhibit the release of thyroid hormones via direct effect on the thyroid gland and inhibits synthesis of thyroid hormones. Also attenuates effects of TSH mediated via cAMPb and decreases vascularity of thyroid gland. When administered before or promptly after radioactive iodine exposure, potassium iodide blocks or reduces accumulation of radioactive iodine in the thyroid gland.

**Drug Characteristics: Potassium Iodide**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Readily absorbed |
| **Dose Adjustment Renal** | Not required | **Distribution** | Iodide concentrates in the thyroid gland, salivary glands, gastric mucosa, choroid plexus, placenta, and mammary glands |
| **Dialyzable** | Yes | **Metabolism** | Taken up by the thyroid; not metabolized |
| **Pregnancy Category** | D | **Elimination** | Renal elimination is 85-90% |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to potassium iodide | **Black Box Warnings** | None |




Upsher-Smith 1 g/mL solution pictured

### Medication Safety Issues: Potassium Iodide

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Potassium iodine | No |

### Drug Interactions: Potassium Iodide

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Warfarin | Hyperthyroid patients metabolize clotting factors more quickly than normal. By decreasing thyroid hormone production, potassium iodide may alter metabolism of clotting factors and affect the INR | Monitor INR carefully and adjust warfarin dose as required |

### Adverse Reactions: Potassium Iodide

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Stomach upset, diarrhea, nausea, vomiting, stomach pain | Rash, salivary gland swelling or tenderness | Goiter, hypothyroidism, thyroid adenoma, immune hypersensitivity reaction |

**Efficacy Monitoring Parameters.** Thyroid function tests.

**Toxicity Monitoring Parameters.** Serum potassium, SCr, BUN, signs/symptoms of goiter, hypothyroidism, thyroid adenoma, allergic reaction, hyperkalemia.

**Key Patient Counseling Points.** To minimize GI irritation, administer with food. Take with 4 oz of water. Other liquids can be used; dilution in chocolate milk can mask the taste. During a radiation emergency, understand the nature of the radiation hazard and the potential benefits and adverse effects of potassium iodide. Administer potassium iodide only as directed by public health authorities. Adhere to other emergency measures recommended by public health authorities.

**Clinical Pearls.** Potassium iodide has been used in the past as an expectorant and cough suppressant, which is not appropriate given the risk of adverse effects. Potassium iodide crosses into breast milk, but most guidelines consider it compatible with breast-feeding.

# PRAMIPEXOLE: Mirapex, Mirapex ER

**Class:** Dopamine Agonist, Anti-Parkinson

**Dosage Forms. Oral Tablet:** 0.125 mg, 0.25 mg, 0.5 mg, 0.75 mg, 1 mg, 1.5 mg; **Oral Tablet, Extended Release):** 0.375 mg, 0.75 mg, 1.5 mg, 2.25, 3 mg, 3.75 mg, 4.5 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Parkinson disease: Immediate release, 0.125 mg po tid, may titrate to 0.5-1.5 mg po tid; extended release, 0.375 mg po daily, may titrate to 4.5 mg po daily
2. Restless legs syndrome: 0.125 mg po daily taken 2-3 h prior to bedtime, may titrate to 0.5 mg po daily

Boehringer Ingelheim 0.5 mg pictured

**Off-Label Uses.** None

**MOA.** Pramipexole is a nonergot-derived dopamine subtype selective agonist that exerts activity in the CNS at $D_2$ and $D_3$ receptors but has no activity at the $D_1$ receptor. $D_2$ receptors are thought to play an important role in improving the akinesia, bradykinesia, rigidity, and gait disturbances of Parkinson disease.

**Drug Characteristics: Pramipexole**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | No adjustment needed | **Absorption** | F = 90%, food reduces Tmax |
| **Dose Adjustment Renal** | Immediate release: CrCl 35-50 mL/min, 0.125 mg po bid, to *max* of 1.5 mg po bid; CrCl 15-34 mL/min, 0.125 mg po daily, to *max* of 1.5 mg po daily, CrCl <15 mL/min: avoid; Extended release: CrCl 30-50 mL/min, 0.375 mg po qod, to *max* of 2.25 mg po daily; CrCl <30 mL/min: avoid | **Distribution** | Vd = 500 L; 15% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Not metabolized |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 90% with a half-life of 8-12 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to pramipexole | **Black Box Warnings** | None |

### Medication Safety Issues: Pramipexole

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| ER | No | Extended-release tablets | No | MiraLax | No |

### Drug Interactions: Pramipexole

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Cimetidine | Increased pramipexole concentrations | Choose an alternative acid-reducing agent |
| Antipsychotics | May reduce the effectiveness of antipsychotic or dopamine agonists | Avoid, or monitor effect of both agents and increase dose if necessary |

### Adverse Reactions: Pramipexole

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Asthenia, dream disorder, dyskinesia, extrapyramidal movements, nausea, somnolence | Amnesia, confusion, compulsive behavior, constipation, diarrhea, dizziness, fatigue, hallucinations, headache, insomnia, orthostatic hypotension, peripheral edema, xerostomia | Blackouts, heart failure, impulsive behavior, melanoma |

**Efficacy Monitoring Parameters.** Improvement in Parkinson symptoms or restless legs syndrome.

**Toxicity Monitoring Parameters.** Hypotension, drowsiness, hallucinations, or behavior changes; melanoma screening.

**Key Patient Counseling Points.** Take with food if nausea occurs. Avoid activities requiring mental alertness or coordination until drug effects are realized. Rise slowly from a sitting/lying down position. Report new or increased gambling urges, sexual urges, compulsive eating or buying, as well as new-onset or worsening dyskinesia. Do not discontinue abruptly, as this may cause emergent hyperpyrexia and confusion. Do not drink alcohol, and avoid concomitant use of other CNS depressants.

**Clinical Pearls.** Safety and efficacy in children not established. May switch patient from immediate-release to extended-release tablets overnight at same daily dose.

# PRASUGREL: Effient

**Class:** Antiplatelet Agent

**Dosage Forms. Oral Tablet:** 5 mg, 10 mg

Lilly 10 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Prevention of thromboembolism after percutaneous coronary intervention: 60 mg po once, then 10 mg po daily, in combination with aspirin 75-325 mg po daily

**Off-Label Uses.**

1. Prevention of thromboembolism in acute coronary syndrome: 30 mg po once, then 10 mg po daily, in combination with aspirin ≤100 mg po daily

**MOA.** Prasugrel is an inhibitor of platelet activation and aggregation through the irreversible binding of its active metabolite to the $P2Y_{12}$ class of ADP receptors on platelets.

**Drug Characteristics: Prasugrel**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required for mild or moderate impairment; risk in severe impairment not known | **Absorption** | F = 79%, food delays rate but not extent of absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 44-68 L; 98% albumin bound |
| **Dialyzable** | Not known | **Metabolism** | Rapid hepatic metabolism to active metabolite, which is further metabolized in the liver to an active metabolite |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 68-70% with a half-life of 7-8 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Active bleeding, history of transient ischemic attack or stroke | **Black Box Warnings** | Bleeding risk; not recommended in patients ≥75 y of age; CABG |

**Medication Safety Issues: Prasugrel**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Pravastatin | No |

### Drug Interactions: Prasugrel

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| SSRIs | Serotonin released from platelets is necessary for hemostasis; bleeding can result if antiplatelet agents are given with SSRIs | Monitor for bleeding |
| Antiplatelet agents, NSAIDs, and anticoagulants | Additive risk of bleeding | Avoid concurrent use or monitor carefully and adjust dose if necessary |

### Adverse Reactions: Prasugrel

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Hypertension, hyperlipidemia, backache, headache, epistaxis | Atrial fibrillation, colon cancer, major bleeding, TTP, angioedema |

**Efficacy Monitoring Parameters.** Stent patency and prevention of clotting.

**Toxicity Monitoring Parameters.** Monitor for signs and symptoms of bleeding. Consider periodic hematocrit/hemoglobin, as well as platelet function testing.

**Key Patient Counseling Points.** May be given with or without food. Tablet may be crushed, but should not be split for purposes of dividing doses.

**Clinical Pearls.** After percutaneous coronary intervention, continue for 12 mo if stent is placed, and at least 15 mo if drug-eluting stent is placed. In patients weighing <60 kg, may consider dose of 5 mg po daily. May need to hold prior to surgical intervention; consult with cardiologist.

# PRAVASTATIN: Pravachol, Various

**Class:** HMG-CoA Reductase Inhibitor

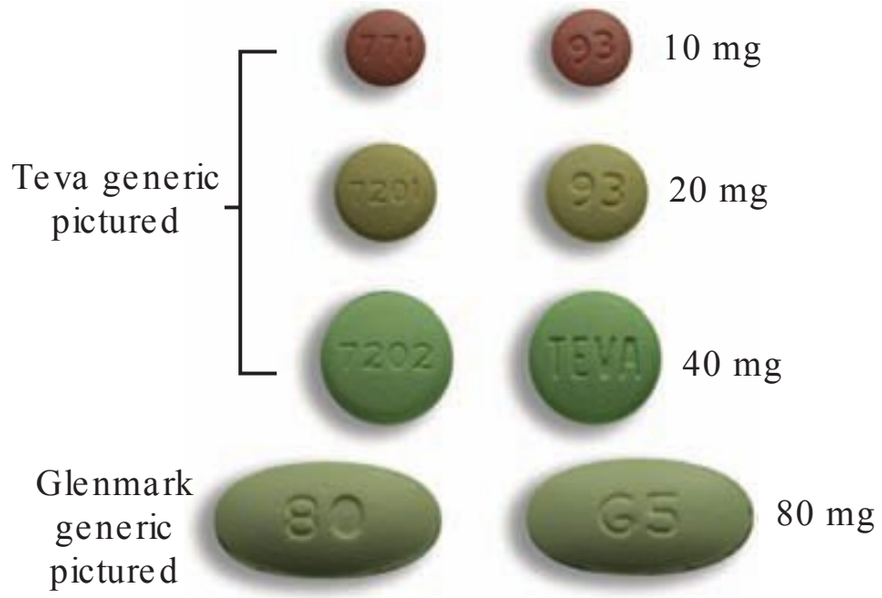
**Dosage Forms. Oral Tablet:** 10 mg, 20 mg, 40 mg, 80 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Cerebrovascular accident (prevention), coronary arteriosclerosis (primary or secondary prevention): 40 mg po daily
2. Familial hypercholesterolemia: Children 8-13 y of age, 20 mg po daily; Children 14-18 y of age, 40 mg po daily
3. Hyperlipidemia: Children (boys and postmenarchal girls) 10-17 y of age, 10 mg po daily, may titrate to 20 mg/d; Adults, 40 mg po daily, may titrate to 40-80 mg po daily

**Off-Label Uses.** None

**MOA.** HMG-CoA reductase inhibitors competitively inhibit conversion of HMG-CoA to mevalonate, an early rate-limiting step in cholesterol synthesis. A compensatory increase in LDL receptors, which bind and remove circulating LDL-cholesterol, results. Production of LDL-cholesterol can decrease because of decreased production of VLDL-cholesterol or increased VLDL removal by LDL receptors.






**Drug Characteristics: Pravastatin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Avoid use in patients with active liver disease or unexplained persistent elevated LFTs | **Absorption** | F = 17%, food has no effect on absorption |
| **Dose Adjustment Renal** | Initial dose 10 mg po daily | **Distribution** | Vd = 0.46 L/kg; 43-55% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic via hydroxylation |
| **Pregnancy Category** | X | **Elimination** | Renal elimination is 20% with a half-life of 2.6-3.2 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | Effective in lowering lipids in patients with the ApoE E2/E2 genotype and Fredrickson type III dysbetalipoproteinemia |
| **Contraindications** | Hypersensitivity to pravastatin, pregnancy or lactation | **Black Box Warnings** | None |

### Medication Safety Issues: Pravastatin

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Prevacid, prasugrel | No |

### Drug Interactions: Pravastatin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Bile acid–binding resins | Binding by bile acid resins decrease efficacy of pravastatin | Give pravastatin 1 h before or 4 h after resin |
| Efavirenz, nelfinavir | Decreased pravastatin levels decreases efficacy of pravastatin | Monitor fasting lipid panels |
| Fibrates, niacin, cyclosporine | Increased risk of myopathy or rhabdomyolysis | Avoid concurrent use or monitor for myopathy and measure creatine kinase levels |

### Adverse Reactions: Pravastatin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Headache, heartburn, increased liver enzymes, influenza-like symptoms, musculoskeletal pain, myalgia, nausea, rash, vomiting | Rhabdomyolysis, tendon rupture |

**Efficacy Monitoring Parameters.** Baseline fasting lipid panel (total cholesterol, LDL, HDL, and triglycerides), repeat 4-12 wk after initiation or dose adjustment.

**Toxicity Monitoring Parameters.** Signs/symptoms of rhabdomyolysis (myalgias, dark urine, arthralgias, fatigue) or hepatotoxicity; LFTs at baseline and if concern for hepatotoxicity; check serum creatine kinase in patients experiencing myopathy.

**Key Patient Counseling Points.** Take in the evening. Contraindicated in pregnancy. Avoid concurrent heavy alcohol use. Pravastatin does not take the place of diet and exercise to lower cholesterol levels.

**Clinical Pearls.** Repeat fasting lipid panel 4-12 wk following initiation or titration. Consider holding pravastatin 4-7 d before major surgery as patient is at higher risk for occurrence of rhabdomyolysis. May increase the risk of diabetes.

# PREDNISOLONE ORAL: Orapred, Prelone, Various



**Class:** Adrenal Glucocorticosteroid

**Dosage Forms.** **Oral Tablet:** 5 mg; **Oral Dispersible Tablet:** 10 mg, 15 mg, 30 mg; **Oral Solution:** 5 mg/5 mL, 10 mg/5 mL, 15 mg/5 mL 20 mg/5 mL; **Oral Syrup:** 15 mg/5 mL; **Oral Suspension:** 15 mg/5 mL

**Common FDA Label Indication, Dosing, and Titration.**

Dosing for indications listed below: Adults, 5-60 mg po daily; Children, 0.1-2 mg/kg/d; adjust dose according to patient response

1. Allergic states (eg, asthma, etc): 1-2 mg/kg/d divided 1-2 times daily, *max* of 60 mg/dose
2. Dermatologic diseases (eg, exfoliative erythroderma, etc)
3. Endocrine disorders (eg, adrenocortical insufficiency, etc)
4. GI diseases (eg, regional enteritis, ulcerative colitis, etc)
5. Hematologic disorders (eg, acquired hemolytic anemia, etc)
6. Neoplastic diseases (eg, palliative management of leukemias and lymphomas, etc)
7. Nervous system (eg, multiple sclerosis, cerebral edema, etc)
8. Renal diseases (eg, idiopathic nephrotic syndrome, systemic lupus erythematosus, etc)
9. Respiratory diseases (eg, idiopathic eosinophilic pneumonia, etc)
10. Rheumatic disorders (eg, rheumatoid arthritis, etc)

**Off-Label Uses.**

1. Croup: 1 mg/kg po once

MGP generic 15 mg /5 mL solution pictured

**MOA.** Glucocorticosteroids are naturally occurring and synthetic adrenocortical steroids that cause varied metabolic effects, modify the body's immune responses to diverse stimuli, and are used primarily for their anti-inflammatory effects in disorders of many organ systems.

**Drug Characteristics: Prednisolone Oral**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 85% |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 1.5 L/kg; 70-90% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, CYP3A4/5 substrate |
| **Pregnancy Category** | C | **Elimination** | Primarily renal elimination with a half-life of 2-4 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to prednisolone or other glucocorticosteroids, administration of live vaccines, fungal infections | **Black Box Warnings** | None |

### Medication Safety Issues: Prednisolone Oral

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| DP, ODT, PRED, 20 | PrednisoLONE | Dispersible tablet | No | PredniSONE | No |

### Drug Interactions: Prednisolone Oral

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Antacids | Decreased absorption of corticosteroids | Separate administration by 2 h |
| CYP3A4/5 inhibitors | Decreased prednisolone metabolism increases risk of prednisolone toxicity | Monitor for toxicity and reduce prednisolone dose if necessary |
| CYP3A4/5 inducers | Increased prednisolone metabolism decreases prednisolone efficacy | Monitor for lack of efficacy and consider dose increase of prednisolone |
| Fluoroquinolones | Concurrent use of steroids and fluoroquinolones can increase risk of tendon rupture, especially in elderly | Avoid concurrent use, or monitor carefully for tendon rupture |
| Phenytoin | Phenytoin increases prednisolone metabolism; prednisolone can increase or decrease phenytoin metabolism | Monitor prednisolone efficacy and phenytoin concentrations |
| Warfarin | Steroids can increase or decrease INR in patients taking warfarin | Monitor INR carefully |

### Adverse Reactions: Prednisolone Oral

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| GI upset | Hypertension, atrophic condition of skin, impaired skin healing, osteoporosis, depression, euphoria, pulmonary tuberculosis, hyperglycemia | Primary adrenocortical insufficiency, Cushing syndrome, decreased body growth, increased risk of infection |

**Efficacy Monitoring Parameters.** Improvement or resolution of clinical signs and symptoms; monitor for decrease in ESR, or improvement of PFT.

**Toxicity Monitoring Parameters.** Hyperglycemia, osteoporosis, adrenocortical insufficiency, and infection. Mood changes may also occur; frequency and severity of adverse effects are dependent on the length of treatment and dose.

**Key Patient Counseling Points.** Take with food or milk to prevent GI upset. Take in the morning to help prevent insomnia. For high-dose or longer term treatment, inform patients to monitor for signs of hyperglycemia, osteoporosis, adrenocortical insufficiency, and infection.

**Clinical Pearls.** Available in a variety of dosage forms and concentrations, including ophthalmic preparations. Use lowest effective dose and discontinue as soon as possible to avoid serious long-term adverse effects. Some formulations taste worse than others; chocolate milk may mask taste best; oral disintegrating tablets are an expensive alternative. Taper required after chronic use (courses >14 d). 1 mg prednisolone is typically equivalent to 1 mg prednisone.

# PREDNISONE: Deltasone, Various



**Class:** Adrenal Corticosteroid

**Dosage Forms. Oral Tablet:** 1 mg, 2.5 mg, 5 mg, 10 mg, 20 mg, 50 mg; **Oral Tablet, Delayed Release:** 1 mg, 2 mg, 5 mg; **Oral Solution:** 5 mg/1 mL; 5 mg/5 mL

**Common FDA Label Indication, Dosing, and Titration.**

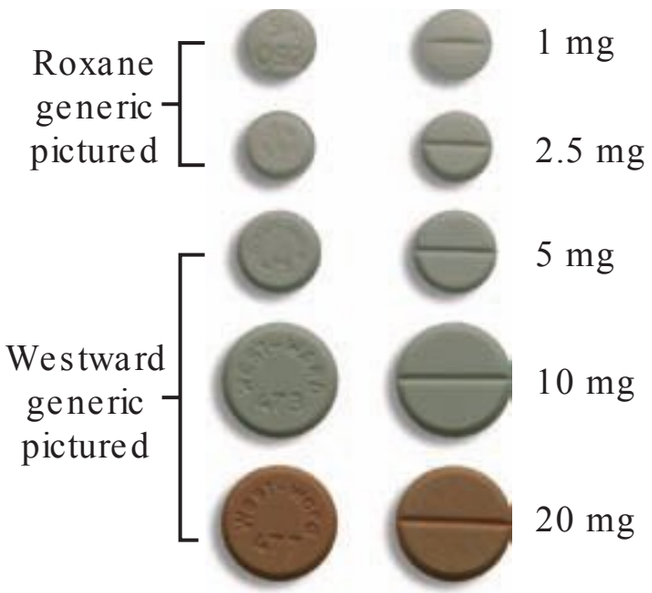
Dosing for indications listed below: Adults and Children, 5-60 mg po daily; for all patients, adjust dose according to patient response

1. Allergic states (eg, asthma, etc)
2. Dermatologic diseases (eg, exfoliative erythroderma, etc)
3. Endocrine disorders (eg, adrenocortical insufficiency, etc)
4. GI diseases (eg, regional enteritis, ulcerative colitis, etc)
5. Hematologic disorders (eg, acquired hemolytic anemia, etc)
6. Neoplastic diseases (eg, palliative management of leukemias and lymphomas, etc)
7. Nervous system (eg, multiple sclerosis, cerebral edema, etc)
8. Renal diseases (eg, idiopathic nephrotic syndrome, systemic lupus erythematosus, etc)
9. Respiratory diseases (eg, idiopathic eosinophilic pneumonia, etc)
10. Rheumatic disorders (eg, rheumatoid arthritis, etc)

**Off-Label Uses.**

1. Graft-versus-host disease: 60 mg/m$^2$ po daily

**MOA.** Glucocorticosteroids are naturally occurring and synthetic adrenocortical steroids that cause varied metabolic effects, modify the body's immune responses to diverse stimuli, and are used primarily for their anti-inflammatory effects in disorders of many organ systems.




**Drug Characteristics: Prednisone**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 92% |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 0.4-1 L/kg |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, CYP3A4/5 substrate |
| **Pregnancy Category** | C | **Elimination** | Primarily renal elimination with a half-life of 2.6-3 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to prednisone or other glucocorticosteroids, administration of live vaccines, fungal infections | **Black Box Warnings** | None |

### Medication Safety Issues: Prednisone

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| Intensol | PredniSONE | Delayed-release formulation | No | prednisoLONE | No |

### Drug Interactions: Prednisone

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Antacids | Decreased absorption of corticosteroids | Separate administration by 2 h |
| CYP3A4/5 inhibitors | Decreased prednisone metabolism increases risk of prednisone toxicity | Monitor for toxicity and reduce prednisone dose if necessary |
| CYP3A4/5 inducers | Increased prednisone metabolism decreases prednisone efficacy | Monitor for lack of efficacy and consider dose increase of prednisolone |
| Fluoroquinolones | Concurrent use of steroids and fluoroquinolones can increase risk of tendon rupture, especially in elderly | Avoid concurrent use, or monitor carefully for tendon rupture |
| Phenytoin | Phenytoin increases prednisone metabolism; prednisone can increase or decrease phenytoin metabolism | Monitor prednisone efficacy and phenytoin concentrations |
| Warfarin | Steroids can increase or decrease INR in patients taking warfarin | Monitor INR carefully |

### Adverse Reactions: Prednisone

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| GI upset | Hypertension, atrophic condition of skin, impaired skin healing, osteoporosis, depression, euphoria, pulmonary tuberculosis, hyperglycemia | Primary adrenocortical insufficiency, Cushing syndrome, decreased body growth, increased risk of infection |

**Efficacy Monitoring Parameters.** Improvement or resolution of clinical signs and symptoms.

**Toxicity Monitoring Parameters.** Monitor for signs of hyperglycemia, osteoporosis, adrenocortical insufficiency, and infection; frequency and severity of adverse effects are dependent on the length of treatment and dose.

**Key Patient Counseling Points.** Take with food or milk to prevent GI upset. Take in the morning to help prevent insomnia. For high-dose or longer term treatment, inform patients to monitor for signs of hyperglycemia, osteoporosis, adrenocortical insufficiency, and infection.

**Clinical Pearls.** See National Heart, Lung, and Blood Institute guidelines for dosing of prednisone for moderate to severe asthma exacerbation; after chronic use (>2 wk), dose tapering required prior to discontinuation of therapy.

# PREGABALIN: Lyrica



**Class:** Analgesic, Anticonvulsant. C-V

**Dosage Forms. Oral Capsule:** 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg, 300 mg; **Oral Solution:** 20 mg/mL

Pfizer pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Neuropathic pain, diabetes associated or spinal cord injury associated: 50-100 mg po tid
2. Fibromyalgia: 75-150 mg po bid; may titrate to *max* 225 mg bid
3. Partial seizure, adjunct: 25-75 mg po bid; may titrate to *max* 600 mg/d in 2-3 divided doses
4. Postherpetic neuralgia: Initial, 75 mg po bid; may titrate to 300 mg/d; maintenance 75-150 mg bid or 50-100 mg tid; may titrate to *max* 600 mg/d

**Off-Label Uses.** None

**MOA.** Pregabalin is a GABA analogue that strongly binds to the $\alpha_2$-delta site (a subunit of voltage-gated calcium channels) in CNS tissues. Binding to the $\alpha_2$-delta subunit may be involved in pregabalin's effects on neuropathic pain and seizure control. Pregabalin reduces the calcium-dependent release of several neurotransmitters; however, the exact mechanism of action is unknown.

## Drug Characteristics: Pregabalin

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F >90%, food has no effect on absorption |
| **Dose Adjustment Renal** | CrCl 30-60 mL/min, 75-300 mg/d; CrCl 15-30 mL/min, 25-150 mg/d; CrCl <15 mL/min, 25-75 mg/d | **Distribution** | Vd = 0.5 L/kg; no protein binding |
| **Dialyzable** | Yes | **Metabolism** | Negligible hepatic metabolism |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 90-99% with a half-life of 5-6.5 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to pregabalin | **Black Box Warnings** | None |

## Medication Safety Issues: Pregabalin

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Lopressor, Hydrea | No |

### Drug Interactions: Pregabalin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CNS depressants | Additive CNS depression | Consider dose reduction of pregabalin or other agent |

### Adverse Reactions: Pregabalin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Dizziness, somnolence, ataxia, headache, peripheral edema | Arthralgia, asthenia, blurred vision, confusion, constipation, diplopia, disturbance in thinking, euphoria, fatigue, incoordination, increased appetite, muscle spasm, tremor, vomiting, weight gain, xerostomia | Angioedema |

**Efficacy Monitoring Parameters.** Reduction in seizure frequency, improvement in pain, reduced symptoms of fibromyalgia.

**Toxicity Monitoring Parameters.** Creatine kinase, emergence or worsening of depression, suicidal behavior or ideation, or unusual changes in behavior, symptoms of angioedema, during initial and chronic therapy.

**Key Patient Counseling Points.** Solution must be used within 45 d of first opening the bottle. Avoid activities requiring mental alertness or coordination until drug effects are realized. Avoid sudden discontinuation of drug due to risk of withdrawal, including increased seizure frequency. Avoid drinking alcohol.

**Clinical Pearls.** Safety and efficacy have not been established in children. Data suggest an increased risk of suicidal behavior or ideation may exist in patients receiving therapy with AEDs.

# PRENATAL VITAMIN: Various

**Class:** Vitamin Supplement

**Dosage Forms. Oral Tablet:** Containing various combinations of vitamins and minerals, including folic acid and iron

Amneal generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Diet supplementation during pregnancy: 1 tablet po daily

**Off-Label Uses.** None

**MOA.** Provide vitamin and mineral supplementation throughout pregnancy and during the postnatal period for both the lactating and the nonlactating mother. It is also useful for improving nutritional status prior to conception.

**Drug Characteristics: Prenatal Vitamin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Unknown |
| **Dose Adjustment Renal** | Not required | **Distribution** | Unknown |
| **Dialyzable** | Not dialyzable | **Metabolism** | Unknown |
| **Pregnancy Category** | A | **Elimination** | Unknown |
| **Lactation** | Compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to any component of vitamin and mineral supplement | **Black Box Warnings** | Iron toxicity |

**Medication Safety Issues: Prenatal Vitamin**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | No |

**Drug Interactions: Prenatal Vitamin.** None known

**Adverse Reactions: Prenatal Vitamin**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Nausea, vomiting, constipation | |

**Efficacy Monitoring Parameters.** Improvement in nutritional status.

**Toxicity Monitoring Parameters.** Seek medical attention if severe GI distress occurs.

**Key Patient Counseling Points.** May contain iron, so important to keep out of the reach of children.

**Clinical Pearls.** Various prescription and OTC products are available. May take with food to avoid GI upset, but administration with milk will decrease extent of iron absorption.

# PROCHLORPERAZINE: Compazine, Various

**Class:** Phenothiazine

**Dosage Forms. Oral Tablet:** 5 mg, 10 mg; **Rectal Suppositories:** 25 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Nausea and vomiting: Adults, 5-10 mg po 3-4 times daily; daily dosages above 40 mg should be used only in resistant cases; Children ≥2 y of age and 20-29 lb, 2.5 mg po or pr daily-bid, *max* of 7.5 mg/d; Children 30-39 lb, 2.5 mg po or pr bid-tid, *max* 10 mg/d; Children 40-85 lb, 2.5-5 mg po or pr tid, *max* of 15 mg/d

**Off-Label Uses.** None

**MOA.** Prochlorperazine is dopamine ($D_2$) receptor antagonist that belongs to the phenothiazine class of antipsychotic agents.

Goldline 10 mg generic pictured



**Drug Characteristics: Prochlorperazine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 12.5%, food has minimal effect on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 12.9-17 L/kg |
| **Dialyzable** | Not dialyzable | **Metabolism** | Not metabolized |
| **Pregnancy Category** | C | **Elimination** | Half-life of 7-9 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to phenothiazines, bone marrow depression, children <20 lb or 2 y of age, comatose or greatly depressed states, severe hypotension | **Black Box Warnings** | Mortality in elderly with dementia |

**Medication Safety Issues: Prochlorperazine**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | ChlorproMAZINE | No |

### Drug Interactions: Prochlorperazine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Agents that prolong the QT interval | Additive QT prolongation | Use with caution in combination with other agents that may prolong QTc or in congenital long QT syndrome |
| Barbiturates, benzodiazepines, centrally acting muscle relaxants, opioids | Additive CNS depression | Monitor and consider dose adjustments |
| Dopamine agonists | Decreased effect of dopamine agonists | Avoid concurrent use |
| MAOIs | Additive respiratory depression, increased risk of serotonin syndrome | Contraindicated |

### Adverse Reactions: Prochlorperazine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Somnolence | Headache | Respiratory depression, hypotension, neuroleptic malignant syndrome, agranulocytosis, extrapyramidal symptoms (increased risk in children <5 y of age), seizures, QTc prolongation |

**Efficacy Monitoring Parameters.** Resolution of nausea and vomiting.

**Toxicity Monitoring Parameters.** Excessive drowsiness, decreased breathing, seizures, unusual bruising or bleeding.

**Key Patient Counseling Points.** May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid concurrent use of other CNS depressants.

**Clinical Pearls.** Use caution in elderly; appear more sensitive to the effects. Prochlorperazine is FDA approved for schizophrenia, although seldom used. Atypical antipsychotics are generally more effective and less toxic. Injection contains benzyl alcohol, which can cause gasping syndrome in neonates; should be avoided.

# PROGESTERONE: Prometrium, Various



**Class:** Progestin Hormone

**Dosage Forms.** **Oral Capsule:** 100 mg, 200 mg; **Vaginal Jelly:** 4%, 8%

**Common FDA Label Indication, Dosing, and Titration.**

1. Prevention of estrogen-induced endometrial hyperplasia: 200 mg po daily hs × 12 sequential d per 28-d cycle while conjugated estrogens are administered
2. Secondary physiologic amenorrhea: 400 mg po daily hs × 10 d

**Off-Label Uses.** None

**MOA.** Progesterone transforms proliferative endometrium into secretory endometrium. Parenterally administered progesterone inhibits gonadotropin production, which in turn prevents follicular maturation and ovulation.

Solvay 100 mg pictured

**Drug Characteristics: Progesterone**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Mild, moderate, lower dose; severe, avoid | **Absorption** | F = 10-15%, food increases AUC |
| **Dose Adjustment Renal** | Not required | **Distribution** | 90% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, CYP3A4/5 and CYP2C19 substrate |
| **Pregnancy Category** | B | **Elimination** | Renal elimination of metabolites, 50-60%, with half-life of 25 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Abnormal vaginal bleeding, history of estrogen- or progesterone-dependent neoplasia, active or history of DVT or PE, known or suspected pregnancy | **Black Box Warnings** | Cardiovascular disorders, breast cancer, dementia risk |

**Medication Safety Issues: Progesterone**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Yes | No | No | No |

### Drug Interactions: Progesterone

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP2C19, CYP3A4/5 inducers | Increased progesterone metabolism reduces progesterone effectiveness | Consider dose increases of progesterone |
| CYP2C19, CYP3A4/5 inhibitors | Decreased progesterone metabolism increases risk of progesterone toxicity | Consider dose decreases of progesterone |
| Warfarin | Progesterone may increase or decrease warfarin effectiveness; mechanism unknown | Monitor INR |

### Adverse Reactions: Progesterone

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Weight change, headache, amenorrhea, breast tenderness, abdominal pain | Nausea, asthenia, feeling nervous, break-through bleeding | Thromboembolism (DVT, PE), thrombophlebitis, osteoporosis |

**Efficacy Monitoring Parameters.** Resolution of clinical signs of abnormal bleeding or symptoms being managed with this product.

**Toxicity Monitoring Parameters.** Annual physical including BP monitoring and annual breast exam; diagnostic evaluation to rule out malignancy in event of persistent or recurring vaginal bleeding.

**Key Patient Counseling Points.** Advise patients that menstrual bleeding should occur 3-7 d after last dose. Patient should report if menstruation does not occur within 7 d after last dose.

**Clinical Pearls.** Injectable depot formulation of progesterone (medroxyprogesterone) is used for contraception (150 mg IM q3mo). Topical formulation is also available for other indications. Combination of estrogens and progestins should not be used for the prevention of cardiovascular disease. Increased risk of myocardial infarction, stroke, invasive breast cancer, PE, and DVT has been shown in postmenopausal women. Evidence regarding teratogenicity is conflicting; some studies show birth defects, and other studies show no effect.

# PROMETHAZINE: Phenergan, Various

**Class:** Phenothiazine Antihistamine

**Dosage Forms. Oral Syrup:** 6.25 mg/5 mL; **Oral Tablet:** 12.5 mg, 25 mg, 50 mg; **Oral Solution:** 6.25 mg/5 mL; **Rectal Suppository:** 12.5 mg, 25 mg, 50 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Motion sickness: Adults, 25 mg po or pr bid; Children ≥2 y of age, 12.5-25 mg po or pr bid
2. Allergy: Adults, 25 mg po or pr daily hs or 12.5 mg po or pr tid; Children ≥2 y of age, 25 mg po or pr daily hs or 6.25 mg po or pr tid
3. Nausea and vomiting: Adults, 25 mg po or pr q4-6h prn; Children ≥2 y of age, 12.5 mg po or pr q4-6h prn

Sandoz generic 25 mg pictured

**Off-Label Uses.** None

**MOA.** Promethazine hydrochloride is a phenothiazine derivative that competitively blocks histamine $H_1$ receptors without blocking the secretion of histamine. The drug has sedative, antimotion-sickness, antiemetic, and anticholinergic effects, but it has no dopaminergic action due to a structural difference with other phenothiazines.

**Drug Characteristics: Promethazine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required, but use with caution | **Absorption** | Well absorbed with high first-pass metabolism; minimal effect of food absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 171 L; 93% protein bound |
| **Dialyzable** | Unknown | **Metabolism** | Hepatic, CYP2B6 and CYP2D6 substrate |
| **Pregnancy Category** | C | **Elimination** | Renal elimination of metabolites with a half-life of 9-16 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to promethazine, asthma, children <2 y, comatose state | **Black Box Warnings** | Children <2 y (fatal respiratory depression), tissue injury (IV) |

**Medication Safety Issues: Promethazine**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | Yes (IV only) | PredniSONE, chlorproMAZINE | Avoid. Highly anticholinergic |

### Drug Interactions: Promethazine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP2B6 inducers | Increased promethazine metabolism reduces promethazine effectiveness | Consider dose increases of promethazine |
| CYP2B6, CYP2D6 inhibitors | Decreased promethazine metabolism increases risk of promethazine toxicity | Consider dose decreases of promethazine |
| Anticholinergics | Additive anticholinergic effects | Avoid concurrent use |
| Agents that prolong the QT interval | Additive QT prolongation | Use with caution in combination with other agents that may prolong QTc or in congenital long QT syndrome |
| Barbiturates, benzodiazepines, centrally acting muscle relaxants, opioids | Additive CNS depression | Monitor and consider dose adjustments |
| MAOIs | Additive respiratory depression, increased risk of serotonin syndrome | Contraindicated |

### Adverse Reactions: Promethazine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Somnolence, xerostomia | Constipation, nausea | Respiratory depression, hypotension, neuroleptic malignant syndrome, agranulocytosis, extrapyramidal symptoms, seizures, photosensitivity |

**Efficacy Monitoring Parameters.** Relief of nausea or allergy symptoms.
**Toxicity Monitoring Parameters.** Mental status, vital signs.
**Key Patient Counseling Points.** May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol.
**Clinical Pearls.** Use caution in elderly; appear more sensitive to the anticholinergic adverse effects.

# PROPRANOLOL: Inderal, Inderal LA, Inderal XL, Various

**Class:** β-Adrenergic Blocker, Nonselective

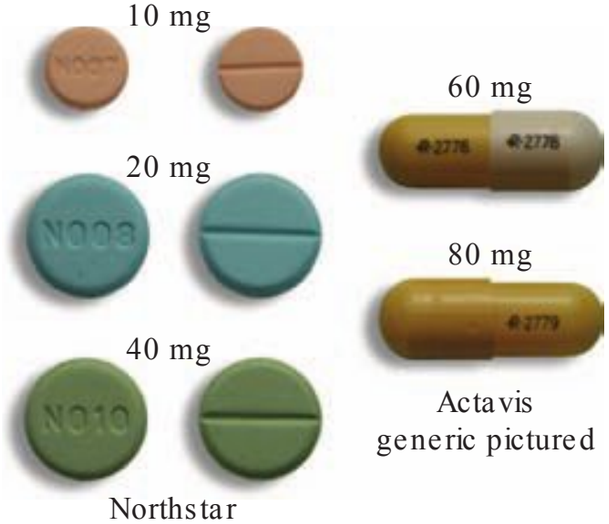
**Dosage Forms. Oral Tablet:** 10 mg, 20 mg, 40 mg, 60 mg, 80 mg; **Oral Capsule, Extended Release:** 60 mg, 80 mg, 120 mg, 160 mg; **Oral Solution:** 20 mg/5 mL, 40 mg/5 mL, 4.28 mg/mL

**Common FDA Label Indication, Dosing, and Titration.**

1. Angina pectoris, chronic: Immediate release, 80-320 mg po daily in 2-4 doses; extended release, 80-160 mg po daily
2. Cardiac dysrhythmia: Adults, 10-30 mg po tid-qid; Children, 2-6 mg/kg po in 3-4 doses, *max* 60 mg/d
3. Hypertension: Adults, immediate release, 40 mg po bid, may titrate to 240 mg po daily in 2-3 doses; Adults, extended release, 80 mg po daily, may titrate to 160 mg po daily; Children, immediate release, 0.5-1 mg/kg po daily in 3-4 doses, may titrate to 16 mg/kg/d
4. Migraine, prophylaxis: Immediate release, 80 mg po daily in divided doses, may titrate to 240 mg po daily; extended release, 80 mg po daily; may titrate to 240 mg po daily

**Off-Label Uses.**

1. Anxiety: 10 mg po 1 h prior to event




**MOA.** Propranolol is a nonselective β-adrenergic blocker (class II antiarrhythmic) that competitively blocks $\beta_1$ and $\beta_2$ receptors, thereby preventing β-adrenergic stimulation. The mechanism of its antihypertensive and antimigraine effects is not completely understood.

**Drug Characteristics: Propranolol**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Titrate with caution | **Absorption** | F = 30-70%, food increases absorption |
| **Dose Adjustment Renal** | Titrate with caution | **Distribution** | Vd = 6 L/kg; 93% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, CYP1A2, CYP2D6 substrate |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 1% with a half-life of 3-4 h |
| **Lactation** | Compatible | **Pharmacogenetics** | Use with caution in CYP2D6 poor metabolizers |
| **Contraindications** | Hypersensitivity to propranolol; asthma; sinus bradycardia, AV block, sick sinus syndrome, cardiogenic shock | **Black Box Warnings** | Avoid abrupt withdrawal |

**Medication Safety Issues: Propranolol**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| LA, XL | No | Extended-release formulations | Yes | Adderall, Isordil, prasugrel | No |

### Drug Interactions: Propranolol

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP1A2 inducers | Increased propranolol metabolism reduces propranolol effectiveness | Consider dose increases of propranolol |
| CYP1A2, CYP2D6 inhibitors | Decreased propranolol metabolism increases risk of propranolol toxicity | Consider dose decreases of propranolol |
| NSAIDs | Decreased antihypertensive effect of propranolol | Avoid concurrent use or monitor BP |
| Antidiabetic drugs | Decreased glycemic control | Monitor blood glucose levels |
| Calcium channel blockers, alpha-blockers | Increased risk of hypotension and/or bradycardia and AV block | Avoid concurrent use, or monitor BP and HR |
| Digoxin | Increased risk of AV block | Monitor HR, ECG, and serum digoxin concentrations |

### Adverse Reactions: Propranolol

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Hypotension | Bradyarrhythmias, bronchospasm, constipation, dizziness, dyspnea, disorder of glucose regulation, fatigue, headache, heart block, impotence, nausea, pruritus, rash, vomiting, urticaria | Heart failure, interstitial nephritis |

**Efficacy Monitoring Parameters.** Decreased BP, chest pain, number of angina attacks, nitroglycerin use, signs/symptoms of CHF, reduction in tremors, frequency of migraines.

**Toxicity Monitoring Parameters.** Signs/symptoms of CHF, decreased HR, bronchospasm, increased FPG, exacerbations of angina pectoris, or acute coronary insufficiency. Monitor HR and BP.

**Key Patient Counseling Points.** Take immediate-release tablets on an empty stomach; ER can be taken with or without food but consistently. Avoid alcohol. Avoid abrupt discontinuation; exacerbations of angina may occur. Report signs/symptoms of hypotension, CHF, or exacerbation of angina with initial dosing and dose changes. This medicine may cause dizziness. Diabetic patients should carefully follow blood glucose as beta-blockers may mask symptoms of hypoglycemia.

**Clinical Pearls.** When discontinuance of propranolol is planned, dosage should be gradually reduced. Avoid in patients with poorly controlled asthma or bronchospasm as beta-blockade may exacerbate symptoms. Consider cardioselective beta-blocker as an alternative.

# QUETIAPINE: Seroquel, Seroquel XR, Various

**Class:** Antipsychotic (Atypical)

**Dosage Forms.** **Oral Tablet:** 25 mg, 50 mg, 100 mg, 200 mg, 300 mg, 400 mg; **Oral Tablet, Extended Release:** 50 mg, 150 mg, 200 mg, 300 mg, 400 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Bipolar disorder or schizophrenia, therapy initiation: Adults, immediate release, 50 mg po bid × 1 d, increase 50 mg/d × 3 d, may titrate to 800 mg/d; Adults, extended release, 300 mg po hs × 1 d, then 600 mg po hs × 1 d, may titrate to 800 mg/d; Children 10-17 y of age, immediate release, 50 mg po × 1 d, then 100 mg po × 1 d, then 200 mg po × 1 d, then 300 mg po × 1 d, then 400 mg po × 1 d, may titrate to 600 mg/d
2. Bipolar disorder or schizophrenia, maintenance: Adults, immediate release: 400-800 mg/d po; Adults, extended release, 400-800 mg/d po; Children 10-17 y of age, regular release, titrate to lowest effective dose
3. Major depressive disorder: Adults, extended release, 50 mg po daily hs, may titrate to 300 mg/d

**Off-Label Uses.**

1. Delirium in the critically ill: Adults, extended release, 50 mg po daily hs, may titrate to 300 mg/d
2. **MOA.** Quetiapine is an antagonist at multiple neurotransmitter receptors in the brain. It antagonizes serotonin 5-$HT_{1A}$ and 5-$HT_2$, dopamine $D_1$ and $D_2$, histamine $H_1$, and adrenergic $\alpha_1$ and $\alpha_2$ receptors. Efficacy in schizophrenia and bipolar disorder is due to the antagonism of a combination of $D_2$ and 5-$HT_2$ receptors. Quetiapine also has no affinity for cholinergic muscarinic and benzodiazepine receptors.

AstraZeneca pictured

**Drug Characteristics: Quetiapine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Regular release, initiate at 25 mg po daily; extended release, initiate at 50 mg po daily | **Absorption** | F = 9%, Cmax and AUC of extended-release tablet increased by high-fat meal |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 6-14 L/kg; 83% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, CYP3A4/5 substrate |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 73% with a half-life of 6-7 h |
| **Lactation** | Weigh risks and benef ts | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to quetiapine, drugs that increase QT interval | **Black Box Warnings** | Mortality in elderly with dementia, suicidality, not approved for children <10 y |

### Medication Safety Issues: Quetiapine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| XR | QUEtiapine, SEROquel | XR formulation | No | OLANZapine, SINEquan | Avoid use for behavioral problems of dementia unless nonpharmacologic options have failed and patient is threat to self or others |

### Drug Interactions: Quetiapine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inducers | Increased quetiapine metabolism reduces quetiapine effectiveness | Consider dose increases of quetiapine |
| CYP3A4/5 inhibitors | Decreased quetiapine metabolism increases risk of quetiapine toxicity | Consider dose decreases of quetiapine |
| Agents that increase QT interval | Increased risk of QT prolongation (torsades de pointes, cardiac arrest) | Use with caution in combination with other agents that may prolong QTc; avoid in congenital long QT syndrome |

### Adverse Reactions: Quetiapine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Agitation, headache, hypertension, somnolence, weight gain, xerostomia | Abdominal pain, asthenia, anxiety, backache, cataracts, constipation, dizziness, extrapyramidal effects, fatigue, hyperglycemia, hyperlipidemia, hyperprolactinemia, increased appetite, indigestion, insomnia, lethargy, nasal congestion, nausea, orthostatic hypotension, rash, tachycardia, tremor, vomiting | Neuroleptic malignant syndrome, neutropenia, pancreatitis, sudden cardiac death, syncope, tardive dyskinesia |

**Efficacy Monitoring Parameters.** Improvement in signs and symptoms of schizophrenia, manic or mixed episodes associated with bipolar disorder, depression.

**Toxicity Monitoring Parameters.** BP, FPG, and CBC with differential, eye examination at baseline and periodically during therapy; fasting lipid profile/$HgA_{1c}$ at baseline, 3 mo, and annually; weight, growth, BMI; TSH/T4; patients at high risk for suicide should be closely supervised.

**Key Patient Counseling Points.** Take with food but avoid alcohol. Avoid activities requiring mental alertness or coordination. Use caution with activities leading to an increased core temperature. Rise slowly from a sitting/supine position. Report signs/symptoms of hyperglycemia, bradycardia, arrhythmia, tardive dyskinesia, or neuroleptic malignant syndrome.

**Clinical Pearls.** Regular release may be switched to extended release at the equivalent total daily dose taken once daily; individual dosage adjustments may be required. Elderly patients with dementia-related psychosis taking quetiapine are at an increased risk of death compared to placebo.

# QUINAPRIL: Accupril, Various

**Class:** ACE-I, Antihypertensive

**Dosage Forms.** **Oral Tablet:** 5 mg, 10 mg, 20 mg, 40 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Heart failure: 5 mg po bid, may titrate to 20-40 mg po bid
2. Hypertension: 10-20 mg po daily, may titrate to 80 mg po daily

**Off-Label Uses.**

1. Diabetic nephropathy: 20-40 mg po daily

**MOA.** Quinapril is a competitive ACE-I; it prevents conversion of angiotensin I to angiotensin II (a vasoconstrictor). It also reduces serum aldosterone leading to decreased sodium retention, potentiates the vasodilator kallikrein–kinin system and alters prostanoid metabolism, inhibits sympathetic nervous system, and inhibits the tissue renin–angiotensin system.

Greenstone 10 mg generic pictured



**Drug Characteristics: Quinapril**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 60%, food decreases rate and extent of absorption |
| **Dose Adjustment Renal** | CrCl 30-60 mL/min, 5 mg po daily; CrCl 10-30 mL/min, 2.5 mg po daily | **Distribution** | Vd = 0.7 L/kg; 97% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic to active metabolite (quinaprilat) but not via CYP450 |
| **Pregnancy Category** | D | **Elimination** | Renal elimination is 50-60% with a half-life of 25 h (metabolite) |
| **Lactation** | Weigh risks and benef ts | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to quinapril or other ACE-Is, history of ACE-I–induced angioedema | **Black Box Warnings** | Pregnancy |

**Medication Safety Issues: Quinapril**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | AcipHex, Accutane | No |

### Drug Interactions: Quinapril

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Antacids | Binding and decreased absorption of quinapril | Separate administration by 2 h |
| Potassium-sparing diuretics | Increased risk of hypotension, hyperkalemia | Avoid concurrent use or monitor BP and serum potassium levels |
| Angiotensin receptor blockers | Increased risk of hypotension, hyperkalemia, nephrotoxicity | Avoid concurrent use or monitor BP, SCr, and potassium levels |
| Potassium supplements | Increased risk of hyperkalemia and cardiac arrhythmias | Avoid concurrent use or monitor serum potassium levels |
| NSAIDs | Decreased antihypertensive effect of quinapril, increased risk of nephrotoxicity | Avoid concurrent use or monitor BP and SCr levels |
| Aliskiren | Increased risk of hyperkalemia | Monitor serum potassium levels |
| Azathioprine | Increased risk of myelosuppression | Avoid concurrent use; monitor for anemia or leukopenia |
| Diuretics | Increased risk of postural hypotension due to hypovolemia | Monitor BP; rise from seated position slowly |

### Adverse Reactions: Quinapril

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Diarrhea, dizziness, dry cough, fatigue, headache, hypotension, hyperkalemia, nausea, nephrotoxicity, rash, tachycardia, vomiting | Angioedema, birth defects, liver failure |

**Efficacy Monitoring Parameters.** BP, signs/symptoms of heart failure.

**Toxicity Monitoring Parameters.** Signs/symptoms of angioedema, persistent dry cough, hypotension; monitor baseline and periodic electrolytes, SCr, BUN, urine protein.

**Key Patient Counseling Points.** Avoid pregnancy. Avoid sudden discontinuation; rebound hypertension can occur. Use potassium supplements or salt substitutes only under medical supervision. May cause dizziness that may worsen if dehydrated.

**Clinical Pearls.** Safety and efficacy not established in children (captopril and enalapril are more commonly used in children). The full effect may not be observed for 2-4 wk. Dry cough associated with ACE-I is typically a class effect; consider switching to an ARB. Can lead to increases in SCr and potassium; recheck electrolytes within a week of initiation.

# RABEPRAZOLE: AcipHex

**Class:** Proton Pump Inhibitor

**Dosage Forms.** **Oral Tablet, Delayed Release:** 20 mg; **Oral Capsule, Oral Sprinkle**: 20 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Duodenal ulcer disease: 20 mg po daily × up to 4 wk
2. *H. pylori* GI infection: 20 mg po bid × 10-14 d in combination with amoxicillin 1000 mg and clarithromycin 500 mg po bid
3. Gastric hypersecretion: 60 mg po daily, may titrate to 60 mg po bid
4. GERD, erosive or ulcerative, for symptom control, initial treatment, or maintenance: Adults and Children >12 y of age, 20 mg po daily

Eisai 20 mg pictured

**Off-Label Uses.**

1. Drug-induced GI disturbance, indigestion: 20 mg po daily
2. Gastric ulcer disease: 20-40 mg po daily

**MOA.** Rabeprazole is a proton pump inhibitor (PPI) that, when protonated in the secretory canaliculi of the parietal cells, covalently binds to $H^+/K^+$-ATPase (proton pump), which is the final pathway for acid secretion. Rabeprazole produces a profound and prolonged antisecretory effect and inhibits basal, nocturnal, and pentagastrin- and food-stimulated gastric acid secretion.

**Drug Characteristics: Rabeprazole**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Required for hepatic dysfunction | **Absorption** | F = 52%, food delays absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | 96% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, substrate for CYP3A4/5, 2C19; moderate inhibitor of CYP2C8 |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 90% with a half-life of 1-2 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | CYP2C19 poor metabolizers have greater gastric acid suppression |
| **Contraindications** | Hypersensitivity to rabeprazole | **Black Box Warnings** | None |

**Medication Safety Issues: Rabeprazole**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | RABEprazole | Do not crush tablets, sprinkle capsules may be opened but not chewed | No | Aricept, ARIPiprazole | No |

### Drug Interactions: Rabeprazole

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5, 2C19 inducers | Increased rabeprazole metabolism reduces rabeprazole effectiveness | Monitor and consider dose increases of rabeprazole |
| CYP3A4/5, 2C19 inhibitors | Decreased rabeprazole metabolism increases risk of rabeprazole toxicity | Monitor and consider dose decreases of rabeprazole |
| CYP2C8 substrates | Decreased substrate metabolism may result in substrate toxicity | Monitor and consider decreasing dose of substrate |
| pH-dependent drugs | Lower gastric pH reduces absorption | Monitor pH-dependent drug and adjust dose as necessary |
| Clopidogrel | May decrease the effect of clopidogrel on platelet inhibition, resulting in cardiovascular events (MI, stroke, death) | Avoid concurrent use; consider alternative acid-reducing agent such as $H_2$ inhibitor |
| Warfarin | Increased INR and risk of bleeding | Monitor INR and consider dose adjustment |

### Adverse Reactions: Rabeprazole

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Headache, rash | Stevens-Johnson syndrome, fracture of bone, rhabdomyolysis, acute interstitial nephritis |

**Efficacy Monitoring Parameters.** Resolution of GI symptoms, (reflux, ulcers, *H. pylori*, infection)

**Toxicity Monitoring Parameters.** Headache, SCr or blistering skin rash.

**Key Patient Counseling Points.** Open sprinkle capsules into a small quantity of room-temperature soft food or liquid and administer within 15 min. If used for duodenal ulcers, administer with breakfast.

**Clinical Pearls.** Multiple *H. pylori* regimens exist that include different combinations of PPIs and antibiotics; patients should complete full regimen if prescribed for *H. pylori* management. Many PPI and $H_2$ antagonists available OTC; warn patients not to take multiple products concurrently to avoid additive risk of adverse effects. Possible increased risk of osteoporosis. Use for shortest period of time and avoid use in those at risk for osteoporosis if possible.

# RALOXIFENE: Evista

**Class:** Selective Estrogen Receptor Modulator

**Dosage Forms. Oral Tablet:** 60 mg

Lilly 60 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Breast cancer, invasive, in postmenopausal women at high risk; prophylaxis: 60 mg po daily
2. Postmenopausal osteoporosis, prevention or treatment: 60 mg po daily

**Off-Label Uses.** None

**MOA.** Raloxifene is a selective estrogen receptor modulator (SERM) and binds to estrogen receptors, resulting in activation of estrogenic pathways in some tissues (agonism) and blockade of estrogenic pathways in others (antagonism). Raloxifene appears to act as an estrogen agonist in bone, decreasing bone resorption and bone turnover and increasing BMD.



## Drug Characteristics: Raloxifene

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 2%, food has no effect on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 2583 L/kg; 95% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic; not via CYP |
| **Pregnancy Category** | X | **Elimination** | Fecal elimination with a half-life of 32 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to raloxifene; pregnancy or lactation, current or history of thromboembolic disorders | **Black Box Warnings** | Venous thromboembolism, stroke |

## Medication Safety Issues: Raloxifene

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | AVINza | No |

### Drug Interactions: Raloxifene

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Bile acid sequestrants | Reduced absorption of raloxifene | Avoid concurrent use |

### Adverse Reactions: Raloxifene

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Hot f ashes, arthralgia, f u-like symptoms | Rash, sweating, weight gain, f atulence, nausea, vaginitis, bronchitis | Edema, hypertriglyceridemia venous thrombo-embolism, cerebrovascular accident, pulmonary embolism |

**Efficacy Monitoring Parameters.** DEXA scan (BMD), mammogram.

**Toxicity Monitoring Parameters.** Weight gain, shortness of breath, symptoms of stroke, DVT (swelling of the leg, redness, pain); triglycerides.

**Key Patient Counseling Points.** Raloxifene increases the risk of blood clots, especially during the first 4 mo of therapy. Avoid sitting for long periods and be aware of the symptoms of DVT. If taking for osteoporosis, consider calcium and vitamin D supplementation.

**Clinical Pearls.** Tamoxifen and raloxifene are equivalent in efficacy of preventing breast cancer; however, raloxifene causes less endometrial hyperplasia, thromboembolic events, and cataracts. Medication guide required at dispensing.

# RALTEGRAVIR: Isentress

**Class:** Antiretroviral Agent, Integrase Inhibitor

**Dosage Forms. Oral Tablet:** 400 mg; **Oral Chewable Tablet:** 25 mg; 100 mg; **Powder for Oral Suspension:** 100 mg/packet

Merck 400 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Treatment of HIV-1 infection in combination with other antiretroviral agents: Adults and Children ≥12 y of age, 400 mg po bid; Children <12 y of age, dose is weight based

**Off-Label Uses.**

1. Occupational HIV postexposure prophylaxis: 400 mg po bid with concomitant emtricitabine/tenofovir

**MOA.** Raltegravir inhibits the catalytic activity of integrase HIV-1 integrase, thus preventing integration of the proviral gene into human DNA.



**Drug Characteristics: Raltegravir**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Use with caution if severe hepatic impairment | **Absorption** | F = 30-40%, no food effect |
| **Dose Adjustment Renal** | Not required | **Distribution** | CSF, semen |
| **Dialyzable** | No | **Metabolism** | Metabolized by UGT1A1 to an inactive metabolite |
| **Pregnancy Category** | C | **Elimination** | 50% of the metabolites in feces, 30% renally eliminated as parent, half-life 9-12 h |
| **Lactation** | Weight risks and benefits | **Pharmacogenetics** | Resistance is associated with HIV mutations |
| **Contraindications** | None | **Black Box Warnings** | None |

**Medication Safety Issues: Raltegravir**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Do not chew or crush oral tablets | Yes | No | No |

### Drug Interactions: Raltegravir

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Aluminum salt, magnesium salts | Decreased absorption of raltegravir | Contraindicated |
| Fosamprenavir | Decreased amprenavir concentrations, unknown mechanism | Avoid |
| PPIs and $H_2$-blockers | Increased absorption of raltegravir with increased pH | Monitor for toxicity and consider dose reductions of raltegravir |
| Rifampin | Decreased raltegravir via induction of UGT by rifampin | Increase raltegravir dose to 800 mg bid |

### Adverse Reactions: Raltegravir

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Hyperglycemia, insomnia, headache, neutropenia, elevated LFTs | Anemia, cerebellar ataxia, depression, hepatitis, hypersensitivity, myopathy, nephrolithiasis, psychomotor hyperactivity (children), renal failure, rhabdomyolysis, Stevens-Johnson syndrome, suicidal ideation/behavior, thrombocytopenia, toxic epidermal necrolysis |

**Efficacy Monitoring Parameters.** HIV viral load, CD4 count, HIV resistance testing.

**Toxicity Monitoring Parameters.** LFTs, bilirubin, CBC, glucose.

**Key Patient Counseling Points.** Take with or without food. May chew or crush the chewable tablet. For the oral suspension, add contents of foil pack (100 mg) to 5 mL water and swirl for 30-60 s. Use oral syringe to obtain correct dose. Administer within 30 min. Does not prevent transmission of HIV; practice safe sex.

**Clinical Pearls.** Not recommended for children <2 y of age. Recommended as a first-line therapy with tenofovir/emtricitabine in antiretroviral naïve patients. Chewable tablet and oral suspension have higher bioavailability than oral tablet; do not interchange these products.

# RAMIPRIL: Altace, Various

**Class:** ACE-I, Antihypertensive

**Dosage Forms.** **Oral Capsule:** 1.25 mg, 2.5 mg, 5 mg, 10 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Heart failure post-MI: 1.25-2.5 mg po bid × 7 d, may titrate to 5 mg po bid
2. Hypertension: 2.5 mg po daily, may titrate to 2.5-20 mg po daily
3. Reduce risk of myocardial infarction, stroke and death from cardiovascular causes: 2.5 mg po bid × 7 d, may titrate as tolerated to 10 mg daily.

**Off-Label Uses.**

1. Diabetic nephropathy, kidney disease: 1.25-10 mg po daily

**MOA.** Ramipril is a competitive ACE-I. It is also a prodrug for the more potent ACE-I ramiprilat. ACE-I prevents conversion of angiotensin I to angiotensin II (a vasoconstrictor). It also reduces serum aldosterone, leading to decreased sodium retention, potentiates the vasodilator kallikrein–kinin system, and inhibits the tissue renin–angiotensin system.

Lupin generic 10 mg pictured



**Drug Characteristics: Ramipril**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 60%, food has no effect on absorption |
| **Dose Adjustment Renal** | CrCl <40 mL/min: use 25% of normal dose | **Distribution** | 73% protein bound |
| **Dialyzable** | Yes | **Metabolism** | Metabolized in liver to active metabolite (ramiprilat) not via CYP |
| **Pregnancy Category** | C (1st trimester), D (2nd and 3rd trimesters) | **Elimination** | Renal elimination is 50-60% with a half-life of 13-17 h (metabolite) |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to ramipril or other ACE-Is, history of ACE-I–induced angioedema | **Black Box Warnings** | Pregnancy |

**Medication Safety Issues: Ramipril**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Capsule | No | Amaryl, enalapril | No |

### Drug Interactions: Ramipril

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Antacids | Binding and decreased absorption | Separate administration by 2 h |
| Potassium-sparing diuretics | Increased risk of hypotension, hyperkalemia | Avoid concurrent use or monitor BP and serum potassium levels |
| Angiotensin receptor blockers | Increased risk of hypotension, hyperkalemia, nephrotoxicity | Avoid concurrent use or monitor BP, SCr, and potassium levels |
| Potassium supplements | Increased risk of hyperkalemia and cardiac arrhythmias | Avoid concurrent use or monitor serum potassium levels |
| NSAIDs | Decreased antihypertensive effect of ramipril, increased risk of nephrotoxicity | Avoid concurrent use or monitor BP and SCr levels |
| Aliskiren | Increased risk of hyperkalemia | Monitor serum potassium levels |
| Azathioprine | Increased risk of myelosuppression | Avoid concurrent use; monitor for anemia or leukopenia |
| Diuretics | Increased risk of postural hypotension due to hypovolemia | Monitor BP; rise from seated position slowly |

### Adverse Reactions: Ramipril

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Diarrhea, dizziness, dry cough, headache, hypotension, hyperkalemia, nausea, nephrotoxicity, rash, tachycardia, vomiting | Angioedema, birth defects, liver failure |

**Efficacy Monitoring Parameters.** BP, progression of heart failure.

**Toxicity Monitoring Parameters.** Angioedema (swelling of the face, eyes, lips, tongue, or throat), persistent dry cough, hypotension; baseline and periodic potassium, SCr, BUN, and urine protein.

**Key Patient Counseling Points.** Avoid pregnancy. Use potassium supplements or salt substitutes only under medical supervision. May cause dizziness that may worsen if dehydrated.

**Clinical Pearls.** Contents of capsule may be mixed with water, apple juice, or apple sauce for administration but do not chew. Dry cough associated with ACE-I is typically a class effect; consider switching to an ARB. Can lead to increases in SCr and $K^+$; recheck electrolytes within 1 wk of initiation.

# RANITIDINE: Zantac, Various

**Class:** Histamine $H_2$ Receptor Antagonist

**Dosage Forms. Oral Tablet:** 75 mg, 150 mg, 300 mg; **Oral Capsule:** 150 mg, 300 mg; **Oral Syrup:** 15 mg/mL; **Oral Suspension:** 22.4 mg/mL

Amneal generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Duodenal ulcer, acute or maintenance, gastric ulcer, acute or maintenance, erosive esophagitis, acute or maintenance: Children 1 mo to 16 y of age, 2-4 mg/kg po bid, *max* of 300 mg/d; Adults, 150 mg po bid or 300 mg po daily hs
2. Indigestion, prevention or treatment: 75-150 mg po bid
3. *H. pylori* GI tract infection, quadruple therapy: 150 mg po bid × 10-14 d in combination with metronidazole 250 mg po qid, bismuth subsalicylate 525 mg po qid, and tetracycline 500 mg po qid

**Off-Label Uses.**

1. Stress ulcer prophylaxis: 150 mg po bid

**MOA.** Ranitidine competitively inhibits histamine $H_2$ receptors and inhibits gastric acid secretion. Both the acid concentration and volume of gastric secretion are suppressed by ranitidine, while changes in pepsin secretion are proportional to volume output.

**Drug Characteristics: Ranitidine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 50%, food has no effect on absorption |
| **Dose Adjustment Renal** | CrCl <50 mL/min, *max* of 150 mg po daily | **Distribution** | Vd = 1.4 L/kg; 15% protein bound |
| **Dialyzable** | Yes | **Metabolism** | Minor hepatic, not via CYP |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 30-70% with a half-life of 2-3 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to ranitidine or other $H_2$ antagonists | **Black Box Warnings** | None |

### Medication Safety Issues: Ranitidine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| FusePaq, Maximum strength | No | No | No | Xanax, Zofran, Zyrtec | No |

### Drug Interactions: Ranitidine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| pH-dependent drugs | Lower gastric pH reduces absorption | Separate administration by 12 h or use alternative agents |

### Adverse Reactions: Ranitidine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Constipation, diarrhea, nausea | Skin rash | Stevens-Johnson syndrome, increased liver enzymes, acute interstitial nephritis |

**Efficacy Monitoring Parameters.** Resolution of GERD symptoms, resolution of peptic ulcers, gastric pH (if indicated).

**Toxicity Monitoring Parameters.** SCr, AST, ALT

**Key Patient Counseling Points.** Advise patients to take at bedtime. Patients may take with food or antacids, if needed.

**Clinical Pearls.** This and other PPI and $H_2$ antagonists available OTC; warn patients not to take multiple products concurrently to avoid additive risk of adverse effects. Injectable dosage form also available; when the intravenous route is used, treatment should be converted to oral route as soon as possible to avoid cost and risks associated with intravenous therapy. If taking as needed to prevent heartburn, take 30-60 min before problem foods.

# RANOLAZINE: Ranexa

**Class:** Antianginal agent

**Dosage Forms.** **Oral Tablet, Extended Release:** 500 mg, 1000 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Chronic angina: Initial, 500 mg po bid, may titrate to *max* dose 1000 mg po bid

**Off-Label Uses.** None

**MOA.** Ranolazine inhibits the late phase of the inward sodium channel during cardiac repolarization reducing intracellular sodium concentrations and thereby reducing calcium influx via $Na^{+}$-$Ca^{2+}$ exchange that in turn reduces ventricular tension and myocardial oxygen consumption.



## Drug Characteristics: Ranolazine

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Avoid if severe hepatic dysfunction | **Absorption** | F = 76%, food has no effect on absorption |
| **Dose Adjustment Renal** | Avoid if acute renal failure | **Distribution** | 62% protein bound |
| **Dialyzable** | Unknown | **Metabolism** | Hepatic, CYP3A4/5 substrate, P-glycoprotein substrate |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 75% with a half-life of 7 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hepatic cirrhosis, strong CYP3A4 inducers or inhibitors | **Black Box Warnings** | None |

## Medication Safety Issues: Ranolazine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Do not chew, crush, or break | No | CeleXA | No |

### Drug Interactions: Ranolazine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inducers | Increased ranolazine metabolism reduces ranolazine effectiveness | Strong inducers contraindicated. Moderate or weak inducers; monitor and consider dose increase of ranolazine |
| CYP3A4/5 inhibitors | Decreased ranolazine metabolism increases risk ranolazine toxicity | Strong inhibitors contraindicated. *Max* dose is 500 mg bid if concurrent strong inhibitors |
| P-glycoprotein inducers | Increased ranolazine transport reduces ranolazine effectiveness | Monitor and consider dose increase of ranolazine |
| P-glycoprotein inhibitors | Decreased ranolazine transport increases risk ranolazine toxicity | Contraindicated |
| Agents that prolong the QTc interval | Additive QTc prolongation | Use with caution in combination with other agents that may prolong QTc or in congenital long QT syndrome |

### Adverse Reactions: Ranolazine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Dizziness, headache, bradycardia, hypotension, edema, constipation, nausea, xerostomia, blurred vision | Angioedema, pancytopenia, pulmonary fibrosis, arrhythmia, renal failure, syncope, QTc prolongation |

**Efficacy Monitoring Parameters.** Improvement in angina symptoms, improved exercise tolerance.

**Toxicity Monitoring Parameters.** Baseline and follow-up ECG to evaluate QTc if concerns for prolongation, monitor BP and renal function at baseline and periodically.

**Key Patient Counseling Points.** Do not crush or chew, but may be taken with or without meals. There are multiple significant drug interactions so talk to pharmacist or physician before starting any new medications or herbal supplements. Ranolazine will not stop an acute angina episode.

**Clinical Pearls.** May be used in combination with beta-blockers or alone in patients who do not respond to or tolerate beta-blockers.

# REPAGLINIDE: Prandin

**Class:** Meglitinide, Antidiabetic

**Dosage Forms. Oral Tablet:** 0.5 mg, 1 mg, 2 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Diabetes mellitus, type 2: 0.5-4 mg po bid-qid (with meal), may titrate to 16 mg po daily

**Off-Label Uses.** None

**MOA.** Repaglinide is a meglitinide agent that stimulates insulin release from the pancreas via inhibition of adenosine triphosphate (ATP)-potassium channels on the beta-cell membrane and potassium efflux. The resulting depolarization and calcium influx induces insulin secretion.

Novo Nordisk 2 mg pictured

**Drug Characteristics: Repaglinide**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 56%, food has no effect on absorption |
| **Dose Adjustment Renal** | CrCl 20-40 mL/min: initial dose of 0.5 mg po daily and titrate carefully | **Distribution** | Vd = 24-31 L; 98% protein bound |
| **Dialyzable** | Unknown | **Metabolism** | Hepatic substrate of CYP3A4/5, 2C8 |
| **Pregnancy Category** | C | **Elimination** | Fecal elimination is 90% with a half-life of 1 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to repaglinide, diabetic ketoacidosis, type 1 diabetes, concurrent gemfibrozil | **Black Box Warnings** | None |

**Medication Safety Issues: Repaglinide**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | Yes | Avandia | No |

### Drug Interactions: Repaglinide

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Beta-blockers, SSRIs, NSAIDs, MAOI | Altered glucose metabolism and increased risk of hypoglycemia | Monitor carefully and manage as appropriate |
| CYP2C8, CYP3A4/5 inducers | Increased repaglinide metabolism reduces repaglinide effectiveness | Monitor and consider dose increases of repaglinide |
| CYP2C8, CYP3A4/5 inhibitors | Decreased repaglinide metabolism increases risk of repaglinide toxicity | Monitor and consider dose decreases of repaglinide |

### Adverse Reactions: Repaglinide

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Hypoglycemia, headache | Arthralgia nasopharyngitis, nausea, diarrhea, chest pain | Angina, hypertension, arrhythmia, thrombocytopenia, hypersensitivity, hepatotoxicity, Stevens-Johnson syndrome |

**Efficacy Monitoring Parameters.** Preprandial blood glucose between 70 and 130 mg/dL, $HbC_{1c}$ <7%.

**Toxicity Monitoring Parameters.** Hypoglycemia (symptoms include nausea, sweating, loss of consciousness, mental status changes, nervousness, headache, shaking, and seizures). Monitor BP, HR, CBC, and LFT.

**Key Patient Counseling Points.** Monitor blood glucose in frequent intervals (2-4 times/d). Take 15-30 min before each meal, up to 4 times/day. Do not take if skipping a meal. Add a dose if eating an extra meal. Counsel on recognition and treatment of hypoglycemia. Encourage healthy lifestyle choices to improve glucose control.

**Clinical Pearls.** Compared with sulfonylureas, repaglinide has a quicker onset and shorter duration of action, resulting in a lower risk of prolonged hypoglycemia. No studies evaluate use in children; avoid. Repaglinide is usually considered a third-line therapy for type 2 diabetes, but could be first-line therapy in patients with contraindications to metformin (impaired renal function) or intolerance to sulfonylureas. Also available as combination tablet with metformin. Use caution in combination with beta-blockers, which can mask hypoglycemia.

# RISEDRONATE: Actonel, Atelvia

**Class:** Bisphosphonate

**Dosage Forms.** **Oral Tablet:** 5 mg, 30 mg, 35 mg, 150 mg; **Oral Tablet, Delayed Release:** 35 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Postmenopausal osteoporosis: Delayed release, 35 mg po once weekly immediately following breakfast; immediate release, 5 mg po daily, 35 mg po once weekly, or 150 mg po once a month; all with supplemental calcium and vitamin D
2. Paget disease: Immediate release, 30 mg po daily for 2 mo
3. Osteoporosis (glucocorticoid induced) prevention and treatment: Immediate release, 5 mg po daily
4. Osteoporosis (male): Immediate release, 35 mg po once weekly

**Off-Label Uses.** None

**MOA.** Risedronate binds to bone hydroxyapatite and inhibits osteoclast activity at the cellular level, thereby modulating bone metabolism.

Procter & Gamble
35 mg pictured

R

**Drug Characteristics: Risedronate**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F <1%, food impairs absorption, take 30-60 min prior to meal |
| **Dose Adjustment Renal** | CrCl <30 mL/min, avoid | **Distribution** | Vd = 13.8 L; 24% protein bound |
| **Dialyzable** | Unknown | **Metabolism** | Not metabolized |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 50% with a half-life of 561 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Known hypersensitivity to risedronate, esophageal abnormalities that delay esophageal emptying, hypocalcemia, inability to sit or stand upright for at least 30 min | **Black Box Warnings** | None |

## Medication Safety Issues: Risedronate

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Do not chew or crush either formulation | No | Alendronate, Actos | No |

## Drug Interactions: Risedronate

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Aluminum, calcium-containing products | Decreased bisphosphonate absorption | Separate administration by 1-2 h |
| $H_2$-blockers and PPIs | Decreased bisphosphonate absorption | Separate administration by 12 h, avoid XR formulation |

## Adverse Reactions: Risedronate

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Rash, abdominal pain, constipation, diarrhea, nausea, indigestion, backache, UTI | Asthenia, flu-like illness, edema, arrhythmias, nephrolithiasis, myalgia, bone pain | Osteonecrosis of the jaw, hypersensitivity reaction |

**Efficacy Monitoring Parameters.** Increased BMD, decreased incidence of fractures, normalization of alkaline phosphatase (Paget's).

**Toxicity Monitoring Parameters.** Baseline SCr, calcium. Severe skin rash, chest pain, difficulty in swallowing, swelling, tooth problems, pain with urination, severe pain.

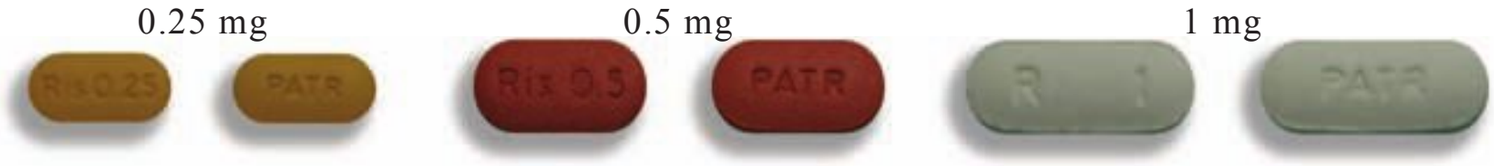
**Key Patient Counseling Points.** Take as soon as you get out of bed in the morning, before you eat or have anything to drink. Swallow tablet whole with 240 mL of plain water only (not mineral water, coffee, juice, or any other liquid). Do not chew tablet. Do not take the medicine while you are still in bed, and do not take it at bedtime. Wait at least 30 min after you swallow the tablet before you eat or drink anything or take any other medicines. Do not lie down for at least 30 min after taking this medicine, and do not lie down until after you have eaten some food.

**Clinical Pearls.** Concurrent chemotherapy and poor oral hygiene increase the risk for osteonecrosis of the jaw. Atypical fractures of the thigh (subtrochanteric and diaphyseal femur fractures) have been reported in patients taking bisphosphonates for osteoporosis; discontinue therapy in patients who develop evidence of a femoral shaft fracture. Atelvia is the brand name of the extended-release product. Medication guide required at dispensing.

# RISPERIDONE: Risperdal, Various

**Class:** Benzisoxazole, Antipsychotic

**Dosage Forms. Oral Tablet:** 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg; **Oral Dispersible Tablet:** 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg; **Oral Solution:** 1 mg/mL




## Common FDA Label Indication, Dosing, and Titration.

1. Autistic disorder, irritability: Children ≥5 y of age and weighing <20 kg, 0.25 mg po daily, titrate to response; Children ≥5 y of age and weighing >20 kg, 0.5 mg po daily, titrate to response
2. Bipolar I disorder: Adults, 2-3 mg po daily, may titrate to 6 mg/d; Children ≥10 y of age, 0.5 mg po daily, may titrate to 2.5 mg/d
3. Schizophrenia: Adults, 1 mg po bid, may titrate to 18 mg/d; Children ≥13 y of age, 0.5 mg po daily, may titrate to 3 mg/d

## Off-Label Uses.

1. Posttraumatic stress disorder: 0.5-8 mg po once daily
2. Tourette syndrome: 0.25-0.5 mg po daily, may titrate to *max* dose of 6mg po daily
3. Pervasive developmental disorder: Children ≥5 y of age, 0.01 mg/kg/dose po daily, may titrate to 0.06 mg/kg/d

**MOA.** Risperidone is a potent serotonin-5-$HT_2$ antagonist with weaker dopamine-$D_2$ antagonism. Whereas typical antipsychotics are dopamine antagonists, the additional serotonin antagonism increases efficacy for negative symptoms of schizophrenia and reduces the likelihood of extrapyramidal symptoms.

## Drug Characteristics: Risperidone

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Severe hepatic impairment, initiate at 0.5 mg po bid, titrate slowly | **Absorption** | F = 70%, food has no effect on absorption |
| **Dose Adjustment Renal** | Severe renal impairment, initiate at 0.5 mg po bid, titrate slowly | **Distribution** | Vd = 1-2 L/kg; 90% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, substrate of CYP2D6, to active metabolite (9-hydroxyrisperidone), P-glycoprotein substrate |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 70% with a half-life of 3-20 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | CYP2D6 poor metabolizers have higher risperidone and lower metabolite levels; limited clinical implication as both parent and metabolite are active |
| **Contraindications** | Hypersensitivity to risperidone, agents that increase QT interval | **Black Box Warnings** | Mortality in elderly with dementia |

## Medication Safety Issues: Risperidone

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| Consta, M-Tab | RisperiDONE, RisperDAL | Dispersible tablet | No | Reserpine, rOPINIRole | Avoid use for behavioral problems of dementia unless nonpharmacologic options have failed and patient is threat to self or others |

## Drug Interactions: Risperidone

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP2D6, P-glycoprotein inhibitors | Decreased risperidone metabolism increases risk of risperidone toxicity | Monitor and consider dose decreases of risperidone; *max* dose 8 mg/d in combination w/fluoxetine or paroxetine |
| P-glycoprotein inducers | Increased risperidone excretion reduces risperidone effectiveness | Monitor and consider dose increases of risperidone |
| Agents that increase QT interval | Increased risk of QT prolongation (torsades de pointes, cardiac arrest) | Use with caution in combination with other agents that may prolong QTc; avoid in congenital long QT syndrome |
| Valproic acid | Increased valproic acid concentrations | Monitor for adverse effects, monitor valproic acid serum levels, adjust dose as needed |
| Anticholinergics | Additive anticholinergic activity | Avoid combination |

## Adverse Reactions: Risperidone

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Extrapyramidal symptoms, insomnia, anxiety, fatigue, metabolic changes (hyperglycemia, dyslipidemia, weight gain, DM) | Abdominal pain, akathisia, GI symptoms (constipation, N/V, diarrhea, dyspepsia), cough, dizziness, hyperprolactinemia, orthostatic hypotension, edema, rash, rhinitis, tachycardia, tremor, xerostomia, dysphagia | Neuroleptic malignant syndrome, pancreatitis, stroke, pancytopenia, sudden cardiac death, syncope, tardive dyskinesia, priapism |

**Efficacy Monitoring Parameters.** Improvement in signs and symptoms of schizophrenia, manic or mixed episodes associated with bipolar disorder, depression.

**Toxicity Monitoring Parameters.** BP (including orthostatics), FPG, A1C in diabetic patients, lipid panel, weight, BMI, abdominal circumference, CBC w/differential, symptoms of tardive dyskinesia; closely supervise patients at high risk for suicide.

**Key Patient Counseling Points.** Take with food. Avoid alcohol or other CNS depressants. Avoid activities requiring mental alertness or coordination until drug effects are known. Use caution during activities leading to an increased core temperature. Rise slowly from a sitting/supine position. Report signs/symptoms of hyperglycemia, arrhythmia, tardive dyskinesia, or neuroleptic malignant syndrome. Keep dispersible tablet in blister pack until use. Place on tongue and swallow after dissolved. Oral solution may be mixed with water, coffee, orange juice, or low fat milk, but should not be mixed with cola or tea.

**Clinical Pearls.** Monitor closely for tardive dyskinesia; tics may become permanent if not treated appropriately. Increases risk of death in elderly patients with dementia-related psychosis. If initiating Risperdal CONSTA (IM injection Q2 wk), continue oral antipsychotic for 3 wk after 1st injection, then discontinue.

# RIVAROXABAN: Xarelto

**Class:** Anticoagulant, Factor Xa inhibitor

**Dosage Forms. Oral Tablet:** 10 mg, 15 mg, 20 mg

Janssen 20 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Prevention of thromboembolism in patients after orthopedic surgery: 10 mg po daily beginning at least 6 h after surgery × 12-14 d for knee replacement or 35 d for hip replacement; if CrCl 30-50 mL/min no dose adjustment, use with caution; do not use if CrCl <30 mL/min
2. Prevention of thromboembolism in patients with nonvalvular atrial fibrillation: 20 mg po daily if CrCl >50 mL/min; 15 mg po daily if CrCl 15-50 mL/min; do not use if CrCl <15 mL/min
3. Treatment and secondary prevention of DVT or pulmonary embolism: 15 mg po bid × 21 d, then 20 mg po daily; do not use if CrCl <30 mL/min

**Off-Label Uses.** None

**MOA.** Rivaroxaban is an orally bioavailable factor Xa inhibitor that selectively blocks the active site of factor Xa and does not require a cofactor (such as anti-thrombin III) for activity. Activation of factor X to factor Xa via the intrinsic and extrinsic pathways plays a central role in the cascade of blood coagulation.

**Drug Characteristics: Rivaroxaban**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Avoid use in moderate to severe dysfunction | **Absorption** | F = 66-100%; food increases extent of absorption at higher doses |
| **Dose Adjustment Renal** | Dose adjustments based on indication, see above | **Distribution** | Vd = 50 L; 95% albumin bound |
| **Dialyzable** | Use in ESRD should be avoided; hemodialysis removes 60% of drug in 2-3 h | **Metabolism** | Hepatic, CYP3A4/5 substrate |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 66% with a half-life of 5-9 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Active bleeding | **Black Box Warnings** | Premature discontinuation increases thrombotic risk, risk of spinal/epidural hematoma |

### Medication Safety Issues: Rivaroxaban

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| Starter Pack | No | No | Yes | No | No |

### Drug Interactions: Rivaroxaban

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inducers | Increased rivaroxaban metabolism reduces rivaroxaban effectiveness | Avoid strong CYP3A/5 inducers. Monitor carefully for clotting |
| CYP3A4/5 inhibitors | Decreased rivaroxaban metabolism increases risk of rivaroxaban toxicity | Avoid strong CYP3A4/5 inhibitors. Monitor carefully for bleeding |
| Antiplatelet agents, NSAIDs, and anticoagulants | Additive risk of bleeding | Avoid concurrent use if possible or monitor carefully for bleeding |

### Adverse Reactions: Rivaroxaban

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Bleeding | Peripheral edema, dizziness, headache, fatigue, bruising, pruritus, rash, nausea, vomiting | Syncope, major bleeding, epidural hematoma, anaphylaxis, intracranial bleeding |

**Efficacy Monitoring Parameters.** Prevention of clotting or recurrence of clotting. Routine monitoring of anticoagulation tests is not necessary with rivaroxaban. If used, anti-Xa activity is the preferred test.

**Toxicity Monitoring Parameters.** Monitor for signs and symptoms of bleeding. Monitor renal function for potential dose adjustment. Monitor CBC, vital signs.

**Key Patient Counseling Points.** Administer with the evening meal. Educate patient on signs and symptoms of bleeding and interactions with other anticoagulant or antiplatelet medications, including OTC medications. Warn of risks of epidural (spinal) anesthesia while taking rivaroxaban.

**Clinical Pearls.** Detailed dosing conversion protocols to convert patients from warfarin or parenteral anticoagulants to rivaroxaban are available in the product package insert. Many drug-drug interactions; monitor concurrent drug use carefully. Tablets may be crushed and mixed with apple sauce immediately prior to administration; may mix with water for NG tube administration.

# ROPINIROLE: Requip, Requip XL, Various

**Class:** Dopamine Agonist

**Dosage Forms.** **Oral Tablet:** 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg, 5 mg; **Oral Tablet, Extended Release:** 2 mg, 4 mg, 6 mg, 8 mg, 12 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Parkinson disease: Immediate release, 0.25 mg po tid × 1 wk, then 0.5 mg po tid × 1 wk, then 0.75 mg po tid × 1 wk, then 1 mg po tid, then may titrate to 24 mg/d; extended release, 2 mg po daily × 1-2 wk, then may titrate to 24 mg/d
2. Restless legs syndrome: Immediate release only, 0.25 mg po daily hs × 2 d, then 0.5 mg po daily hs × 5 d, then 1 mg po daily × 1 wk, then 1.5 mg po daily hs for 1 wk, then 2 mg po daily hs, then may titrate to 4 mg po daily hs

**Off-Label Uses.** None

**MOA.** Ropinirole is a nonergoline dopamine agonist that has a higher specificity to $D_3$ than to $D_2$ and $D_4$ subtypes of dopamine receptors. The drug has a moderate affinity for opioid receptors and has insignificant effects on $D_1$, 5-hydroxytryptamine 1 (5-$HT_1$), 5-$HT_2$, benzodiazepine, GABA, muscarinic, $\alpha_1$-, $\alpha_2$-, and β-adrenoreceptors. It is suggested that ropinirole stimulates the postsynaptic $D_2$-type receptor found in the brain's caudate putamen in Parkinson disease.

0.25 mg

0.5 mg

1 mg

3 mg

Core Pharma generic pictured



## Drug Characteristics: Ropinirole

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Use with caution | **Absorption** | F = 45-55%, food increases Tmax and Cmax |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 7.5 L/kg; 40% protein bound |
| **Dialyzable** | Unknown | **Metabolism** | Hepatic, CYP1A2 substrate |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is >80% with a half-life of 6 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to ropinirole | **Black Box Warnings** | None |

## Medication Safety Issues: Ropinirole

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| XL | rOPINIRole | Extended-release tablets | No | RisperDAL, risperiDONE | No |

### Drug Interactions: Ropinirole

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP1A2 inducers | Increased ropinirole metabolism reduces ropinirole effectiveness | Monitor and consider dose increases of ropinirole |
| CYP1A2 inhibitors | Decreased ropinirole metabolism increases risk of ropinirole toxicity | Monitor and consider dose decreases of ropinirole |
| Antipsychotics | May decrease effectiveness of antipsychotics and/or dopamine agonists | Avoid concurrent use, or monitor both agents and consider dose adjustments to one or both |

### Adverse Reactions: Ropinirole

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Dizziness, dyskinesia, nausea, orthostatic hypotension, somnolence, vomiting, hallucinations | Abdominal pain, abnormal vision, constipation, edema, fatigue, headache, increased HR, sleep attack, syncope, vomiting | Sinus node dysfunction |

**Efficacy Monitoring Parameters.** Reduction in extrapyramidal movements, rigidity, tremor, gait disturbances; decrease in desire to move limbs.

**Toxicity Monitoring Parameters.** Signs/symptoms of postural hypotension, BP, CNS depression/somnolence, decreased HR, periodic dermatologic screening.

**Key Patient Counseling Points.** Take with food to reduce nausea. Avoid driving and other activities requiring mental alertness or coordination until drug effects are realized. Rise slowly from sitting/lying-down position. Report new onset or exacerbation of dyskinesia, changes in BP, fainting, or unusual urges. Avoid sudden discontinuation of drug. Do not drink alcohol or take other CNS depressants while using this drug.

**Clinical Pearls.** May switch directly from immediate-release ropinirole to extended-release; start an extended-release dose that matches most closely with the total daily immediate-release dose.

# ROSIGLITAZONE: Avandia

**Class:** Thiazolidinedione Antidiabetic

**Dosage Forms. Oral Tablet:** 2 mg, 4 mg, 8 mg

Glaxo SmithKline 4 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Diabetes mellitus: 4 mg po daily or 2 mg po bid; may titrate to *max* of 8 mg daily as monotherapy or in combination with a sulfonylurea, or metformin

**Off-Label Uses.** None

**MOA.** Rosiglitazone is a thiazolidinedione antihyperglycemic and a potent peroxisome proliferator-activated receptor-gamma (PPAR [γ]) agonist used to improve insulin sensitivity in patients with type 2 diabetes. Insulin-dependent glucose disposal in skeletal muscle is improved and hepatic glucose production is decreased; both actions contribute to rosiglitazone's glucose-lowering effects.

R

**Drug Characteristics: Rosiglitazone**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Avoid in active liver disease or if LFT elevated | **Absorption** | F = 99%, food has no effect on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 17.6 L; 99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, CYP2C8 substrate, moderate inhibitor of CYP2C8 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 64% with a half-life of 3-4 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to rosiglitazone, heart failure, NYHA class III or IV | **Black Box Warnings** | Heart failure, MI risk |

**Medication Safety Issues: Rosiglitazone**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | Yes | Avalide | No |

### Drug Interactions: Rosiglitazone

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP2C8 inducers | Increased rosiglitazone metabolism reduces rosiglitazone effectiveness | Monitor and consider dose increases of rosiglitazone |
| CYP2C8 inhibitors | Decreased rosiglitazone metabolism increases risk of rosiglitazone toxicity | Monitor and consider dose decreases of rosiglitazone |
| CYP2C8 substrates | Decreased substrate metabolism may result in substrate toxicity | Monitor and consider decreasing dose of substrate |
| Psyllium | Psyllium may delay absorption of glucose from meals, leading to less postprandial hyperglycemia and potentially allowing a reduced dosage of the antidiabetic agent | Avoid concurrent use if possible; monitor and consider dose adjustments |
| Corticosteroids | May diminish or increase hypoglycemic effect of rosiglitazone | Monitor and consider rosiglitazone dose adjustment |
| NSAIDs, SSRIs | Altered glucose metabolism and increased risk of hypoglycemia and hyperglycemia | Avoid concurrent use if possible; monitor and consider dose adjustments |
| MAOIs | Stimulation of insulin secretion, hypoglycemic effects | Avoid concurrent use if possible; monitor and consider dose adjustments |

### Adverse Reactions: Rosiglitazone

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Edema, weight gain, increased cholesterol | Myalgia, bone fractures, sinusitis, headache | Heart failure, MI, anemia, hepatotoxicity, diabetic macular edema, hypoglycemia when used in combination with insulin or sulfonylureas |

**Efficacy Monitoring Parameters.** Pre-prandial blood glucose between 70 and 130 mg/dL, $HbA_{1c}$ <7%.

**Toxicity Monitoring Parameters.** Weight for assessment of edema, Hgb, LFTs; symptoms of hypoglycemia include nausea, sweating, and loss of consciousness; seek care for bone pain, yellowing of skin or eyes, eye pain, or shortness of breath. Eye exam.

**Key Patient Counseling Points.** Monitor blood glucose in frequent intervals (2-4 times/d). May take without regard to food. May require several weeks for max effect.

**Clinical Pearls.** Causes edema, which may exacerbate underlying heart failure, use with caution. Premenopausal anovalatory individuals may resume ovulation. Not for use in children. Thiazolidinediones are as effective as metformin, but have greater risk of adverse effects, so used as second line (both as monotherapy and in combination). Rosiglitazone has more CV effects than pioglitazone, so pioglitazone is preferred in this class. Released from REMS program in May 2014.

# ROSUVASTATIN: Crestor

**Class:** HMG-CoA Reductase Inhibitor

**Dosage Forms. Oral Tablet:** 5 mg, 10 mg, 20 mg, 40 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Hyperlipidemia: Adults, 10-20 mg po daily, may titrate to 40 mg po daily; Children 10-17 y of age, 5-20 mg po daily, may titrate to 20 mg po daily
2. Disorder of cardiovascular system, primary prophylaxis, familial hypercholesterolemia, homozygous, hypertriglyceridemia, mixed lipidemia: 10-20 mg po daily, may titrate to 40 mg po daily

**Off-Label Uses.** None

**MOA.** HMG-CoA reductase inhibitors competitively inhibit conversion of HMG-CoA to mevalonate, an early rate-limiting step in cholesterol synthesis. A compensatory increase in LDL receptors, which bind and remove circulating LDL-cholesterol, results. Production of LDL-cholesterol can also decrease because of decreased production of VLDL-cholesterol or increased VLDL removal by LDL receptors.

**Drug Characteristics: Rosuvastatin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Use with caution; contraindicated in active liver disease or unexplained increased LFTs | **Absorption** | F = 20%, food slows absorption |
| **Dose Adjustment Renal** | CrCl <30 mL/min, initial dose 5 mg po daily, may titrate to 10 mg po daily | **Distribution** | Vd = 134 L; 88% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Minimal hepatic |
| **Pregnancy Category** | X | **Elimination** | Fecal elimination is 90% with a half-life of 13-20 h |
| **Lactation** | Contraindicated | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to rosuvastatin, active liver disease, pregnancy or lactation | **Black Box Warnings** | None |

40 mg

20 mg

10 mg

5 mg

AstraZeneca pictured

R

### Medication Safety Issues: Rosuvastatin

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | atorvaSTATin | No |

### Drug Interactions: Rosuvastatin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Antacids | Decreased absorption of rosuvastatin | Separate coadministration by 2 h |
| Bile acid-binding resins | Decreased absorption of rosuvastatin | Give rosuvastatin 1 h before or 4 h after resin |
| Amiodarone, azole antifungals, protease inhibitors, fibrates, niacin, cyclosporine | Increased risk of myopathy or rhabdomyolysis | Avoid concurrent use, or monitor for myopathy and measure creatine kinase levels |
| Warfarin | Increased risk of bleeding | Monitor INR with addition or withdrawal of rosuvastatin |

### Adverse Reactions: Rosuvastatin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Arthralgia | Abdominal pain, asthenia, constipation, diarrhea, indigestion, headache, increased liver enzymes, influenza-like symptoms, myalgia, nasopharyngitis, nausea, pharyngitis, rhinitis | Rhabdomyolysis, tendon rupture |

**Efficacy Monitoring Parameters.** Total cholesterol, LDL-cholesterol, and triglycerides levels; HDL-cholesterol levels.

**Toxicity Monitoring Parameters.** Signs/symptoms of rhabdomyolysis (myalgias, dark urine, arthralgias, fatigue) or hepatotoxicity; LFTs should be performed at baseline, 12 wk after initiation of therapy, and every 6 mo thereafter; serum creatine kinase should be measured in patients experiencing muscle pain and in those receiving other drugs associated with myopathy.

**Key Patient Counseling Points.** Contact prescriber immediately if pregnancy occurs while taking rosuvastatin. Do not drink alcohol. Rosuvastatin does not take the place of diet and exercise to lower cholesterol levels.

**Clinical Pearls.** Lipid-level assessment should be done within 4 wk following dose initiation or titration. Consider holding rosuvastatin 4-7 d before major surgery as patient is at higher risk for occurrence of rhabdomyolysis. May increase risk of diabetes.

# ROTAVIRUS VACCINE, LIVE: Rotarix, RotaTeq

Merck pictured



**Class:** Vaccine, Live, Viral

**Dosage Forms. Suspension for Oral Administration:** Monovalent attenuated human rotavirus vaccine (Rotarix), pentavalent attenuated bovine rotavirus vaccine (RotaTeq)

**Common FDA Label Indication, Dosing, and Titration.**

1. Prophylaxis of viral gastroenteritis due to rotavirus infection: One dose po for all infants at 2 and 4 mo of age (Rotarix, 2 doses required), or 2, 4, and 6 mo of age (RotaTeq, 3 doses required); the 1st dose should be administered between 6 and 14 wk of age; do not start the series if infant >14 wk of age; all doses should be administered at least 4 wk apart and before infant reaches 24 wk of age

**Off-Label Uses.** None

**Drug Characteristics: Rotavirus Vaccine, Live**

| | | | |
|---|---|---|---|
| **Pregnancy Category** | C | **ADME** | None known |
| **Lactation** | Infant risk is minimal | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to rotavirus vaccine or a component of the vaccine, severe combined immunodeficiency; Rotarix may contain latex; history of intussusception | **Black Box Warnings** | None |

### Medication Safety Issues: Rotavirus Vaccine, Live

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Rotarix, RotaTeq | No |

### Drug Interactions: Rotavirus Vaccine, Live

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Moderate- to high-dose corticosteroids | Immunosuppression increases risk of infection caused by live virus and decreases vaccine efficacy | Defer or delay rotavirus vaccine administration until corticosteroid therapy has been discontinued |
| Immunosuppressing agents | Immunosuppression increases risk of infection caused by live virus and decreases vaccine efficacy | Defer or delay rotavirus vaccine administration until immunosuppressive therapy has been discontinued |

### Adverse Reactions: Rotavirus Vaccine, Live

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Vomiting, irritability, fever, otitis media | Diarrhea | Intussusception, anaphylaxis, seizures |

**Efficacy Monitoring Parameters.** Prevention of viral gastroenteritis due to rotavirus infection.

**Toxicity Monitoring Parameters.** Fever, number of stools, abdominal pain.

**Key Patient Counseling Points.** Return to provider for each dose in the series. Contact a health-care provider right away if the child has diarrhea, blood in his stool, vomiting, high fever, or abdominal pain as these may be symptoms of intussusception.

**Clinical Pearls.** If the infant fails to swallow or vomits the vaccine dose, do not readminister the dose. Immunized infant may shed virus in stools. Hand washing after diaper changing is always recommended.

# SAXAGLIPTIN: Onglyza

**Class:** Dipeptidyl Peptidase-4 Inhibitor, Antidiabetic

**Dosage Forms.** **Oral Tablet:** 2.5 mg, 5 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Diabetes mellitus: 2.5-5 mg po daily

**Off-Label Uses.** None

**MOA.** Saxagliptin is a dipeptidyl peptidase-4 (DPP-4) enzyme inhibitor that inhibits the degradation of incretin hormones by DPP-4, and enhances the function of GLP-1 and GIP to increase insulin release and decrease glucagon levels in the circulation in a glucose-dependent manner.

**Drug Characteristics: Saxagliptin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 50-75%, food has no effect on absorption |
| **Dose Adjustment Renal** | CrCl ≤50 mL/min, 2.5 mg po daily | **Distribution** | Vd = 2.7 L/kg; negligible protein binding |
| **Dialyzable** | Yes | **Metabolism** | Hepatic via CYP3A4/5 to metabolite with 50% activity of parent compound; substrate of P-glycoprotein |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 60% with a half-life of 2.5 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to saxagliptin | **Black Box Warnings** | None |

**Medication Safety Issues: Saxagliptin**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | Yes | SitaGLIPtin, SUMAtriptan | No |

### Drug Interactions: Saxagliptin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| P-glycoprotein inducers | Increased saxagliptin transport reduces saxagliptin effectiveness | Monitor and consider dose increases of saxagliptin |
| P-glycoprotein inhibitors | Decreased saxagliptin transport increases risk of saxagliptin toxicity | Monitor and consider dose decreases of saxagliptin |
| CYP3A4/5 inducers | Increased saxagliptin metabolism reduces saxagliptin effectiveness | Monitor and consider dose increases of saxagliptin |
| CYP3A4/5 inhibitors | Decreased saxagliptin metabolism increases risk of saxagliptin toxicity | Reduce dose to 2.5 mg daily if concurrent strong CYP3A4/5 inhibitor. Monitor and consider dose decreases of saxagliptin for moderate CYP3A4/5 inhibitor |
| Corticosteroids (orally inhaled, systemic) | May diminish or increase hypoglycemic effect of saxagliptin | Monitor and consider saxagliptin dose adjustment |
| MAOIs | Stimulation of insulin secretion, hypoglycemic effects | Avoid concurrent use if possible; monitor and consider dose adjustments |

### Adverse Reactions: Saxagliptin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Hypoglycemia | Headaches, nasopharyngitis, peripheral edema, nausea, diarrhea | Pancreatitis, hypersensitivity, acute renal failure, Stevens-Johnson syndrome, rhabdomyolysis |

**Efficacy Monitoring Parameters.** Pre-prandial blood glucose between 70 and 130 mg/dL, $HbA_{1c}$ <7%.

**Toxicity Monitoring Parameters.** Monitor renal function and amylase periodically. Seek medical attention if severe skin rash, severe abdominal pain, muscle weakness or pain, or decreased urine production.

**Key Patient Counseling Points.** Monitor blood glucose in frequent intervals (2-4 times/d). Take with morning meal if once-daily dosing. Take with morning and evening meal if twice-a-day dosing.

**Clinical Pearls.** Not for use in children. Metformin is first-line therapy for type 2 diabetes. Saxagliptin may be used as monotherapy in a patient with contraindications to metformin. Also available in combination dosage form with metformin. Incretin mimetics may increase risk of pancreatitis and pancreatic duct metaplasia.

# SERTRALINE: Zoloft, Various

**Class:** SSRI Antidepressant

**Dosage Forms. Oral Tablet:** 25 mg, 50 mg, 100 mg; **Oral Solution, Oral Syrup:** 20 mg/mL

Northstar Rx generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Depression: 50 mg po daily, may titrate to 200 mg/d
2. OCD: Children 6-12 y of age, 25 mg po daily, may titrate to 200 mg/d; Children 13-17 y of age and Adults, 50 mg po daily, may titrate to 200 mg/d
3. Panic disorder, posttraumatic stress disorder, social phobia disorder: 25 mg po daily for 1 wk, then titrate to 50 mg po daily, may titrate to 200 mg/d
4. Premenstrual dysphoric disorder: 50 mg po daily continuously or only during luteal phase; may titrate to 100 mg/d

**Off-Label Uses.**

1. Binge eating disorder: 25 mg po daily after lunch × 3 d, then titrate to 50 mg po daily, may titrate to 200 mg/d
2. Bulimia nervosa: 50 mg po daily for 1 wk, may titrate to 200 mg/d
3. Generalized anxiety disorder: 25 mg po daily for 1 wk, may titrate to 200 mg/d

**MOA.** Sertraline is an SSRI that indirectly results in a downregulation of β-adrenergic receptors. It has no clinically important effect on noradrenergic or histamine receptors and no effect on MAO. It lacks stimulant, cardiovascular, anticholinergic, and convulsant effects.

**Drug Characteristics: Sertraline**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Lower dose or dose less frequently | **Absorption** | F = 100%, food has minimal effect on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 20 L/kg; 99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic via CYP2D6 to 1 active metabolite; CYP2D6 substrate; moderate inhibitor of CYP2B6, 2C19, and 2D6 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 40-45% with a half-life of 24 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to sertraline; concomitant use of pimozide, thioridazine, or MAOIs | **Black Box Warnings** | Suicidality, not approved for depression in children; approved for OCD in children >6 y |

### Medication Safety Issues: Sertraline

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Zocor, selegiline | No |

### Drug Interactions: Sertraline

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP2D6 inhibitors | Decreased sertraline metabolism increases risk of sertraline toxicity | Monitor and consider dose decreases of sertraline |
| CYP2B6, 2C19, 2D6, substrates | Decreased substrate metabolism may result in substrate toxicity | Monitor and consider decreasing dose of substrate |
| Antiplatelet drugs, NSAIDs | Increased risk of bleeding | Monitor for bleeding |
| Triptans, SSRIs, dextroampheta-mine, tramadol, MAOIs, linezolid | Increased risk of serotonin syndrome | Monitor closely for symptoms of serotonin syndrome (rest-lessness, hyperthermia, hyper-ref exia, incoordination) |

### Adverse Reactions: Sertraline

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Diarrhea, fatigue, head-ache, insomnia, nausea | Abdominal pain, anxiety, bleeding, constipation, dizziness, diaphoresis, disor-der of ejaculation, indigestion, loss of appetite, rash, reduced libido, somno-lence, sweating, tremor, vomiting, weight gain, xerostomia | Serotonin syndrome, suicidal thoughts |

**Efficacy Monitoring Parameters.** Improvement in symptoms of depression, panic disorder, OCD.

**Toxicity Monitoring Parameters.** Worsening of depression, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases; signs/symptoms of abnormal bleeding. Monitor CBC.

**Key Patient Counseling Points.** Avoid activities requiring mental alertness or coordination until drug effects are realized. Symptomatic improvement may not be seen for several weeks. Report worsening depression, suicidal ideation, unusual changes in behavior, or unusual bleeding. Avoid abrupt discontinuation; may precipitate withdrawal symptoms. Do not drink alcohol or use NSAIDs or aspirin while taking this drug.

**Clinical Pearls.** If intolerable withdrawal symptoms occur following a decrease in dose or therapy discontinuation, may need to resume the previous dose and taper at a more gradual rate. Oral concentrate must be diluted before administration. Medication guide required at dispensing.

# SILDENAFIL: Viagra, Revatio, Various

**Class:** Erectile Dysfunction Agent, Pulmonary Hypertension Agent

**Dosage Forms. Oral Tablet:** 20 mg, 25 mg, 50 mg, 100 mg; **Oral Suspension:** 10 mg/mL

Pfizer pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Erectile dysfunction: 25-100 mg po prn 1 h prior to anticipated sexual activity
2. Pulmonary hypertension (WHO group I): 5-20 mg po tid

**Off-Label Uses.**

1. Pulmonary hypertension (WHO group II-IV): 5-20 mg po tid

**MOA.** Inhibition of phosphodiesterase type 5 (PDE5) by sildenafil increases the amount of cyclic guanosine monophosphate (GMP) enhancing erectile function and pulmonary vasculature relaxation. Penile erection during sexual stimulation is mediated by the release of nitric oxide (NO) from nerve terminals and endothelial cells, which stimulates the synthesis of cyclic GMP in smooth muscle cells. Cyclic GMP causes smooth muscle relaxation and increased blood flow into the corpus cavernosum and vasodilation in the pulmonary bed.



**Drug Characteristics: Sildenafil**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Avoid use in severe liver disease | **Absorption** | F = 41%, food has minimal effect on absorption |
| **Dose Adjustment Renal** | CrCl <30 mL/min, 25 mg po if used for ED. Not required for pulmonary artery hypertension (PAH) | **Distribution** | Vd = 105 L; 96% protein bound |
| **Dialyzable** | Unknown | **Metabolism** | Hepatic via CYP3A4/5 |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 13% with a half-life of 4 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to phosphodiesterase inhibitors, concurrent nitrates, concurrent HIV protease inhibitors when used for treating pulmonary hypertension | **Black Box Warnings** | None |

### Medication Safety Issues: Sildenafil

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Silodosin, tadalafil | No |

### Drug Interactions: Sildenafil

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inducers | Increased sildenafil metabolism reduces sildenafil effectiveness | Monitor and consider dose increases of sildenafil |
| CYP3A4/5 inhibitors | Decreased sildenafil metabolism increases risk of sildenafil toxicity | Reduce dose to 25 mg if concurrent strong CYP3A4/5 inhibitors |
| α-Adrenergic agents | Additive hypotension | Monitor for hypotension and consider dose reductions |
| Nitrates | Additive hypotension, potentially severe | Contraindicated |
| Protease inhibitors | Increased concentration of sildenafil and increased risk of toxicity | Reduce dose of sildenafil to 25 mg every 48 h if used for ED; concurrent use is contraindicated if used for PAH |

### Adverse Reactions: Sildenafil

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Flushing, nausea, headache, visual disturbances, lack of blue/green color discrimination | Nasopharyngitis, angina, chest pain, hypotension, retinal hemorrhage | Myocardial infarction, seizures, strokes, sudden hearing loss, priapism |

**Efficacy Monitoring Parameters.** Improvement in sexual function, improvement in respiratory status/functional status.

**Toxicity Monitoring Parameters.** Seek medical attention if severe skin rash, chest pain, erection lasting more than 4 h, tinnitus, dizziness, or shortness of breath.

**Key Patient Counseling Points.** Take 60 min prior to anticipated sexual activity, but do not take more frequently than once q24h.

**Clinical Pearls.** The choice between tadalafil, sildenafil, or vardenafil is largely one of patient preference; tadalafil would be indicated in those desiring "full-day coverage." Sexual stimulation is required to initiate the local release of nitric oxide; the inhibition of PDE5 has no effect in the absence of sexual stimulation. Dose-dependent increase in mortality in children using for PAH; use alternative agent if possible. Revatio is brand name for PAH indication.

# SIMVASTATIN: Zocor, Various

**Class:** HMG-CoA Reductase Inhibitor

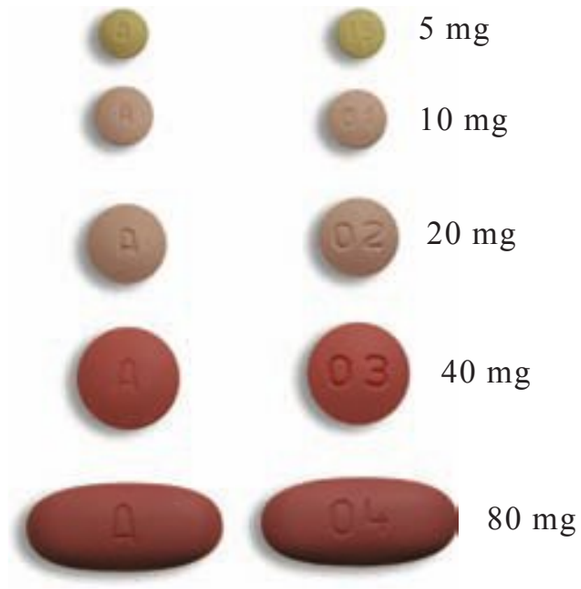
**Dosage Forms. Oral Tablet:** 5 mg, 10 mg, 20 mg, 40 mg, 80 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Hyperlipidemia: 20-40 mg po daily in the evening
2. Primary and secondary preventions of atherosclerotic cardiovascular disease: 20-40 mg po daily in the evening
3. Secondary prevention of cardiovascular events in patients with or at high risk for CAD: 5-40 mg po daily in the evening
4. Familial hypercholesterolemia (homozygous): Children (boys and postmenarchal girls 10-17 y of age), 10 mg po daily, may titrate to 40 mg po daily in the evening; Adults 20-40 mg po daily in the evening

**Off-Label Uses.** None

**MOA.** HMG-CoA reductase inhibitors competitively inhibit conversion of HMG-CoA to mevalonate, an early rate-limiting step in cholesterol synthesis. A compensatory increase in LDL receptors, which bind and remove circulating LDL-cholesterol, results. Production of LDL-cholesterol also can decrease because of decreased production of VLDL-cholesterol or increased VLDL removal by LDL receptors.




Northstar Rx generic pictured



**Drug Characteristics: Simvastatin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Contraindicated in active liver disease | **Absorption** | F <5% |
| **Dose Adjustment Renal** | Severe renal impairment, initiate at 5 mg po daily | **Distribution** | 95% protein bound |
| **Dialyzable** | Unknown | **Metabolism** | Extensive hepatic into 3 active metabolites; CYP3A4/5 substrate |
| **Pregnancy Category** | X | **Elimination** | Fecal elimination is 60% |
| **Lactation** | Contraindicated | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to simvastatin, active liver disease, pregnancy and lactation | **Black Box Warnings** | None |

**Medication Safety Issues: Simvastatin**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Zoloft, ZyrTEC atorvaSTATin | No |

### Drug Interactions: Simvastatin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inducers | Increased simvastatin metabolism reduces simvastatin effectiveness | Monitor and consider dose increases of simvastatin |
| Moderate CYP3A4/5 inhibitors | Decreased simvastatin metabolism increases risk of simvastatin toxicity | With concurrent amiodarone, amlodipine, lomitapide, or ranolazine, *max* dose of simvastatin is 20 mg daily. With concurrent diltiazem, dronedarone or verapamil, *max* dose of simvastatin is 10 mg daily. Monitor and consider dose decreases of simvastatin if used with other inhibitors |
| Strong CYP3A4/5 inhibitors | Decreased simvastatin metabolism increases risk of simvastatin toxicity | Concurrent use contraindicated |
| Fibrates, niacin | Increased risk of myopathy or rhabdomyolysis | Avoid concurrent use, or monitor for myopathy and measure creatine kinase levels |
| Warfarin | Increased risk of bleeding and risk of rhabdomyolysis | Monitor INR with addition or withdrawal of simvastatin; monitor for myopathy and measure creatine kinase levels |

### Adverse Reactions: Simvastatin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Abdominal pain, constipation, diarrhea, headache, increased liver enzymes, myalgia, nausea, rash | Rhabdomyolysis, myopathy, hepatotoxicity, tendon rupture, elevated $HgA_{1c}$, immune-mediated necrotizing myopathy |

**Efficacy Monitoring Parameters.** Reduction in total cholesterol, LDL-cholesterol, and triglycerides levels; increase in HDL-cholesterol levels. Obtain baseline lipid panel, fasting lipid panel 4-12 wk after initiation of therapy and every 3-12 mo thereafter.

**Toxicity Monitoring Parameters.** Obtain baseline LFTs, SCr, and BUN. Repeat LFTs if signs of hepatotoxicity (fatigue, abdominal pain, yellowing of skin or sclera). Consider CPK in patients with symptoms of myopathy (pain cramping, weakness)

**Key Patient Counseling Points.** Contact prescriber immediately if pregnancy occurs. Do not drink alcohol. There are multiple significant drug-drug interactions with simvastatin. Consult a health-care professional prior to starting any new medications, including OTC and herbal drugs. Simvastatin does not take the place of lifestyle changes (diet, exercise) to lower cholesterol levels.

**Clinical Pearls.** May increase fasting blood glucose; however, cardiovascular benefits outweigh the risk of dysglycemia. Myopathy is related to both dose and interacting medications. Simvastatin 80 mg is limited to patients maintained on this dose >12 mo without myopathy or interacting medications. Patients not at LDL goal on 40 mg of simvastatin or requiring high-intensity therapy (eg, LDL >190 mg/dL) should receive alternative therapy.

# SITAGLIPTIN: Januvia

**Class:** Dipeptidyl Peptidase-4 Inhibitor, Antidiabetic

**Dosage Forms. Oral Tablet:** 25 mg, 50 mg, 100 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Diabetes mellitus: 100 mg po daily

**Off-Label Uses.** None

**MOA.** Sitagliptin phosphate is a DPP-4 enzyme inhibitor that inhibits the degradation of incretin hormones by DPP-4, and enhances the function of GLP-1 and GIP to increase insulin release and decrease glucagon levels in the circulation in a glucose-dependent manner.

Merck 100 mg pictured

**Drug Characteristics: Sitagliptin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 87%, food has no effect on absorption |
| **Dose Adjustment Renal** | CrCl 30-50 mL/min, 50 mg po daily; CrCl <30 mL/min, 25 mg po daily | **Distribution** | Vd = 198 L; 38% protein bound |
| **Dialyzable** | Yes | **Metabolism** | Substrate of P-glycoprotein; not metabolized |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 87% with a half-life of 12 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to sitagliptin | **Black Box Warnings** | None |

**Medication Safety Issues: Sitagliptin**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | SitaGLIPtin | No | Yes | Janumet, saxagliptin | No |

### Drug Interactions: Sitagliptin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| P-glycoprotein inducers | Increased sitagliptin transport reduces sitagliptin effectiveness | Monitor and consider dose increases of sitagliptin |
| P-glycoprotein inhibitors | Decreased sitagliptin transport increases risk of sitagliptin toxicity | Monitor and consider dose decreases of sitagliptin |
| Corticosteroids | May diminish or increase hypoglycemic effect of sitagliptin | Monitor and consider sitagliptin dose adjustment |
| MAOIs | Stimulation of insulin secretion, hypoglycemic effects | Avoid concurrent use if possible; monitor and consider dose adjustments |

### Adverse Reactions: Sitagliptin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Hypoglycemia | Headaches, nasopharyngitis, nausea, diarrhea | Pancreatitis, hypersensitivity, acute renal failure, Stevens-Johnson syndrome, rhabdomyolysis |

**Efficacy Monitoring Parameters.** Preprandial blood glucose between 70 and 130 mg/dL, $HbA_{1c}$ <7%.

**Toxicity Monitoring Parameters.** Monitor renal function and amylase periodically. Seek medical attention if severe skin rash, severe abdominal pain, muscle weakness or pain, or decreased urine production.

**Key Patient Counseling Points.** Monitor blood glucose in frequent intervals (2-4 times/d). Take with morning meal if once-daily dosing. Take with morning and evening meal if twice-a-day dosing. When used in combination with insulin or sulfonylureas, risk of hypoglycemia may be increased.

**Clinical Pearls.** Not for use in children. Metformin is first-line therapy for type 2 diabetes. Sitagliptin may be used as monotherapy in a patient with contraindications to metformin. Also available in combination dosage form with metformin. Incretin mimetics may increase risk of pancreatitis and pancreatic duct metaplasia. Medication guide must be dispensed with this product.

# SOLIFENACIN: Vesicare

**Class:** Urinary Antispasmodic; Anticholinergic Agent

**Dosage Forms. Oral Tablet:** 5 mg, 10 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Overactive bladder: 5 mg po daily, may titrate to 10 mg po daily

**Off-Label Uses.** None

**MOA.** Solifenacin is a competitive muscarinic receptor antagonist. Muscarinic receptors play an important role in several major cholinergically mediated functions, including contractions of the urinary bladder smooth muscle and stimulation of salivary secretion.

GlaxoSmithKline 5 mg pictured

**Drug Characteristics: Solifenacin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Moderate hepatic dysfunction, *max* dose of 5 mg po daily; severe hepatic dysfunction, avoid use | **Absorption** | F = 90%, food has no effect on absorption |
| **Dose Adjustment Renal** | CrCl <30 mL/min, *max* 5 mg po daily | **Distribution** | Vd = 600 L; 98% protein bound |
| **Dialyzable** | Unknown | **Metabolism** | Hepatic; CYP3A4/5 substrate |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 70% with a half-life of 45-68 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to solifenacin, gastric retention, uncontrolled glaucoma, urinary retention | **Black Box Warnings** | None |

**Medication Safety Issues: Solifenacin**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | VESIcare | Swallow tablet whole | No | Visicol | No |

### Drug Interactions: Solifenacin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inducers | Increased solifenacin metabolism reduces solifenacin effectiveness | Monitor and consider dose increases of solifenacin |
| CYP3A4/5 inhibitors | Decreased solifenacin metabolism increases risk of solifenacin toxicity | Monitor and consider dose decreases of solifenacin |
| Anticholinergic agents | Additive anticholinergic adverse effects | Avoid concurrent use or monitor carefully for adverse effects |
| Agents that increase QT interval | Increased risk of QT prolongation (torsades de pointes, cardiac arrest) | Avoid concurrent use or monitor carefully |

### Adverse Reactions: Solifenacin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Constipation, xerostomia, blurred vision | Abdominal pain, dizziness, indigestion, urinary retention | Angioedema, QT prolongation, exfoliative dermatitis |

**Efficacy Monitoring Parameters.** Resolution of clinical signs of incontinence and urinary urgency and frequency.

**Toxicity Monitoring Parameters.** Seek medical attention for severe anticholinergic effects (severe dry mouth, cognitive impairment, constipation, vision changes). Monitor vital signs.

**Key Patient Counseling Points.** This drug may cause anticholinergic effects, including constipation, urinary retention, blurred vision, dyspepsia, or xerostomia. Heat prostration (due to decreased sweating) can occur when used in a hot environment and/or exercise.

**Clinical Pearls.** Patients should be advised to exercise caution in driving or other tasks that require alertness until the drug's effects have been determined. May cause decline in cognitive function, especially in the elderly.

# SPIRONOLACTONE: Aldactone, Various

**Class:** Potassium-Sparing Diuretic; Selective Aldosterone Blocker

**Dosage Forms. Oral Tablet:** 25 mg, 50 mg, 100 mg

25 mg

Amneal generic pictured

50 mg

Actavis generic pictured

100 mg

Amneal generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Heart failure, NYHA class III-IV: 12.5-25 mg po daily, may titrate to *max* of 50 mg
2. Edema associated with heart failure: 100 mg po daily in single or divided doses, may titrate to 400 mg/d
3. Nephrotic syndrome: 100 mg po daily in single or divided doses, may titrate to 400 mg/d
4. Hypertension: 50-100 mg po daily in single or divided doses, may titrate to 400 mg/d
5. Hypokalemia: 25-100 mg po daily

**Off-Label Uses.**

1. Ascites, cirrhosis of liver: 100 mg po daily in single or divided doses, may titrate to 400 mg/d
2. Acne vulgaris: 50-200 mg po daily
3. Hirsutism: 50-200 mg po daily for 20 d/mo

**MOA.** Spironolactone is a steroidal competitive aldosterone antagonist that acts from the interstitial side of the distal and collecting tubular epithelium to block sodium-potassium exchange, producing a delayed and mild diuresis. The diuretic effect is maximal in states of hyperaldosteronism. Excretion of sodium and chloride excretion is increased; excretion of potassium and magnesium is decreased. Spironolactone has mild antihypertensive activity and has demonstrated a beneficial effect in NYHA class III and IV heart failure.

**Drug Characteristics: Spironolactone**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Alternate-day dosing may be considered | **Absorption** | F = 73%, food increases absorption |
| **Dose Adjustment Renal** | CrCl <30 mL/min, not recommended | **Distribution** | 90% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic to active metabolites |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 47-57% with a half-life of 1.4 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to spironolactone, anuria, acute renal insufficiency, hyperkalemia | **Black Box Warnings** | Tumorigenic in animal models |

### Medication Safety Issues: Spironolactone

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Aldactazide | Avoid >25 mg/d in patients with heart failure or with a CrCl <30 mL/min |

### Drug Interactions: Spironolactone

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Potassium-sparing diuretics | Increased risk of hypotension, hyperkalemia | Avoid concurrent use or monitor BP and serum potassium levels |
| ACE-Is, angiotensin receptor antagonists | Increased risk of hypotension, hyperkalemia, nephrotoxicity | Avoid concurrent use or monitor BP, SCr, and potassium levels |
| Eplerenone, potassium supplements, salt substitutes | Increased risk of hyperkalemia | Avoid concurrent use or monitor serum potassium levels |
| NSAIDs | Decreased antihypertensive effect of spironolactone, increased risk of hyperkalemia | Avoid concurrent use or monitor BP and potassium levels |
| Digoxin, sotalol | Increased risk of proarrhythmic effects | Monitor ECG and serum potassium and magnesium levels |

### Adverse Reactions: Spironolactone

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Breast tenderness, diarrhea, disorder of menstruation, gastritis, gynecomastia, headache, hyperkalemia, hyponatremia, impotence, lethargy, nausea, rash, stomach cramps, vomiting, urticaria | Cardiac arrhythmias, gastric hemorrhage |

**Efficacy Monitoring Parameters.** Decreased BP, reduction in edema, weight.

**Toxicity Monitoring Parameters.** Monitor SCr, potassium levels, ECG if symptoms of hyperkalemia occur.

**Key Patient Counseling Points.** May cause dizziness. Avoid driving, using machinery, or doing anything else that could be dangerous if not alert. Report signs/symptoms of hyperkalemia (muscle weakness, fatigue, bradycardia) and hyponatremia (confusion, dry mouth, thirst, weakness, hypotension, decreased urination). Avoid potassium supplements, foods/salt substitutes that are high in potassium. Avoid alcohol and NSAIDs.

**Clinical Pearls.** Reduce dose when used in combination with other diuretics. May use loading dose of 2-3 times the daily dose on first day for faster diuresis. Tablets smell like peppermint . . . no kidding.

# SUMATRIPTAN: Imitrex, Various

Dr. Reddy's generic 100 mg pictured

**Class:** Antimigraine Serotonin Receptor Agonist

**Dosage Forms.** **Oral Tablet:** 25 mg, 50 mg, 100 mg; **Nasal Spray:** 5 mg/actuation

**Common FDA Label Indication, Dosing, and Titration.**

1. Migraine: Oral, 25-100 mg po at onset of migraine, may repeat after 2 h prn; *max* 200 mg/d; Nasal, 5-20 mg in 1 nostril, may repeat after 2 h; *max* 40 mg/d

**Off-Label Uses.** None

**MOA.** Sumatriptan binds with high affinity to serotonin (5HT) subtypes 1B, 1D, and 1F receptors. It has no significant affinity or pharmacological activity at adrenergic $\alpha_1$, $\alpha_2$, or $\beta$; dopaminergic $D_1$ or $D_2$; muscarinic; or opioid receptors. Serotonin receptor agonists are believed to be effective in migraine either through vasoconstriction (via activation of 5-$HT_1$ receptors located on intracranial blood vessels) or through activation of 5-$HT_1$ receptors on sensory nerve endings in the trigeminal system resulting in the inhibition of proinflammatory neuropeptide release.

**Drug Characteristics: Sumatriptan**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Hepatic dysfunction, *max* single dose 50 mg | **Absorption** | F = 15%, high-fat meal increases F |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 2.4 L/kg; 14-21% protein bound |
| **Dialyzable** | Unknown | **Metabolism** | Hepatic via monoamine oxidase |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 60% with a half-life of 2.5 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to sumatriptan, cerebrovascular syndromes, hemiplegic or basilar migraine, ischemic bowel disease, ischemic heart disease, peripheral vascular disease, severe hepatic impairment, uncontrolled hypertension | **Black Box Warnings** | None |

**Medication Safety Issues: Sumatriptan**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| STATdose | SUMAtriptan | No | No | ZOLMitriptan, sitaGLIPtin | No |

### Drug Interactions: Sumatriptan

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| SSRIs | Additive pharmacologic effects resulting in excessive serotonergic stimulation | Avoid concurrent use or monitor carefully for signs of serotonin syndrome |
| Other 5HT agonists | Additive pharmacologic effect leading to dangerous toxicity | Administration within 24 h of other serotonin agonists is contraindicated |
| MAOIs | Metabolism of sumatriptan inhibited by MAOI, increasing serotonin levels and risk of serotonin syndrome | Contraindicated |
| Ergot alkaloids | Enhanced vasoconstricting effects | Contraindicated |

### Adverse Reactions: Sumatriptan

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Nausea, asthenia, dizziness, somnolence | Angina, cardiac dysrhythmia, coronary arteriosclerosis, heart block, hypertension, acute myocardial infarction, aphasia, cerebral ischemia, stroke, dystonia, hemiplegia, neuropathy, transient ischemic attack, oculogyric crisis |

**Efficacy Monitoring Parameters.** Resolution of clinical signs of migraine headache.

**Toxicity Monitoring Parameters.** Signs of ischemic bowel disease (eg, sudden severe abdominal pain, bloody diarrhea) or peripheral vascular disease, serotonin syndrome (eg, agitation, hallucinations, tachycardia, hyperthermia, labile BP, hyperreflexia, incoordination, diarrhea, nausea, and vomiting), ischemic cardiac syndrome, or hypertensive crisis.

**Key Patient Counseling Points.** Avoid activities requiring mental alertness or coordination until drug effects are realized, as this drug may cause dizziness or somnolence.

**Clinical Pearls.** Sumatriptan is also available in formulations for injectable administration, and as an oral dosage form in combination with naproxen. These agents are not for prophylaxis; only for the treatment of acute migraine headache. Several serotonin agonists ("triptans") exist for migraine, administered via a variety of routes (oral, inhaled, and injected). Each differs in onset and duration of action. If one agent is ineffective at *max* dose, recommend changing agents or route. Instruct patients to take a 2nd dose 2 or more h after the 1st, if needed, but no more than 200 mg/d. A transdermal form of sumatriptan was approved in 2013, but is not commercially available as of early 2015.

# TACROLIMUS: Prograf, Astragraf XL, Various

**Class:** Calcineurin Inhibitor

**Dosage Forms.** **Oral Capsule:** 0.5 mg, 1 mg, 5 mg; **Oral Capsule, Extended Release:** 0.5 mg, 1 mg, 5 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Cardiac transplant rejection, prophylaxis: 0.075 mg/kg/d po in 2 divided doses, may titrate based on serum levels and tolerability
2. Liver transplant rejection, prophylaxis: Adults, 0.1-0.15 mg/kg/d po in 2 divided doses, may titrate based on clinical response, serum levels, and tolerability; Children, 0.15-0.2 mg/kg/d po in 2 divided doses, may titrate based on serum levels and tolerability
3. Renal transplant rejection, prophylaxis: Immediate release, 0.2 mg/kg/d po in 2 divided doses, may titrate based on serum levels and tolerability; extended release, 0.1-0.2 mg/kg/d po in 1 dose; may titrate based on serum levels and tolerability; immediate-release to extended-release conversion is 1:1

**Off-Label Uses.**

1. Lung, small bowel, transplant rejection; prophylaxis, graft-versus-host disease, prevention: Use liver transplant dose above
2. Treatment of graft-versus-host disease in allogeneic stem cell transplant: 0.06 mg/kg po twice daily

**MOA.** Tacrolimus binds to cyclophilin, which inhibits the antigenic response of helper T lymphocytes, which in turn reduces the production of interleukin-2 and suppresses interferon-γ. Inhibition of the immune response limits inflammation.

Sandoz generic 5 mg pictured

## Drug Characteristics: Tacrolimus

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Use doses at the lower end of the dosing range | **Absorption** | F = 14-32%, food decreases absorption |
| **Dose Adjustment Renal** | Use doses at the lower end of the dosing range | **Distribution** | Vd = 5-65 L/kg; 99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic; substrate of CYP3A4/5 and P-glycoprotein. P-glycoprotein inhibitor |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is <1% with a half-life of 11 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to tacrolimus, concurrent ziprasidone use | **Black Box Warnings** | Risk of infection, risk of malignancies |

## Medication Safety Issues: Tacrolimus

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Extended release | Yes | Gengraf, PROzac, sirolimus | No |

### Drug Interactions: Tacrolimus

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inducers | Increased tacrolimus metabolism reduces tacrolimus effectiveness | Monitor and consider dose increases of tacrolimus |
| CYP3A4/5 inhibitors | Decreased tacrolimus metabolism increases risk of tacrolimus toxicity | Monitor and consider dose decreases of tacrolimus |
| P-glycoprotein substrates | Decreased substrate transport and increased concentrations of substrates | Monitor and consider dose decreases of substrates |
| Amiloride, potassium-sparing diuretics | Increased risk of hyperkalemia | Avoid concurrent use |
| Aminoglycosides, amphotericin, cisplatin, gancyclovir | Increased risk of nephrotoxicity | Avoid concurrent use |
| Agents that increase QT interval | Increased risk of QT prolongation (torsade de pointes, cardiac arrest) | Ziprasidone contraindicated, others, avoid concurrent use or monitor carefully |
| Live vaccines | Risk of severe infections | Avoid concurrent use |

### Adverse Reactions: Tacrolimus

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Chest pain, hypertension, alopecia, diabetes, hyperglycemia, hyperkalemia, hypomagnesemia, hyperlipidemia, constipation, diarrhea, nausea, anemia, leukopenia, thrombocytopenia, infection, arthralgia, dizziness, headache, insomnia, neuropathy, myoclonus, seizure, nephrotoxicity, dyspnea, pleural effusions | Pruritus, elevated LFTs | Cardiomegaly, arrhythmia, Stevens-Johnson syndrome, increased risk of cancer, pancreatitis, acute renal failure |

**Efficacy Monitoring Parameters.** Lack of signs of rejection (elevation in SCr for renal transplant, LFTs for liver transplant). Tacrolimus trough whole blood concentrations (target 5-20 ng/mL).

**Toxicity Monitoring Parameters.** Monitor electrolytes, FPG, BP and SCr, BUN, lipids, and CBC. Itching or hives, swelling of face, hands, mouth facial or throat, chest tightness, trouble breathing, blistering, peeling, or red skin rash, chest pain, change in urination, unusual bruising or bleeding, severe abdominal pain.

**Key Patient Counseling Points.** Take on an empty stomach. Avoid alcohol, grapefruit, and grapefruit juice. Many medications, OTC medications, and foods interact with tacrolimus. Monitor carefully.

**Clinical Pearls.** Tacrolimus is more effective in preventing acute rejection than cyclosporine for patients with liver and kidney transplants. When changing between brand and generic forms, monitor tacrolimus levels. Medication guide required when dispensing this medication. Topical formulation, used for dermatitis, also available.

# TADALAFIL: Cialis, Adcirca

**Class:** Erectile Dysfunction Agent; Pulmonary Hypertension Agent

**Dosage Forms. Oral Tablet:** 2.5 mg, 5 mg, 10 mg, 20 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Erectile dysfunction: Daily use, Cialis only, 2.5-5 mg po daily; PRN use, 10-20 mg po 30 min prior to anticipated sexual activity, *max* frequency is once daily
2. Benign prostatic hyperplasia: Cialis only, 5 mg po daily; when combined with finasteride, tadalafil administration should be discontinued at or before 26 wk.
3. Pulmonary hypertension: Adcirca only, 40 mg po daily

**Off-Label Uses.** None

Lilly pictured

**MOA.** Inhibition of phosphodiesterase type 5 (PDE5) by tadalafil enhances erectile function by increasing the amount of cyclic GMP enhancing erectile function and pulmonary vasculature relaxation. Penile erection during sexual stimulation is mediated by the release of nitric oxide (NO) from nerve terminals and endothelial cells, which stimulates the synthesis of cyclic GMP in smooth muscle cells. Cyclic GMP causes smooth muscle relaxation and increased blood flow into the corpus cavernosum and vasodilation in the pulmonary bed.

## Drug Characteristics: Tadalafil

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Avoid use | **Absorption** | Well absorbed, food has no effect on absorption |
| **Dose Adjustment Renal** | CrCl 31-50 mL/min, *max* dose 10 mg q48h; CrCl <30 mL/min, *max* dose is 5 mg q72h | **Distribution** | Vd = 63-77 L; 94% protein bound |
| **Dialyzable** | Unknown | **Metabolism** | Hepatic, CYP3A4/5 substrate |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 36% with a half-life of 15-35 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to phosphodiesterase inhibitors, concurrent nitrates | **Black Box Warnings** | None |

## Medication Safety Issues: Tadalafil

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Sildenafil, vardenafil | No |

### Drug Interactions: Tadalafil

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inducers | Increased tadalafil metabolism reduces tadalafil effectiveness | Monitor and consider dose increases of tadalafil |
| CYP3A4/5 inhibitors | Decreased tadalafil metabolism increases risk of tadalafil toxicity | Max dose of 2.5 mg daily dose or 10 mg every 72 h as needed if concurrent strong CYP3A4/5 inhibitors. Monitor and consider dose decreases of tadalafil if concurrent moderate CYP3A4/5 inhibitors |
| α-adrenergic agents | Additive hypotension | Monitor for hypotension and consider dose reductions |
| Nitrates | Additive hypotension, potentially severe | Contraindicated |

### Adverse Reactions: Tadalafil

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Flushing, nausea, myalgia, headache | Nasopharyngitis, angina, chest pain, hypotension | Stevens-Johnson syndrome, myocardial infarction, seizures, strokes, sudden hearing loss |

**Efficacy Monitoring Parameters.** Improvement in sexual function, BPH symptoms, or respiratory symptoms.

**Toxicity Monitoring Parameters.** Seek medical attention if severe skin rash, chest pain, erection lasting >4 h, tinnitus, dizziness, or shortness of breath.

**Key Patient Counseling Points.** If taking as needed, take 30 min prior to anticipated sexual activity. Do not take more frequently than once q24h. Avoid driving or other activities that require mental alertness until the drug's effects have been determined.

**Clinical Pearls.** The choice between tadalafil, sildenafil, and vardenafil is largely one of patient preference; tadalafil may be preferred in those desiring "full-day coverage." Sexual stimulation is required to initiate the local release of NO; the inhibition of PDE5 has no effect in the absence of sexual stimulation. Adcirca is FDA approved for pulmonary artery hypertension; Cialis is FDA approved for erectile dysfunction.

# TAMSULOSIN: Flomax, Various



Boehringer Ingelheim 0.4 mg pictured

**Class:** $\alpha_1$-Adrenergic Blocker

**Dosage Forms. Oral Capsule:** 0.4 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Benign prostatic hyperplasia: 0.4 mg po daily, may titrate to 0.8 mg po daily

**Off-Label Uses.**

1. Neurogenic bladder: 0.4 mg po daily
2. Bladder outlet obstruction symptoms: 0.4 mg po daily
3. Ureteral stones, expulsion: 0.4 mg po daily, discontinue after successful expulsion

**MOA.** Tamsulosin is closely related to quinazoline derivatives that selectively block postsynaptic $\alpha_1$-adrenergic receptors. Total peripheral resistance is reduced through arterial and venous dilations. Reflex tachycardia that occurs with other vasodilators is infrequent because there is no presynaptic $\alpha_2$-receptor blockade. The drugs also decrease total cholesterol, increase HDL-cholesterol, and may improve glucose tolerance and reduce left ventricular mass during long-term therapy. They increase urine flow in BPH by relaxing smooth muscle tone in the bladder neck and prostate.

**Drug Characteristics: Tamsulosin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F >90%, fasting increase F by 30% |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 16 L; 94-99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive hepatic; CYP3A4/5 substrate |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 10% with a half-life of 9-13 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to tamsulosin | **Black Box Warnings** | None |

**Medication Safety Issues: Tamsulosin**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Yes | No | Flomax, terazosin | No |

### Drug Interactions: Tamsulosin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| $\alpha_1$-Blockers | Increases risk of hypotension | Contraindicated |
| CYP3A4/5 inducers | Increased tamsulosin metabolism reduces tamsulosin effectiveness | Monitor and consider dose increases of tamsulosin |
| CYP3A4/5 inhibitors | Decreased tamsulosin metabolism increases risk of tamsulosin toxicity | Avoid strong CYP3A4/5 inhibitors. Monitor and consider dose decreases of tamsulosin with concurrent moderate CYP3A4/5 |
| Beta-blockers, calcium channel blockers, MAOIs | Increased risk of hypotension, especially with 1st dose | Monitor BP |

### Adverse Reactions: Tamsulosin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Dizziness, headache, abnormal ejaculation, rhinitis | Asthenia, edema, fatigue, hypotension, nausea, somnolence, vertigo | Retinal detachment, priapism |

**Efficacy Monitoring Parameters.** American Urological Association (AUA) Symptom Score, decrease in residual urine volume, increased urine flow.

**Toxicity Monitoring Parameters.** Sign/symptoms of hypotension, BP.

**Key Patient Counseling Points.** Administer 30 min after same meal daily as fasting increases bioavailability by 30%. Patient should avoid activities requiring coordination until drug effects are realized, as drug may cause vertigo or dizziness. Tell patient to rise slowly from a sitting/lying position, as this drug may cause orthostatic hypotension. Caution patient that syncope or loss of consciousness is possible with first dose or dose increases, especially if patient is in an upright position.

**Clinical Pearls.** Alpha-blockers commonly used for hypertension. Patients with both hypertension and BPH should avoid taking other α-adrenergic blocking agents while taking this drug.

# TEMAZEPAM: Restoril, Various

**Class:** Benzodiazepine. C-IV

**Dosage Forms. Oral Capsule:** 7.5 mg, 15 mg, 22.5 mg, 30 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Insomnia: 7.5-30 mg po daily hs

**Off-Label Uses.** None

**MOA.** Temazepam is a minor metabolite of diazepam. Enhances the postsynaptic effect of the inhibitory neurotransmitter, γ-aminobutyric acid (GABA).

Sandoz generic 15 mg pictured

Mutual Pharmaceutical generic 7.5 mg pictured

## Drug Characteristics: Temazepam

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Well absorbed, food has no effect on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 1.4 L/kg; 96% protein bound |
| **Dialyzable** | Unknown | **Metabolism** | Hepatic via multiple CYP pathways; contribution of each CYP is minor |
| **Pregnancy Category** | X | **Elimination** | Renal elimination is 80-90% with a half-life of 4-18 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to temazepam or other benzodiazepines, narrow-angle glaucoma, pregnancy | **Black Box Warnings** | None |

## Medication Safety Issues: Temazepam

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Vistaril, LORazepam | Avoid benzodiazepines (any type) for treatment of insomnia, agitation, or delirium |

### Drug Interactions: Temazepam

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Alcohol, opioids, and other CNS depressants | Additive CNS and respiratory depression | Avoid if possible and consider dose reductions of both agents |
| Theophylline | Decreased benzodiazepine effectiveness via inhibition of adenosine receptors | Monitor and consider dose increases for benzodiazepines |

### Adverse Reactions: Temazepam

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Drowsiness, somnolence, impaired motor coordination | Hypotension, blurred vision, nausea, diarrhea, confusion, headache | Complex behavior, anaphylaxis, worsening of depression, angioedema, drug dependence |

**Efficacy Monitoring Parameters.** Improved ability to fall asleep and sleep through night.

**Toxicity Monitoring Parameters.** Seek medical attention if severe drowsiness, thoughts of suicide, allergic reaction, or slow or irregular heartbeat. Monitor vital signs.

**Key Patient Counseling Points.** May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol. Take 30 min prior to bedtime. May cause complex behaviors (driving, talking on phone, etc while not fully awake); bed partner should monitor and temazepam should be discontinued.

**Clinical Pearls.** Not for long-term use (usually 7-10 d only). Use caution in elderly, appear more sensitive to the effects; dose reductions of 50% have been recommended. Use CNS depressants with caution; may have additive effects. Avoid abrupt discontinuation after chronic use; may cause seizures.

# TERAZOSIN: Hytrin, Various

Sandoz generic pictured

**Class:** $\alpha_1$-Adrenergic Blocker

**Dosage Forms. Oral Capsule:** 1 mg, 2 mg, 5 mg, 10 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Benign prostatic hyperplasia: 1 mg po daily hs, may titrate to 20 mg/d
2. Hypertension: 1 mg po daily hs, may titrate to 20-40 mg/d

**Off-Label Uses.** None

**MOA.** Terazosin selectively blocks postsynaptic $\alpha_1$-adrenergic receptors. Total peripheral resistance is reduced through arterial and venous dilations. Reflex tachycardia that occurs with other vasodilators is infrequent because there is no presynaptic $\alpha_2$-receptor blockade. Increases urine flow in BPH by relaxing smooth muscle tone in the bladder neck and prostate.



## Drug Characteristics: Terazosin

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Lower doses may be required | **Absorption** | F = 90%, food delays but does not reduce absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 25-30 L; 90-94% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Not metabolized |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 40% with a half-life of 9-12 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to terazosin | **Black Box Warnings** | None |

## Medication Safety Issues: Terazosin

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | Avoid use as an antihypertensive. High risk of orthostatic hypotension |

### Drug Interactions: Terazosin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Beta-blockers, calcium channel blockers, PDEIs other alpha-blockers, MAOI | Increased risk of hypotension, especially with first dose | Monitor BP |

### Adverse Reactions: Terazosin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Asthenia, dizziness | Dyspnea, headache, impotence, nausea, nasal congestion, orthostatic hypotension, palpitations, peripheral edema, priapism, somnolence, syncope | Hepatotoxicity |

**Efficacy Monitoring Parameters.** Decreased BP, improvement in obstructive urinary symptoms.

**Toxicity Monitoring Parameters.** Sign/symptoms of hypotension, increased HR, LFTs.

**Key Patient Counseling Points.** Avoid activities requiring mental alertness or coordination until drug effects are realized, as drug may cause dizziness and somnolence. Rise slowly from a sitting/lying position, as this drug may cause orthostatic hypotension. May experience syncope or loss of consciousness with 1st dose. Take drug at bedtime to minimize side effects, especially the 1st dose. Avoid sudden discontinuation of drug, as this may cause rebound hypertension. Avoid alcohol while taking this drug.

**Clinical Pearls.** JNC 8 guidelines do not recommend the use of terazosin, or other alpha-blockers, for the treatment of hypertension. Clinical use should be restricted to the management of BPH.

# TERBINAFINE: Lamisil, Various

**Class:** Antifungal

**Dosage Forms.** **Oral Tablet:** 250 mg; **Oral Granules:** 125 mg/packet

**Common FDA Label Indication, Dosing, and Titration.**

1. Onychomycosis due to dermatophyte: Tablet only, 250 mg po daily × 6 wk for fingernails and × 12 wk for toe nails
2. Tinea capitis: Granules only, Children <25 kg, but ≥4 y of age, 125 mg po daily; Children 25-35 kg, 187.5 mg po daily; Children >35 kg, 250 mg po daily

Northstar Rx generic 250 pictured

**Off-Label Uses.**

1. Cutaneous sporotrichosis: 500 mg po bid × 2-4 wk after all lesions have healed
2. Lymphocutaneous sporotrichosis: 500 mg po bid × 2-4 wk after all lesions have healed

**MOA.** Terbinafine is an allylamine antifungal that inhibits biosynthesis of ergosterol, an essential component of fungal cell membrane. This results in fungal cell death primarily due to the increased membrane permeability. Terbinafine has been shown to be active against most clinical infections of *T. mentagrophytes* and *T. rubrum*.

**Drug Characteristics: Terbinaf ne**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Hepatic dysfunction, use not recommended | **Absorption** | F = 40%, administration with food increases AUC by 20% |
| **Dose Adjustment Renal** | CrCl <50 mL/min, use not recommended | **Distribution** | Vd = 948 L with 99% protein binding |
| **Dialyzable** | Not dialyzable | **Metabolism** | Rapidly and extensively metabolized hepatically, substrate of CYP2C9, CYP1A2, CYP3A4/5, CYP2C8, and CYP2C19, all <10%. Strong CYP2D6 inhibitor |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 70% with a half-life of 22-26 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | Use with caution in poor CYP2D6 metabolizers |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

**Medication Safety Issues: Terbinaf ne**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| AT | LamISIL | Do not chew granules | No | LaMICtal, Lomotil | No |

### Drug Interactions: Terbinaf ne

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP2D6 substrates | Terbinafine is a CYP2D6 inhibitor and can reduce metabolism of substrates, increasing risk of toxicity | Avoid concurrent use or monitor for signs of toxicity and consider substrate dose reductions |

### Adverse Reactions: Terbinaf ne

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Diarrhea, headache | Rash, fever, increased LFTs | Cutaneous lupus erythematosus, erythema multiforme, Stevens-Johnson syndrome, agranulocytosis, neutropenia, pancytopenia, liver failure, systemic lupus erythematosus |

**Efficacy Monitoring Parameters.** Resolution of infection.

**Toxicity Monitoring Parameters.** Seek medical attention if severe skin reactions occur; if therapy exceeds 6 wk, CBC, LFTs, are warranted.

**Key Patient Counseling Points.** Instruct patients to report signs/symptoms of rash, infection, or hepatotoxicity. Symptomatic improvement of nail beds may not be seen for several months. Granules should be sprinkled on a spoonful of pudding or other soft, nonacidic food (eg, mashed potatoes) and swallowed without chewing; do not mix granules with applesauce or other fruit-based foods.

**Clinical Pearls.** Several topical products containing terbinafine, including both prescription and OTC products, are also available for treatment of skin infections.

# TESTOSTERONE: AndroGel, Androderm

**Class:** Androgen, C-III

**Dosage Forms.** **Transdermal Patch:** 2 mg/24 h, 4 mg/24 h; **Topical Gel:** 1%; 1.62%, 2%; **Transdermal Cream:** 2%; **Mucoadhesive for Buccal Application:** 30 mg; **Topical Solution:** 30 mg/actuation

**Common FDA Label Indication, Dosing, and Titration.**

1. Hypogonadism: 5 g gel (50 mg active drug) daily to clean, dry, intact skin, may titrate dose to 7.5-10 g daily; one 5 mg patch daily × 24 h, may titrate to 7.5 mg/d

**Off-Label Uses.** None

**MOA.** Testosterone is an endogenous androgen. Androgens are responsible for normal growth and development of male sex organs. Testosterone is involved in the growth and maturation of the prostate, seminal vesicles, penis, and scrotum; development of male hair distribution; laryngeal enlargement; vocal cord thickening; alterations in body musculature; and fat distribution.

Solvay Pharmaceuticals pictured

## Drug Characteristics: Testosterone

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Approximately 10% of a topically administered dose is absorbed over 24 h |
| **Dose Adjustment Renal** | Not required | **Distribution** | 98% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Minimal |
| **Pregnancy Category** | X | **Elimination** | Renal elimination is 90% with a half-life of 10-100 min |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to testosterone; men with breast or prostate cancer; women who are pregnant, who may become pregnant, or who are breast-feeding | **Black Box Warnings** | Secondary exposure |

## Medication Safety Issues: Testosterone

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| Pump, MC | No | No | No | T-Gel | Avoid unless indicated for moderate to severe hypogonadism |

### Drug Interactions: Testosterone

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Warfarin | Testosterone suppresses clotting factors II, V, VII, and X, and competes with warfarin for plasma protein binding, increasing risk of bleeding | Avoid concurrent use, or increase warfarin monitoring |

### Adverse Reactions: Testosterone

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Benign prostatic hyperplasia, testicular atrophy, PSA increase | Acne, headache, gynecomastia, alopecia, impotence, aggressive behavior, hypertension | Edema, liver carcinoma, prostate cancer, polycythemia, hepatotoxicity, DVTs |

**Efficacy Monitoring Parameters.** Development of secondary gender characteristics (hair growth, masculinization).

**Toxicity Monitoring Parameters.** Hematocrit levels should be monitored, especially in older men. Instruct patients to report signs and symptoms of unusual bleeding/bruising, rapid weight gain, edema, VTE (leg pain or redness) or liver toxicity (jaundice, dark urine, pale stools).

**Key Patient Counseling Points.** Gel to be applied to clean, dry, intact skin of the shoulders and upper arms and/or abdomen, but should not be applied to genitals. Gel should be allowed to dry well; swimming and showering should be avoided for 5-6 h after application. Patients should keep application site covered, as direct skin contact can transfer drug to others. Virilization has been reported in children who were secondarily exposed to testosterone gel (coming in contact with bare skin around gel application site). Male patients should report too frequent or persistent erections. Female sexual partners of patients using drug should report male-like changes.

**Clinical Pearls.** In addition to topical dosage forms (gel and patch), other dosage forms include subcutaneous implants and injectable, which are indicated for delayed puberty, breast cancer, female-to-male gender identity disorder, and others. Avoid other medications containing testosterone, including those purchased without a prescription in health food stores or on the Internet. The patch may contain metal; remove prior to MRIs.

# TETANUS TOXOID: Daptacel, Adacel, Boostrix

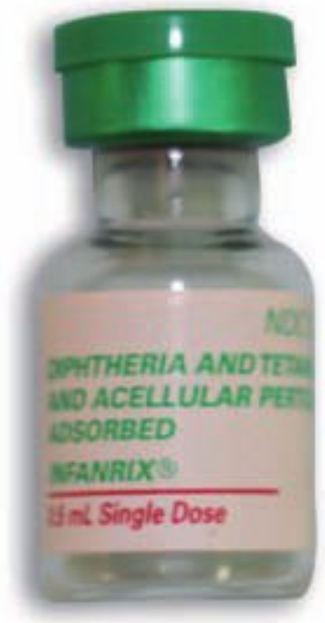
**Class:** Vaccine, Inactivated, Bacterial

**Dosage Forms. Suspension for Intramuscular Injection:** Adults and Children ≥7 y of age, available in combination with tetanus and diphtheria toxoids (Td) or combination with tetanus and diphtheria toxoids and acellular pertussis (Tdap); Children ≤6 y of age, available in combination with tetanus and diphtheria toxoids and acellular pertussis (DTaP), and in combination with other pediatric vaccines.

**Common FDA Label Indication, Dosing, and Titration.**

1. Prevention of tetanus: Children, all infants at 2, 4, 6, and 12-15 mo of age, and a 5th dose at 4-6 y of age, as primary series of DTaP; Tdap at 11-12 y of age; single dose of Tdap for all adults at next opportunity; Td every 10 y for adults

**Off-Label Uses.** None




Infanrix, GlaxoSmithKline pictured



## Drug Characteristics: Tetanus Toxoid

| | | | |
|---|---|---|---|
| **Pregnancy Category** | C | **ADME** | None known |
| **Lactation** | Caution advised; weigh risk and benefit | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to tetanus toxoid or a component of the vaccine (gelatin, latex, thimerosal) | **Black Box Warnings** | None |

## Medication Safety Issues: Tetanus Toxoid

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Adacel, Daptacel, Tdap, DTaP | No |

## Drug Interactions: Tetanus Toxoid

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Moderate- to high-dose corticosteroids | Immunosuppression, reduced efficacy of vaccine | Delay tetanus toxoid administration until corticosteroid therapy has been discontinued if possible; clinical judgment |
| Immunosuppressing agents | Immunosuppression, reduced efficacy of vaccine | Delay tetanus toxoid administration until immunosuppressive therapy has been discontinued if possible |

**Adverse Reactions: Tetanus Toxoid**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Injection site reactions, including erythema and soreness. Fever, headache, fatigue, swelling of limb | GI symptoms | Anaphylaxis, swelling or severe arm pain, Guillain-Barré syndrome |

**Efficacy Monitoring Parameters.** Prevention of tetanus, although antibody concentrations might be measured; routine measurement for vaccine response is not recommended.

**Toxicity Monitoring Parameters.** Monitor for syncope, fever after administration.

**Key Patient Counseling Points.** Return to provider for each dose in the series.

**Clinical Pearls.** Use the same brand of vaccine to complete the entire series, if possible. After childhood immunization, adults should substitute a 1 time dose of Tdap for Td booster then boost with Td (tetanus with diphtheria) vaccination every 10 y. Pregnant women should receive 1 dose of Tdap vaccine during each pregnancy, preferred during 27-36 wk gestation regardless of interval of last Td or Tdap vaccine. Individuals with wounds requiring medical attention should be vaccinated with Td if vaccination status is inadequate or unknown, or if >5 y since last vaccination.

# THYROID: Armour Thyroid, Various

**Class:** Thyroid Supplement

**Dosage Forms. Oral Tablet:** 15 mg, 16.25 mg, 30 mg, 32.4 mg, 32.5 mg, 48.75 mg, 60 mg, 64.8 mg, 65 mg, 81.25 mg, 90 mg, 97.5 mg, 113.75 mg, 120 mg, 130 mg, 146.25 mg, 162.5 mg, 180 mg, 195 mg, 240 mg, 260 mg, 300 mg, 325 mg

Forest Laboratories pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Hypothyroidism: Dosing individualized based on clinical response and serum TSH levels; Infants birth to 6 mo of age, 4.8-6.8 mg/kg/d po daily; Infants 6-12 mo of age, 3.6-4.8 mg/kg/d po daily; Children 1-5 y of age, 3-3.6 mg/kg/d po daily; Children 6-12 y of age, 2.4-3 mg/kg/d po daily; Children >12 y of age, 1.2-1.8 mg/kg/d po daily; Adults, 15-120 mg po daily

**Off-Label Uses.** None

**MOA.** Thyroid hormone is a naturally derived thyroid replacement containing both levothyroxine ($T_4$) and liothyronine ($T_3$). The endogenous thyroid hormones, $T_3$ and $T_4$, diffuse into the cell nucleus and bind to thyroid receptor proteins attached to DNA. This hormone nuclear receptor complex activates gene transcription and synthesis of messenger RNA and cytoplasmic proteins.

**Drug Characteristics: Thyroid**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 48-79%, increases with fasting |
| **Dose Adjustment Renal** | Not required | **Distribution** | 99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Approximately 80% of levothyroxine sodium is deiodinated into $T_3$ in the liver, kidney, and other tissues; it can also be metabolized by conjugation with glucuronides and sulfates and then enter into enterohepatic recirculation |
| **Pregnancy Category** | A | **Elimination** | Renal excretion is 50% with a half-life of 7 d |
| **Lactation** | Compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to thyroid, nontoxic diffuse goiter or nodular thyroid disease, thyrotoxicosis, acute MI, treatment of obesity or weight loss, uncorrected adrenal insufficiency; may precipitate acute adrenal crisis | **Black Box Warnings** | Ineffective and potentially toxic when used for weight loss |

### Medication Safety Issues: Thyroid

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| NP, P | No | No | No | No | Avoid. Concerns about cardiac effects |

### Drug Interactions: Thyroid

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Warfarin | Increased risk of bleeding | Monitor INR and consider warfarin does adjustments |

### Adverse Reactions: Thyroid

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | | Aggravation of preexisting cardiovascular disease, hyperthyroidism |

**Efficacy Monitoring Parameters.** Serum TSH, $T_3$, and $T_4$ levels: resolution of symptoms of hypothyroidism, fatigue, edema, hair loss, cold intolerance, lethargy.

**Toxicity Monitoring Parameters.** Monitor patients with preexisting cardiovascular disease for exacerbation of symptoms.

**Key Patient Counseling Points.** You may have to take this medicine for 6-8 wk before your symptoms improve. Do not stop using this medicine suddenly without asking your doctor. You may need to slowly decrease your dose before stopping it completely. Take on an empty stomach, with water.

**Clinical Pearls.** $T_3$ normal range is 100-200 ng/dL. $T_4$ normal range is 4.5-11.2 mcg/dL. TSH level should be between 0.5 and 3.0 mIU/L in those successfully treated for a thyroid disorder. When used for weight loss, high doses may cause life-threatening adverse effects.

# TIOTROPIUM: Spiriva

**Class:** Anticholinergic Bronchodilator

**Dosage Forms. Inhalation Capsule:** 18 mcg

**Common FDA Label Indication, Dosing, and Titration.**

1. COPD: Inhale contents of 1 capsule (18 mcg) daily using manufacturer-provided device (do not swallow capsules)

**Off-Label Uses.** None

**MOA.** Tiotropium is a long-acting antimuscarinic agent, which is often referred to as an anticholinergic. It has similar affinity to the subtypes of muscarinic receptors, M1 to M5. In the airways, it exhibits pharmacological effects through inhibition of M3-receptors at the smooth muscle leading to bronchodilation. The bronchodilation following inhalation of tiotropium is predominantly a site-specific effect.

Pfizer/Boehringer Ingelheim pictured

**Drug Characteristics: Tiotropium**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | After inhalation, well absorbed into the lung; <19.5% of dose is absorbed systemically |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 32 L/kg; 72% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Minimal |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 14% (unchanged) with a half-life of 5-6 d |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to tiotropium, ipratropium, or milk protein | **Black Box Warnings** | None |

**Medication Safety Issues: Tiotropium**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Capsules for inhalation, not oral use | No | Inspra, Serevent | No |

### Drug Interactions: Tiotropium

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Other anticholinergic agents | Additive effect with tiotropium | Avoid concurrent use |

### Adverse Reactions: Tiotropium

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Xerostomia, upper respiratory infection | Constipation, pharyngitis, sinusitis, headache, dysphonia, application site irritation | Bowel obstruction, cerebrovascular accident; bronchospasm |

**Efficacy Monitoring Parameters.** Monitor pulmonary function tests, shortness of breath.

**Toxicity Monitoring Parameters.** Seek medical attention if severe anticholinergic side effects occur, including bladder obstruction, narrow angle glaucoma, prostatic hyperplasia, and urinary retention or difficulty.

**Key Patient Counseling Points.** Advise patients that this drug is not indicated for acute bronchospasm (rescue therapy). This drug may cause increased HR, dry mouth, constipation, urinary difficulty and retention, respiratory tract infection, and sinusitis. Warn patients that the drug capsules are for inhalation only and are not to be swallowed; instruct patients on the use of the inhalation device.

**Clinical Pearls.** Paradoxical bronchospasm has occurred with tiotropium; when it occurs, therapy should be permanently discontinued.

# TIZANIDINE: Zanaflex, Various

**Class:** Centrally Acting Skeletal Muscle Relaxant, $\alpha_2$-Agonist

**Dosage Forms.** **Oral Capsule:** 2 mg, 4 mg, 6 mg; **Oral Tablet:** 2 mg, 4 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Muscle Spasticity: 2 mg po up to tid, may titrate to 8 mg po q6-8h with *max* dose of 36 mg/d

**Off-Label Uses.**

1. Acute low back pain: 12 mg/d po alone or in combination with NSAIDs

**MOA.** Tizanidine is a centrally acting muscle relaxant. The drug is an imidazole derivative, structurally unrelated to other muscle relaxants. Tizanidine is an agonist of $\alpha_2$-adrenergic receptors, which decreases spasticity by increasing presynaptic inhibition; however, it does not have antihypertensive properties.

Sandoz generic pictured

## Drug Characteristics: Tizanidine

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Use not recommended | **Absorption** | F = 40%, extensive first-pass metabolism; food increases extent of absorption of tablets by 30% but decreases extent of absorption of capsules by 10% |
| **Dose Adjustment Renal** | CrCl <25 mL/min, reduce dose | **Distribution** | Vd = 2.4 L/kg; 30% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Extensive (95%) hepatic metabolism to inactive metabolites, substrate of CYP1A2 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 60% with a half-life of 2 h |
| **Lactation** | Avoid | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to tizanidine; coadministration with CYP1A2 inhibitors | **Black Box Warnings** | None |

## Medication Safety Issues: Tizanidine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | TiZANidine | No | No | tiaGABine | No |

### Drug Interactions: Tizanidine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP1A2 inhibitors | Inhibition of tizanidine metabolism and increased toxicity | Do not coadminister; select alternative antispasmodic |
| Phenytoin, fosphenytoin | Unknown mechanism; results in increased serum concentrations of phenytoin and resulting phenytoin toxicity | Monitor for signs of phenytoin toxicity and adjust dose accordingly |
| CNS depressants | Additive CNS depression | Avoid concurrent use |

### Adverse Reactions: Tizanidine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Mild hypotension, xerostomia, asthenia, dizziness, somnolence, muscle weakness | Constipation, vomiting, dyskinesia, amblyopia, feeling nervous, syncope, depression | Myocardial infarction, thrombocytopenia, hepatitis, pulmonary embolism, hypersensitivity, death |

**Efficacy Monitoring Parameters.** Reduction in pain and muscle spasms, reduction in passive limb movement.

**Toxicity Monitoring Parameters.** Monitor BP, LFTs, SCr, CBC.

**Key Patient Counseling Points.** Be cautious of risk of dizziness and somnolence when initiating therapy; do not drive until effects of drug are known. Rise slowly from a lying/sitting position, as this drug may cause hypotension. May cause xerostomia (dry mouth) and asthenia (weakness).

**Clinical Pearls.** While this drug may be taken with or without food, patients should take the drug in the same way (fasting or fed) every time to avoid inconsistent absorption patterns and resulting changes in efficacy and adverse effects. Effect of food on extent of absorption differs for tablets and capsules. Abrupt discontinuation can cause rebound hypertension and tachycardia. Taper if used at high dose (20-28 mg daily) or for an extended period of time.

# TOLTERODINE: Detrol, Detrol LA

**Class:** Antimuscarinic

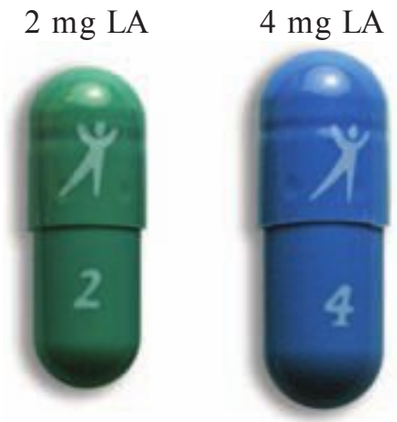
**Dosage Forms.** **Oral Tablet:** 1 mg, 2 mg; **Oral Capsule, Extended Release:** 2 mg, 4 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Bladder muscle dysfunction, overactive: Immediate release, 1-2 mg po bid; Extended release, 2-4 mg po daily; may titrate dose to tolerability and response

**Off-Label Uses.** None

**MOA.** Tolterodine, a competitive muscarinic receptor antagonist, has a high binding affinity for the cholinergic muscarinic receptors that mediates contraction of the urinary bladder and decreases salivation. The drug exerts its significant effects on the lower urinary tract by increasing the residual urine and decreasing detrusor pressure.



Pfizer pictured

## Drug Characteristics: Tolterodine

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Hepatic dysfunction, limit dose to 2 mg po daily | **Absorption** | F = 77%; no effect of food on absorption |
| **Dose Adjustment Renal** | CrCl 10-30 mL/min, limit dose to 2 mg po daily | **Distribution** | Vd = 113 L; >90% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, CYP2D6 and CYP3A4/5 substrate |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 77% (10% unchanged) and 17% in feces (20% unchanged), with a half-life of 1.9-3.7 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | Consider lower dose in CYP2D6 poor metabolizers |
| **Contraindications** | Hypersensitivity to tolterodine, gastric retention, uncontrolled narrow-angle glaucoma, urinary retention | **Black Box Warnings** | None |

## Medication Safety Issues: Tolterodine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| LA | No | Do not chew or crush LA formulation | No | Fesoterodine | No |

### Drug Interactions: Tolterodine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Amiodarone, propafenone, quinidine | Increased QT interval prolongation | Avoid concurrent use |
| CYP3A4/5 and CYP2D6 inhibitors | Decreased tolterodine metabolism increases risk of toxicity | Reduce dose to 2 mg po daily |
| CYP3A4/5 inducers | Increased tolterodine metabolism reduces tolterodine effectiveness | Monitor for efficacy and consider dose increases |
| Warfarin | Increased risk of bleeding | Monitor INR |

### Adverse Reactions: Tolterodine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Xerostomia | Constipation, dizziness, headache, increased HR, indigestion, somnolence, vertigo, chest pain | Tachycardia, QT prolongation, angioedema, hallucinations |

**Efficacy Monitoring Parameters.** Subjective improvement of urge incontinence (reduced desire to urinate), and urinary frequency.

**Toxicity Monitoring Parameters.** Assess renal and hepatic function at baseline; monitor vital signs.

**Key Patient Counseling Points.** Patients should avoid activities requiring mental alertness or coordination until drug effects are realized, as this drug may cause blurred vision, dizziness, and drowsiness. Swallow extended-release capsule whole; do not crush, break, or chew. In the presence of a high environmental temperature, heat prostration can occur with drug use (fever and heat stroke due to decreased sweating). If symptoms occur, the drug should be discontinued and supportive measures instituted.

**Clinical Pearls.** May note decline in cognitive function, particularly in elderly. Lifestyle changes can also improve urinary symptoms. Patients should lose weight and avoid beverages containing alcohol or caffeine. Long-acting product is generally better tolerated.

# TOLVAPTAN: Samsca

**Class:** Vasopressin Antagonist

**Dosage Forms. Oral Tablet:** 15 mg, 30 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Hypervolemic or euvolemic hyponatremia: 15 mg po daily, may titrate to *max* of 60 mg po daily

**Off-Label Uses.** None

**MOA.** Tolvaptan is a selective vasopressin $V_2$-receptor antagonist with an affinity for the $V_2$-receptor that is 1.8 times that of native arginine vasopressin (AVP). When taken orally, tolvaptan antagonizes the effect of vasopressin and causes an increase in urine water excretion that results in an increase in free water clearance, a decrease in urine osmolality, resulting in the restoration of normal serum sodium levels.

Otsuka 30 mg pictured

**Drug Characteristics: Tolvaptan**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Avoid in liver disease | **Absorption** | F = 40% |
| **Dose Adjustment Renal** | Avoid use if CrCl <10 mL/min | **Distribution** | Vd = 3 L/Kg; 99% protein bound |
| **Dialyzable** | Not known | **Metabolism** | Hepatic, CYP3A4/5 substrate |
| **Pregnancy Category** | C | **Elimination** | Nonrenal routes with half-life of 2.8-12 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Anuria, concurrent use of strong CYP3A4/5 inhibitors, hypovolemic hyponatremia | **Black Box Warnings** | Initiate in hospital to monitor serum sodium. Too rapid correction (eg, >12 mEq/24 h) can results in seizures, coma and death; correct sodium gradually |

**Medication Safety Issues: Tolvaptan**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | No |

### Drug Interactions: Tolvaptan

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inducers | Increased tolvaptan metabolism reduces tolvaptan effectiveness | Monitor and consider dose increases of tolvaptan |
| CYP3A4/5 inhibitors | Decreased tolvaptan metabolism increases risk of tolvaptan toxicity | Concurrent strong CYP3A4/5 inhibitors is contraindicated, monitor and consider dose decreases of tolvaptan if concurrent moderate CYP3A4/5 inhibitors |

### Adverse Reactions: Tolvaptan

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Increased thirst, nausea, xerostomia, polyuria | Hyperglycemia, constipation, dizziness, dehydration | Hypovolemia, hepatic failure, osmotic demyelination syndrome |

**Efficacy Monitoring Parameters.** Monitor serum sodium levels carefully; normalization of serum sodium is the efficacy parameter.

**Toxicity Monitoring Parameters.** Monitor for dehydration, serum electrolytes, neurologic status, signs and symptoms of syndrome of inappropriate antidiuretic hormone secretion. Monitor LFTs and discontinue if increased.

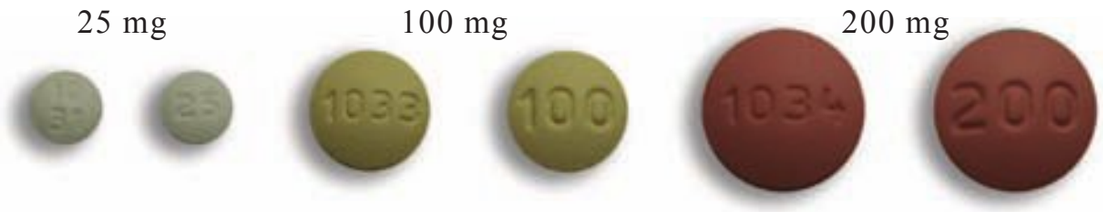
**Key Patient Counseling Points.** May be taken with or without food. Avoid fluid restriction for the first 24 h of therapy. Resume fluid restriction on discontinuation.

**Clinical Pearls.** Initiate and reinitiate therapy only in the hospital setting, monitoring serum sodium carefully. Should not be used for >30 d in patients with underlying liver disease.

# TOPIRAMATE: Topamax, Various

**Class:** Anticonvulsant

**Dosage Forms.** **Oral Capsule, Sprinkle:** 15 mg, 25 mg; **Oral Tablet:** 25 mg, 50 mg, 100 mg, 200 mg; **Oral Capsule, Extended Release, 24 H**: 25 mg, 50 mg, 100 mg, 200 mg; **Oral Capsule, Extended Release, 24 H Sprinkle:** 25 mg, 50 mg, 100 mg, 150 mg, 200 mg



Forest Laboratories generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Partial or tonic-clonic seizure, monotherapy or adjunct: Children 2-16 y of age, 1-3 mg/kg/d (*max* 25 mg) po daily × 1 wk, may titrate to 5-9 mg/kg/d; Children ≥17 y of age and Adults, 25 mg po bid × 1 wk, may titrate to *max* of 200 mg po bid
2. Migraine prophylaxis: Immediate release only, initial 25 mg po daily × 1 wk, may titrate to *max* of 50 mg po bid

**Off-Label Uses.**

1. Cluster headache prophylaxis: 25 mg po daily, may titrate to *max* of 200 mg/d

**MOA.** The exact mechanisms by which topiramate exerts its anticonvulsant and migraine prophylaxis effects are unknown. Electrophysiological and biochemical evidence suggests that topiramate blocks voltage-dependent sodium channels, augments the activity of the neurotransmitter gamma-aminobutyrate at some subtypes of the GABA-A receptor, antagonizes the AMPA/kainate subtype of the glutamate receptor, and inhibits the carbonic anhydrase enzyme, particularly isozymes II and IV.



## Drug Characteristics: Topiramate

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Hepatic disease, adjust dose and monitor carefully for adverse effects | **Absorption** | F = 80%, no effect of food on absorption |
| **Dose Adjustment Renal** | CrCl <70 mL/min, reduce initial and incremental dose adjustments by 50% | **Distribution** | Vd = 0.6-0.8 L/kg; 15-41% protein bound |
| **Dialyzable** | Yes | **Metabolism** | Minor |
| **Pregnancy Category** | D | **Elimination** | Renal elimination is 70% unchanged with a half-life of 21 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity, alcohol use for the ER formulation (within 6 h prior to and 6 h after administration) | **Black Box Warnings** | None |

### Medication Safety Issues: Topiramate

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| XR | No | Qudexy XR may be opened and sprinkled on food. Do not open Trokendi XR capsule. | No | Sporanox, Toprol XL | No |

### Drug Interactions: Topiramate

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Amitriptyline | Concomitant use of amitriptyline and topiramate may increase plasma concentrations of amitriptyline; mechanism unknown | Avoid concurrent use or adjust amitriptyline dose as necessary to avoid amitriptyline toxicity |
| Oral contraceptives | When used concurrently with estrogen-progestin combination contraceptives, AUC of the estrogenic component is decreased, reducing contraceptive efficacy | Avoid concurrent use or use an alternative nonhormonal contraceptive method of birth control |

### Adverse Reactions: Topiramate

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Ataxia, loss of appetite, nausea dizziness, impaired psychomotor performance, somnolence, fatigue, nystagmus, low serum bicarbonate | Disorder of language, diplopia, weight loss, depression, nausea, nephrolithiasis | Erythema multiforme, Stevens-Johnson syndrome, hypohidrosis, increased body temperature, metabolic acidosis, liver failure, glaucoma, myopia, suicidal ideation |

**Efficacy Monitoring Parameters.** Decreased seizure frequency or frequency of migraine headaches.

**Toxicity Monitoring Parameters.** Monitor electrolytes, SCr, hydration, and occurrence of suicidal thoughts.

**Key Patient Counseling Points.** Avoid activities requiring mental alertness and coordination until drug effects are realized. Drug may cause dizziness and somnolence, especially if taken with alcohol or other CNS depressants. May cause nausea, diplopia, nervousness, confusion, and many other CNS effects. Do not discontinue drug abruptly, as this may cause increased seizure activity. Seek medical attention for new eye problems or high body temperature. May decrease sweating; avoid hot temperatures (including hot tubs and saunas).

**Clinical Pearls.** When adjusting dose, make small changes slowly ("start low and go slow") to avoid acute adverse effects.

# TRAMADOL: Ultram, Various

**Class:** Opioid Analgesic. C-IV

**Dosage Forms.** **Oral Tablet:** 50 mg; **Oral Tablet, Extended Release:** 100 mg, 200 mg, 300 mg; **Oral Capsule, Extended Release:** 100 mg (composed of 25 mg immediate release followed by 75 mg extended release), 200 mg (composed of 50 mg immediate release followed by 150 mg extended release), 300 mg (composed of 50 mg immediate release followed by 250 mg extended release); **Oral Suspension:** 10 mg/mL; **Topical Cream:** 5%, 8%

Amneal generic 50 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Pain, chronic, moderate to moderately severe: Immediate release, 50 mg po prn, may titrate to 200 mg/d; extended release, initial, 100 mg po daily, may titrate to 300 mg/d; to convert from immediate release, convert 1:1 and round down to nearest 100 mg dose

**Off-Label Uses.** None

**MOA.** Tramadol is a mu agonist and a weak inhibitor of serotonin and norepinephrine reuptake. Mu receptors are responsible for analgesia, respiratory depression, miosis, decreased GI motility, and euphoria. In the CNS, it promotes analgesia and respiratory depression by decreasing brain stem respiratory centers' response to carbon dioxide tension and electrical stimulation.

**Drug Characteristics: Tramadol**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Moderate or severe, immediate release, 50 mg po q12h; avoid extended-release formulation | **Absorption** | Immediate release: F = 75%, no food effect. Extended release: F = 70%, variable food effect |
| **Dose Adjustment Renal** | CrCl <30 mL/min, immediate release, extend interval to q12h (*max* dose of 200 mg po daily); avoid extended-release formulation | **Distribution** | Vd = 3 L; 20% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | >90% hepatic, CYP3A4/5 and CYP2D6 substrate |
| **Pregnancy Category** | C | **Elimination** | Renal elimination of 30%, with a half-life of 6 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | CYP2D6 poor metabolizers have higher concentrations of parent compound and may require lower doses |
| **Contraindications** | Hypersensitivity to tramadol or other opioids, paralytic ileus, respiratory depression, bronchial asthma | **Black Box Warnings** | None |

### Medication Safety Issues: Tramadol

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| ODT | TraMADol | Do not chew or crush ER | No | Tapentadol, Toradol, Trandate, traZODone, Voltaren | No |

### Drug Interactions: Tramadol

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Barbiturates, benzodiazepines, centrally acting muscle relaxants, opioids, phenothiazines | Additive CNS depression | Monitor and consider dose adjustments |
| Buprenorphine, opioid agonists/antagonists, opioid antagonists | Precipitation of withdrawal symptoms | Avoid concurrent use with opioids |
| CYP3A4/5 inducers | Increased tramadol metabolism reduces tramadol efficacy | Consider dose increases of tramadol |
| CYP3A4/5 or CYP2D6 inhibitors | Decreased tramadol metabolism increases risk of tramadol toxicity | Consider dose decreases of tramadol |
| MAOIs | Additive respiratory depression, increased risk of serotonin syndrome | Contraindicated |

### Adverse Reactions: Tramadol

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Constipation, GI distress, dizziness, sedation, edema, sweating, pruritus, headaches, flushing | Dyspnea, xerostomia, depression, orthostatic hypotension | Cardiac arrest, physical dependence, tolerance, seizures, pancreatitis, suicidal ideation, anemia |

**Efficacy Monitoring Parameters.** Relief of pain.

**Toxicity Monitoring Parameters.** Excessive drowsiness; decreased breathing, severe constipation, chest pain, dizziness, signs of tolerance. Monitor vital signs.

**Key Patient Counseling Points.** Use a stool softener and stimulant or laxative for preventing constipation if used chronically. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol and other CNS depressants.

Extended-release products must not be crushed or chewed, but may be taken with or without food, and always the same way to avoid variability in absorption.

**Clinical Pearls.** Tolerance and physical dependence may occur with chronic use; avoid abrupt discontinuation. Tramadol-related deaths have been reported in patients with histories of emotional disturbances; suicidal ideation/attempts; or tranquilizer, alcohol, and other CNS-active drug misuse. Suspension and creams are available in compounding kits.

# TRAVOPROST: Travatan Z

**Class:** Prostaglandin, Antiglaucoma Agent

**Dosage Forms. Ophthalmic Solution:** 0.004%

**Common FDA Label Indication, Dosing, and Titration.**

1. Ocular hypertension: 1 drop in affected eyes daily in the evening
2. Open-angle glaucoma: 1 drop in affected eyes daily in the evening

**Off-Label Uses.** None

**MOA.** Travoprost is a prostaglandin F2-alpha analogue. It is believed to reduce intraocular pressure by increasing the outflow of aqueous humor. Studies suggest that the main mechanism of action is increased uveoscleral outflow, but the exact mechanism is unknown.

Alcon 0.004% solution pictured

## Drug Characteristics: Travoprost

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Travoprost is absorbed through the cornea where the isopropyl ester prodrug is hydrolyzed to the acid form to become biologically active; systemic absorption following ocular instillation is very low |
| **Dose Adjustment Renal** | Not required | **Distribution** | Unknown |
| **Dialyzable** | Not dialyzable | **Metabolism** | Metabolized within the cornea; any entering systemic circulation is metabolized in the liver, extent unknown |
| **Pregnancy Category** | C | **Elimination** | Extent of renal elimination unknown, but half-life of 45 min |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

## Medication Safety Issues: Travoprost

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Xalatan | No |

**Drug Interactions: Travoprost.** None known

**Adverse Reactions: Travoprost**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Blurred vision, hyperpigmentation of eyelid, iris pigmentation | Blepharitis, pain in eye, reduced visual acuity, foreign-body sensation | Cataract |

**Efficacy Monitoring Parameters.** Reduction in IOP.

**Toxicity Monitoring Parameters.** Seek medical attention if symptoms of ocular irritation are severe.

**Key Patient Counseling Points.** Wash your hands and remove contact lenses before using the medicine. For administration, lie down or tilt your head back. With your index finger, pull down the lower lid of your eye to form a pocket. Hold the dropper close to your eye with the other hand. Drop the correct number of drops into the pocket made between your lower lid and eyeball. Gently close your eyes. Place your index finger over the inner corner of your eye for 1 min. Do not rinse or wipe the dropper or allow it to touch anything, including your eye. Put the cap on the bottle right away. Do not exceed once-daily dosing (may decrease efficacy). Separate administration of other ophthalmic agents by at least 5 min.

**Clinical Pearls.** Advise patients that there is a risk of permanent increased iris pigmentation associated with instillation of this product. May change length and number of eye lashes.

# TRAZODONE: Desyrel, Oleptro, Various

**Class:** Antidepressant

**Dosage Forms.** **Oral Tablet:** 50 mg, 100 mg, 150 mg, 300 mg; **Oral Tablet, Extended Release:** 150 mg, 300 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Depression: Immediate release, 150 mg po daily in divided doses, may titrate to 400 mg/d; extended release, 150 mg po daily hs, may titrate to 375 mg/d

**Off-Label Uses.**

1. Insomnia: Adults, 50 po daily hs

**MOA.** The mechanism of antidepressant action is not fully understood, but suspected to be related to its potentiation of serotonergic activity in the CNS by inhibiting reuptake of serotonin. Trazodone also significantly blocks histamine ($H_1$) and $\alpha_1$-adrenergic receptors.

Teva generic pictured

Mylan generic pictured

## Drug Characteristics: Trazodone

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Hepatic dysfunction, initial dose 25 mg po daily | **Absorption** | F = 65%; food increases absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | 89-95% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | >90% hepatic; CYP3A4/5 substrate |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 70-75% and 21% in feces, with a half-life of 7-10 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity, use of MAOI | **Black Box Warnings** | Suicidal ideation, not for use in children |

## Medication Safety Issues: Trazodone

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | TraZODone | Do not crush or chew ER formulation | No | traMADol, ziprasidone | No |

### Drug Interactions: Trazodone

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Amiodarone, agents that prolong QT interval | Increased risk of QT prolongation and torsades de pointes | Avoid concomitant use |
| CYP3A4/5 inhibitors | Decreased trazodone metabolism increases risk of trazodone toxicity | Consider lower trazodone dose; monitor for adverse effects |
| CYP3A4/5 inducers | Increased trazodone metabolism reduces trazodone efficacy | Monitor trazodone levels |
| Digoxin | Increased digoxin concentrations and risk of toxicity | Monitor digoxin levels |
| Fluoxetine, linezolid, paroxetine, venlafaxine | Increased risk of trazodone side effects or serotonin syndrome | Monitor for adverse effects |

### Adverse Reactions: Trazodone

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Dizziness, sedation, headache, nausea, somnolence, xerostomia | Backache, blurred vision, constipation, diarrhea, fatigue, feeling nervous, headache, hypotension, insomnia, syncope, tremor, vomiting | Bleeding risk, cardiac dysrhythmia, fractures, priapism, prolonged QT, serotonin syndrome, suicidal thoughts, torsade de pointes |

**Efficacy Monitoring Parameters.** Improvement in depressive symptoms (depressed mood, suicidal thoughts or intent, change in appetite, lack of energy, change in sleep patterns, lack of pleasure/interest in usual activities, feeling of excessive guilt/worthlessness, psychomotor retardation or agitation, difficulties in thinking/concentration/memory).

**Toxicity Monitoring Parameters.** Worsening of depression, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases. Irregular HR in patients with cardiac disease and/or risk factors associated with QT prolongation. Signs/symptoms of peripheral edema, increased HR, signs/symptoms of liver damage. Monitor ECG, LFT, SCr, BUN, and vital signs.

**Key Patient Counseling Points.** Extended-release tablet may be broken in half, but do not chew or crush. Extended-release tablets should be taken on an empty stomach, but the immediate-release tablets should be taken with food. Patients should avoid driving and other activities requiring mental alertness or coordination until drug effects are realized, as this medicine may cause dizziness or somnolence. Report signs/symptoms of priapism immediately. Report use of MAOI within the past 14 d. Advise patients against sudden discontinuation of drug. Do not drink alcohol, or use barbiturates or other CNS depressants while taking this drug.

**Clinical Pearls.** Antidepressants increased the risk of suicidal thinking and behavior in children, adolescents, and young adults in short-term studies with major depressive disorder (MDD) and other psychiatric disorders. This risk must be balanced with the clinical need. Monitor patients closely for clinical worsening, suicidality, or unusual changes in behavior.

# TRIAMCINOLONE NASAL: Nasacort AQ

**Class:** Intranasal Adrenal Glucocorticosteroid

**Dosage Forms. Nasal Spray:** 55 mcg/actuation

**Common FDA Label Indication, Dosing, and Titration.**

1. Perennial or seasonal allergic rhinitis: Children 2-5 y of age, 1 spray/nostril daily, *max* of 110 mcg/d; Children 6-12 y of age, 1 spray/nostril daily, *max* of 220 mcg/d; Children >12 y of age and Adults, initial, 2 spray/nostril daily, *max* of 220 mcg/d; maintenance, 1 spray/nostril daily, *max* of 110 mcg/d

**Off-Label Uses.** None

**MOA.** Triamcinolone has anti-inflammatory, antipruritic, and vasoconstrictive properties. Corticosteroids are thought to act by the induction of phospholipase A2 inhibitory proteins, lipocortins, resulting in suppression of the immune system. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor, arachidonic acid.

Sanofi-Aventis pictured

## Drug Characteristics: Triamcinolone Nasal

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | <2% of dose absorbed systemically after nasal administration |
| **Dose Adjustment Renal** | Not required | **Distribution** | Not absorbed |
| **Dialyzable** | Not dialyzable | **Metabolism** | Not absorbed |
| **Pregnancy Category** | C | **Elimination** | Not absorbed |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

## Medication Safety Issues: Triamcinolone Nasal

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | NasalCrom, do not use TAC as an abbreviation for triamcinolone | No |

**Drug Interactions: Triamcinolone Nasal.** None known

**Adverse Reactions: Triamcinolone Nasal**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Nasal irritation and burning, headache, pharyngitis | Epistaxis, taste perversion | Severe hypersensitivity, glaucoma, pneumonia, secondary hypocortisolism; osteoporosis |

**Efficacy Monitoring Parameters.** Control of rhinitis signs and symptoms.

**Toxicity Monitoring Parameters.** While only small amounts of triamcinolone reach systemic circulation, BMD and growth and development in children should be monitored. Routine ophthalmologic examinations should be performed. Monitor for signs and symptoms of adrenal suppression and infection.

**Key Patient Counseling Points.** Advise patients on the proper administration technique for this product. Instruct patients to monitor for signs of toxicity, especially adrenal insufficiency.

**Clinical Pearls.** Injectable, oral inhalation, and topical dosage forms of triamcinolone also available for treatment of other allergic disorders. While oral antihistamines (either OTC or prescription) remain the mainstay for treatment of rhinitis, nasal steroids are a recommended option if symptoms are severe, unresolved with oral antihistamines, or if oral antihistamines cause undesirable adverse effects. Available OTC.

# TRIAMCINOLONE TOPICAL: Various

**Class:** Topical Corticosteroid

**Dosage Forms.** **Topical Cream:** 0.025%, 0.1%, 0.5%; **Topical Lotion:** 0.025%, 0.1%; **Topical Ointment:** 0.025%, 0.05%, 0.1%, 0.5%

**Common FDA Label Indication, Dosing, and Titration.**

1. Skin disorders: Apply thin layer topically to affected area daily or bid

**Off-Label Uses.** None

**MOA.** Triamcinolone has anti-inflammatory, antipruritic, and vasoconstrictive properties. Corticosteroids are thought to act by the induction of phospholipase A2 inhibitory proteins, lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor, arachidonic acid.

Fougera generic 0.025% cream pictured

## Drug Characteristics: Triamcinolone Topical

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | Minimal absorption unless covering large surface area or covering areas lacking skin integrity |
| **Dose Adjustment Renal** | Not required | **Distribution** | Not absorbed |
| **Dialyzable** | Not dialyzable | **Metabolism** | Not absorbed |
| **Pregnancy Category** | C | **Elimination** | Not absorbed |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

## Medication Safety Issues: Triamcinolone Topical

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Ketalar | No |

**Drug Interactions: Triamcinolone Topical.** None known

**Adverse Reactions: Triamcinolone Topical**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| | Dry skin, burning sensation, stinging, pruritus/atrophy at site of administration | HPA suppression has been reported when used with occlusive dressings over larger surface areas |

**Efficacy Monitoring Parameters.** Improvement in clinical signs of skin disorder.

**Toxicity Monitoring Parameters.** Seek medical attention if severe skin irritation or symptoms worsen after administration.

**Key Patient Counseling Points.** Apply thin layer to affected area of skin. Skin should be clean and intact at site of application. Avoid contact with eyes and do not ingest by mouth. Avoid occlusive dressings or tight-fitting clothes over site of administration.

**Clinical Pearls.** Large number of dosage formulations (foams, gels, shampoos, etc), both by prescription and OTC, are available. Oral and inhaled formulations, administered for systemic action, also available and used for similar indications as other oral corticosteroids. Application to large surface areas, prolonged use, and occlusive dressings increase risk of systemic absorption and toxicity; pediatric patients are more susceptible to systemic absorption. TAC is an error-prone abbreviation; avoid.

# TRIAMTERENE/HYDROCHLOROTHIAZIDE: Dyazide, Maxzide, Various

**Class:** Potassium Sparing/Thiazide Diuretic Combination

**Dosage Forms. Oral Capsule:** (Triamterene/Hydrochlorothiazide) 37.5 mg/25 mg, 50 mg/25 mg; **Oral Tablet:** (Triamterene/Hydrochlorothiazide) 37.5 mg/25 mg, 50 mg/25 mg, 75 mg/50 mg

37.5 mg/25 mg

50 mg/25 mg

75 mg/50 mg

Sandoz generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Edema: 37.5 mg/25 mg, 1-2 tablets or capsules po daily
2. Hypertension: 37.5 mg/25 mg, 1 tablet or capsule po daily, may titrate to 75 mg/50 mg po daily

**Off-Label Uses.** None

**MOA.** Triamterene acts directly from the distal tubular lumen on active sodium exchange for potassium and hydrogen, producing a mild diuresis that is independent of aldosterone concentration. Antihypertensive activity is inconsistent and less pronounced than with thiazides or spironolactone. Hydrochlorothiazide is a thiazide diuretic that increases sodium and chloride excretion by interfering with their reabsorption in the cortical diluting segment of the nephron; a mild diuresis of slightly concentrated urine results.

**Drug Characteristics: Triamterene/Hydrochlorothiazide**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 60-80% for hydrochlorothiazide, 30-70% for triamterene; food delays absorption |
| **Dose Adjustment Renal** | CrCl <25 mL/min, avoid use | **Distribution** | Hydrochlorothiazide is 40% protein bound, distribution limited to extracellular f uid space and kidneys; protein binding is 55-67% for triamterene |
| **Dialyzable** | Hydrochlorothiazide is not dialyzable; triamterene is removed by dialysis | **Metabolism** | Hydrochlorothiazide is not metabolized; extensive liver metabolism for triamterene |
| **Pregnancy Category** | C | **Elimination** | Hydrochlorothiazide is eliminated 50-70% unchanged in urine, with a half-life of 10-12 h; triamterene is eliminated in urine (5-10% unchanged), with a half-life of 4.3-6.5 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to hydrochlorothiazide, sulfonamides or triamterene; concomitant use of potassium supplements, potassium-containing salt substitutes, or other potassium-sparing diuretics; or in patients with anuria, acute/ chronic renal insufficiency, or hyperkalemia | **Black Box Warnings** | Hyperkalemia |

### Medication Safety Issues: Triamterene/Hydrochlorothiazide

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| -25 | No | No | No | Diazoxide, Dynacin | No |

### Drug Interactions: Triamterene/Hydrochlorothiazide

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Aliskiren, ACE-Is, angiotensin-receptor blockers, potassium-sparing diuretics | Increased risk of hypotension, hyperkalemia | Avoid concurrent use or monitor BP and serum potassium levels |
| Eplerenone, potassium supplements, salt substitutes | Increased risk of hyperkalemia and cardiac arrhythmias | Avoid concurrent use or monitor serum potassium levels |
| Calcium supplements | Increased risk of hypercalcemia | Avoid concurrent use or monitor serum calcium levels |
| Antidiabetic medications | Decreased hypoglycemic effect | Monitor FBG |
| NSAIDs | Decreased antihypertensive and diuretic effect, increased risk of nephrotoxicity | Avoid concurrent use or monitor BP and SCr |

### Adverse Reactions: Triamterene/Hydrochlorothiazide

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Hypotension, dizziness, headache | Altered sense of taste, cramps, constipation, diarrhea, dry mouth, hyperglycemia, hyperuricemia, hypokalemia, hypomagnesemia, hyponatremia, impotence, loss of appetite, nausea, orthohypotension, photosensitivity, rash, tachycardia, urticaria, vomiting | Cardiac arrhythmias, hepatitis, hyperkalemia, gout, pancreatitis, Stevens-Johnson syndrome, decreased visual acuity |

**Efficacy Monitoring Parameters.** Decreased BP, reductions in edema.

**Toxicity Monitoring Parameters.** Altered serum and urine electrolytes (calcium, magnesium, potassium, sodium), decreased renal function (increased SCr or decreased urine output), increased serum uric acid or blood glucose. Seek medical attention if skin rash, yellowing of eyes or skin, decreased urine output or symptoms of gout occur.

**Key Patient Counseling Points.** May cause dizziness. Avoid foods that are high in potassium, potassium supplements or potassium-containing salt substitutes. Avoid alcohol and NSAIDs. May cause photosensitivity; use sunscreen. Use with caution in patients with sulfonamide allergy.

**Clinical Pearls.** Safety and effectiveness not established in children.

# TRIMETHOPRIM (TMP)/SULFAMETHOXAZOLE (SMZ): Bactrim, Septra, Various

**Class:** Sulfonamide Antibiotic

**Dosage Forms.** **Oral Tablet:** (SMZ/TMP) 400 mg/80 mg (single strength), 800 mg/160 mg (double strength); **Oral Suspension:** (SMZ/TMP) 200 mg/40 mg/5 mL

Amneal generic pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Acute infective exacerbation of COPD: 800 mg SMZ and 160 mg TMP po bid × 21 d
2. HIV infection, *Pneumocystis* pneumonia: 1600 mg SMZ and 320 mg TMP po bid × 21 d
3. HIV infection, *Pneumocystis* pneumonia, prophylaxis: Adults, 800 mg SMZ and 160 mg TMP po daily; Children ≥1 mo of age, 750 mg/m$^2$/d SMZ and 150 mg/m$^2$/d TMP in 2 divided doses po 3 times/wk on consecutive days
4. Traveler's diarrhea: 800 mg SMZ and 160 mg TMP po bid × 5 d
5. Urinary tract infection: Adult, 800 mg SMZ and 160 mg TMP po bid × 10-14 d; Children ≥2 mo of age, 8 mg/kg TMP component/d po bid × 10 d

**Off-Label Uses.**

1. Sinusitis: 800 mg SMZ and 160 mg TMP po bid × 10-14 d

**MOA.** SMZ competitively inhibits the synthesis of dihydropteric acid (an inactive folic acid precursor) in microorganisms. TMP inhibits the enzymatic reduction of dihydrofolic acid to tetrahydrofolic acid. The combination is active against many bacteria and *P. carinii*. TMP/SMZ has in vitro activity against methicillin-resistant *S. aureus* (MRSA), but clinical success has been variable and unpredictable.



**Drug Characteristics: Trimethoprim/Sulfamethoxazole**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 90%, no effect of food on absorption |
| **Dose Adjustment Renal** | CrCl 15-30 mL/min, reduce dose by 50%; CrCl <15 mL/min, avoid, or reduce by 50% and increase interval to 24 h | **Distribution** | CSF |
| **Dialyzable** | Hemodialysis requires supplemental dose | **Metabolism** | Hepatic metabolism >90%, trimethoprim is CYP2C9 and CYP3A4/5 substrate. Trimethoprim is moderate inhibitor of CYP2C8 and CYP2C9 |
| **Pregnancy Category** | D | **Elimination** | SMZ: renal elimination 10-30% with a half-life of 8-11 h; TMP: renal elimination 50-75% with a half-life of 6-17 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | Individuals with G6PD deficiency are more likely to develop hemolytic anemia caused by SMZ/TMP |
| **Contraindications** | Hypersensitivity to sulfonamides, children <2 mo, pregnant patients at term, megaloblastic anemia due to folate deficiency | **Black Box Warnings** | None |

### Medication Safety Issues: Trimethoprim/Sulfamethoxazole

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| DS | No | No | No | Bacitracin, Bactine, Bactroban | No |

### Drug Interactions: Trimethoprim/Sulfamethoxazole

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Antiarrhythmic agents, agents that prolong the QT interval | Increased risk of QT prolongation and other cardiac events | Avoid concurrent use or monitor carefully and consider dose reductions |
| CYP2C8 and CYP2C9 substrates | TMP is a CYP2C8 and CYP2C9 inhibitor, decreased metabolism of substrates, increases risk of substrate toxicity | Consider decreased dose of CYP2C8 and CYP2C9 substrates |
| CYP3A4/5 and CYP2C9 inducers | Increased TMP metabolism reduces TMP efficacy | Monitor and consider dose increases of TMP |
| CYP3A4/5 and CYP2C9 inhibitors | Decreased TMP metabolism increases risk of TMP toxicity | Monitor and consider dose decreases of TMP |
| Methotrexate | Increased toxicity of methotrexate through synergistic antifolate effects of TMP | Avoid concurrent use or consider methotrexate dose reduction or monitoring methotrexate levels |

### Adverse Reactions: Trimethoprim/Sulfamethoxazole

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Diarrhea, nausea | Skin rash | Severe hypersensitivity, renal failure, hepatic failure, pancytopenia, arrhythmias, Stevens-Johnson syndrome, hyperkalemia, hypoglycemia, hemolytic anemia |

**Efficacy Monitoring Parameters.** Resolution of signs of infection within 2-3 d. Decreased episodes of *Pneumocystis* pneumonia.

**Toxicity Monitoring Parameters.** Monitor potassium in those with concurrent ACI-Is. Monitor FPG with concurrent sulfonylureas. CBC monthly if using for PCP prophylaxis. Seek medical attention for severe diarrhea, dark urine, yellowing of skin or eye, unusual bruising or bleeding, blistering skin rash, or shortness of breath.

**Key Patient Counseling Points.** Complete full course of therapy. For the suspension, shake well and store at room temperature. Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner. May cause photosensitivity; use sunscreen. Maintain adequate hydration during therapy to prevent kidney complications.

**Clinical Pearls.** Avoid use in patients with G6PD deficiency (increased risk of hemolytic anemia). Preferred agent for *Pneumocystis* pneumonia prevention in HIV-infected patients when CD4 count is <200.

# VALACYCLOVIR: Valtrex, Various

**Class:** Viral DNA Polymerase Inhibitor

**Dosage Forms. Oral Tablet:** 500 mg, 1000 mg

Ranbaxy generic 500 mg pictured

**Common FDA Label Indication, Dosing, and Titration.**

1. Genital herpes simplex: Initial episode, 1 g po bid × 10 d; recurrent, 500 mg bid × 3 d
2. Genital herpes simplex: Suppressive therapy, immunocompetent, 1 g po daily; HIV infected, 500 mg po bid
3. Herpes zoster, shingles: 1 g po tid × 7 d
4. Varicella: Children ≥2 y of age, 20 mg/kg po tid × 5 d
5. Herpes labialis (cold sores): 2 g po bid × 1 d

**Off-Label Uses.**

1. CMV prophylaxis in allogeneic stem cell transplant: 2 g po qid
2. Herpes simplex or varicella zoster in cancer patients: Prophylaxis, 500 mg po bid-tid; treatment, 1 g po tid

**MOA.** Valacyclovir is a prodrug of acyclovir. Acyclovir is an acyclic nucleoside analogue of deoxyguanosine that is selectively phosphorylated by the virus-encoded thymidine kinase to its monophosphate form. Cellular enzymes then convert the monophosphate to the active antiviral acyclovir triphosphate, which inhibits viral DNA synthesis by incorporation into viral DNA, resulting in chain termination. Acyclovir has potent activity against herpes simplex virus (HSV) I and II and varicella-zoster virus (VZV).

**Drug Characteristics: Valacyclovir**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 10-20%, no effect of food on absorption |
| **Dose Adjustment Renal** | Moderate: increase interval to q8h; Severe: increase interval to q12h | **Distribution** | Placenta, CSF, kidney, brain, lung, heart |
| **Dialyzable** | Hemodialysis removes 60% of dose. Administer dose after dialysis | **Metabolism** | Hepatic; valacyclovir is rapidly and nearly completely converted to acyclovir and l -valine by first-pass effect; acyclovir is hepatically metabolized to a very small extent by aldehyde oxidase and by alcohol and aldehyde dehydrogenase |
| **Pregnancy Category** | B | **Elimination** | Renal elimination is 61-90% with a half-life of 2-3 h |
| **Lactation** | Compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

### Medication Safety Issues: Valacyclovir

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | ValACYclovir | No | No | Acyclovir, valGANciclovir, vancomycin | No |

### Drug Interactions: Valacyclovir

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Phenytoin, fosphenytoin, valproic acid | Decreased absorption and lower plasma concentration of phenytoin | Monitor phenytoin levels and adjust if necessary |
| Varicella virus vaccine | Decreased vaccine effectiveness via antagonism | Avoid concurrent use |

### Adverse Reactions: Valacyclovir

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Malaise, headache, increased LFTs | Nausea, vomiting | Severe hypersensitivity, renal failure, TTP |

**Efficacy Monitoring Parameters.** Resolution or prevention of clinical signs of infection (lesions).

**Toxicity Monitoring Parameters.** Seek medical attention if decreased urination, unusual bruising or bleeding, blistering skin rash, or shortness of breath. Monitor CBC, LFTs, and SCr.

**Key Patient Counseling Points.** Symptoms should improve within 2-3 d; if they worsen, seek follow-up with health-care practitioner. If using for prophylaxis, this medication should reduce the number of breakouts.

**Clinical Pearls.** Not indicated for children <2 y of age. Use caution with concurrent nephrotoxins. Not for use in adults with chicken pox (varicella). Drug of choice for herpes zoster infection. Improved oral bioavailability over acyclovir, allowing bid dosing of valacyclovir (compared to 5 times/d dosing of acyclovir).

# VALSARTAN: Diovan

**Class:** Angiotensin II Receptor Antagonist

**Dosage Forms. Oral Tablet:** 40 mg, 80 mg, 160 mg, 320 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Heart failure: 40 mg po bid, may titrate to 320 mg/d
2. Hypertension: 80-160 mg po daily, may titrate to 320 mg po daily
3. Myocardial infarction: 20 mg po bid, may titrate to 320 mg po daily

**Off-Label Uses.** None

**MOA.** Valsartan is a selective, reversible, competitive antagonist of the angiotension II receptor, which is responsible for the physiologic effects of angiotensin II, including vasoconstriction, aldosterone secretion, sympathetic outflow, and stimulation of renal sodium reabsorption.

Novartis pictured

**Drug Characteristics: Valsartan**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 25%, food does not affect absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 17 L; 95% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Minimal liver metabolism |
| **Pregnancy Category** | D | **Elimination** | Renal elimination is 7-13% and bile elimination is 89% with a half-life 6-9 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity, pregnancy | **Black Box Warnings** | Pregnancy |

**Medication Safety Issues: Valsartan**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Losartan, Valstar | No |

### Drug Interactions: Valsartan

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Potassium-sparing diuretics | Increased risk of hypotension, hyperkalemia | Avoid concurrent use or monitor BP and serum potassium levels |
| ACE-Is | Increased risk of hypotension, hyperkalemia, nephrotoxicity | Avoid concurrent use or monitor BP, SCr, and potassium levels |
| Potassium supplements, salt substitutes | Increased risk of hyperkalemia and cardiac arrhythmias | Avoid concurrent use or monitor serum potassium level |
| NSAIDs | Decreased antihypertensive and natriuretic effect of valsartan, increased risk of nephrotoxicity | Avoid concurrent use or monitor BP and SCr |
| Diuretics | Increased risk of postural hypotension due to hypovolemia | Monitor BP; rise from seated position slowly |

### Adverse Reactions: Valsartan

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Dizziness | Back pain, cough, diarrhea, drowsiness, headache, hyperkalemia, hypotension, nausea, nephrotoxicity, rash, tachycardia | Angioedema, rhabdomyolysis |

**Efficacy Monitoring Parameters.** Decreased BP, signs/symptoms of heart failure.

**Toxicity Monitoring Parameters.** Signs/symptoms of hypotension, tachycardia, angioedema (swelling of the face, eyes, lips, tongue, or throat), hyperkalemia (confusion, body weakness, uneven heartbeat, or numbness/tingling in hands or feet), reduction in urination, jaundice, or skin rash. Monitor vital signs, weight, LFTs.

**Key Patient Counseling Points.** Do not discontinue abruptly. Use potassium supplements or salt substitutes only under medical supervision. This medicine may cause dizziness. Avoid driving, using machinery, or doing anything else that could be dangerous if not alert. Recommend avoiding alcohol and NSAIDs while taking this drug.

**Clinical Pearls.** ARBs can cause injury or death to the developing fetus when used during 2nd and 3rd trimesters. Therapy should be stopped as soon as possible when pregnancy is detected. In hypertensive patients with chronic kidney disease, either an ACE-I or ARB is recommended as first-line therapy to improve kidney outcomes. While ACE-Is are recommended as first-line therapy, in patients with heart failure or with ST-elevation myocardial infarctions, ARBs are recommended for patients unable to tolerate ACE-Is.

# VARDENAFIL: Levitra, Staxyn

**Class:** Erectile Dysfunction Agent

**Dosage Forms. Oral Tablet:** 2.5 mg, 5 mg, 10 mg, 20 mg; **Oral Dispersible Tablet:** 10 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Erectile dysfunction: 10-20 mg po 60 min prior to anticipated sexual activity; *max* frequency is once daily

**Off-Label Uses.** None

Bayer pictured

**MOA.** Inhibition of phosphodiesterase type 5 (PDE5) by vardenafil enhances erectile function by increasing the amount of cyclic GMP. Penile erection during sexual stimulation is mediated by the release of nitric oxide (NO) from nerve terminals and endothelial cells, which stimulates the synthesis of cyclic GMP in smooth muscle cells. Cyclic GMP causes smooth muscle relaxation and increases blood flow into the corpus cavernosum.

## Drug Characteristics: Vardenafil

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Moderate hepatic impairment, decrease dose to 5-10 mg po prior to anticipated sexual activity; severe impairment, avoid use | **Absorption** | F = 15%, minimal food effect, water reduces the absorption of orally disintegrating tablet, take without liquid |
| **Dose Adjustment Renal** | Not required, but avoid use in dialysis patients | **Distribution** | Vd = 209 L; 95% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | 90-95% hepatic, CYP3A4/5 substrate |
| **Pregnancy Category** | B | **Elimination** | <2-6% renal elimination with a half-life of 4-6 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to PDE inhibitors, concurrent nitrates | **Black Box Warnings** | None |

## Medication Safety Issues: Vardenafil

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Dispersible tablet | No | Sildenafil, tadalafil | No |

### Drug Interactions: Vardenafil

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| α-Adrenergic agents | Additive hypotension | Monitor for hypotension and consider dose reductions |
| CYP3A4/5 inducers | Increased vardenafil metabolism reduces vardenafil efficacy | Consider dose increases of vardenafil |
| CYP3A4/5 inhibitors | Decreased vardenafil metabolism increases risk of vardenafil toxicity | Reduce vardenafil dose to 2.5 mg q72h if concurrent strong inhibitors and 5 mg q24h if moderate inhibitors |
| Nitrates | Additive hypotension, potentially severe | Contraindicated |

### Adverse Reactions: Vardenafil

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Flushing, headache | Nasopharyngitis, angina, chest pain, hypotension | Myocardial infarction, seizures, strokes, sudden hearing loss, priapism |

**Efficacy Monitoring Parameters.** Improvement in sexual functioning.

**Toxicity Monitoring Parameters.** Seek medical attention if chest pain, erection lasting >4 h, tinnitus, dizziness, shortness of breath.

**Key Patient Counseling Points.** Take 60 min prior to anticipated sexual activity. Do not take more frequently than once q24h. The orally disintegrating tablet should be placed on tongue immediately upon removal from packaging; the tablet should be taken whole and not crushed or split, do not take with any liquids. Oral tablet can be taken without regard to food. If erection lasts >4 h, seek medical attention.

**Clinical Pearls.** The choice between tadalafil, sildenafil, or vardenafil is largely one of patient preference; tadalafil would be indicated in those desiring "full-day coverage." Sexual stimulation is required to initiate the local release of NO; the inhibition of PDE5 has no effect in the absence of sexual stimulation.

# VARENICLINE: Chantix

**Class:** Smoking Cessation Agent

**Dosage Forms. Oral Tablet:** 0.5 mg, 1 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Smoking cessation: Initial dose, 0.5 mg po daily × 3 d, then 0.5 mg po bid × 4 d, then 1 mg po bid for the following 11 wk; may repeat additional 12 wk treatment if patient has not stopped smoking, and if patient has stopped, may increase likelihood of long-term abstinence

**Off-Label Uses.** None

**MOA.** Varenicline binds with high affinity and selectivity at α4β2 neuronal nicotinic acetylcholine receptors. Its efficacy in smoking cessation is believed to be the result of activity at α4β2 subtype of the nicotinic receptor where its binding produces agonist activity, while simultaneously preventing nicotine binding to these receptors.

Pfizer pictured

**Drug Characteristics: Varenicline**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 99%, food has no effect on absorption |
| **Dose Adjustment Renal** | CrCl <30 mL/min, initial dose 0.5 mg po daily, and titrate up to 0.5 mg po bid; patients with end-stage renal disease, use with caution at *max* dose of 0.5 mg po daily | **Distribution** | 20% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Minimal metabolism |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 92% unchanged with a half-life of 24 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | Neuropsychiatric effects, weigh risk/benefit |

**Medication Safety Issues: Varenicline**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | No |

### Drug Interactions: Varenicline

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Bupropion, $H_2$-antagonsits, quinolone antibiotics, trimethoprim | May increase varenicline serum concentration via unknown mechanisms | Monitor for adverse effects and consider dose decreases |

### Adverse Reactions: Varenicline

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Dream disorder, nausea, headache, insomnia | Constipation, f atulence, vomiting | Abnormal behavior, suicidal thoughts, angioedema, hypersensitivity reactions, increased risk of accidents, increased risk of cardiovascular related events |

**Efficacy Monitoring Parameters.** Abstinence from tobacco

**Toxicity Monitoring Parameters.** Seek medical attention if patient experiences severe abnormal behavior or suicidal thoughts.

**Key Patient Counseling Points.** Take drug after eating and with a full glass (8 oz) of water. If agitation, depressed mood, changes in behavior or thinking, or suicidal ideation, stop taking and contact health-care provider. May be used with other nicotine replacement products to help alleviate withdrawal from nicotine.

**Clinical Pearls.** Serious neuropsychiatric symptoms have been reported in patients being treated with varenicline. It may occur in patients without a history of psychiatric illness, although patients with bipolar disorder, depression, schizophrenia, or suicidal ideation appear to be at increased risk. Patients who continue to smoke are also at increased risk. FAA has banned its use in pilots and air traffic controllers. Patients and health-care providers should weigh the risks of taking varenicline against the benefits of smoking cessation. In a recent meta-analysis, there was an increased, but not statistically significant, incidence of major adverse cardiovascular events (a combined outcome of cardiovascular-related death, nonfatal myocardial infarction, and nonfatal stroke) in patients using varenicline when compared to placebo. Dispense with FDA-approved medication guide.

# VARICELLA VACCINE, LIVE: Varivax

**Class:** Vaccine, Live, Viral

**Dosage Forms.** **Lyophilized Powder for Subcutaneous Injection:** 0.5 mL after reconstitution with diluent supplied; also available in combination with measles, mumps, and rubella vaccine

**Common FDA Label Indication, Dosing, and Titration.**

1. Prevention of varicella infection: Adults, 2 doses separated by at least 4 wk; Children, 1 dose at 12 mo of age with a 2nd dose at 4-6 y of age, prior to entering school

**Off-Label Uses.** None

Merck pictured

| | | | |
|---|---|---|---|
| **Pregnancy Category** | Contraindicated | **ADME** | None known |
| **Lactation** | Infant risk is likely minimal | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to varicella vaccine or a component of the vaccine; immunosuppression; pregnancy | **Black Box Warnings** | None |

**Medication Safety Issues: Varicella Vaccine, Live**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | V-ZIG | No |

**Drug Interactions: Varicella Vaccine, Live**

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Aspirin, salicylates | Increased risk of Reye syndrome | Avoid giving salicylates to children for the 6 wk following varicella vaccine administration |
| Moderate- to high-dose corticosteroids | Immunosuppression and increased risk of infection by vaccine | Delay varicella vaccine administration until corticosteroid therapy has been discontinued |
| Immunosuppressing agents, including cyclosporine, cancer chemotherapy | Immunosuppression and increased risk of infection by vaccine | Delay varicella vaccine administration until immunosuppressive therapy has been discontinued |
| Immune globulin or blood products | Interference with immune response to live vaccines | Delay varicella vaccine administration for a period of time depending on type and dose of immune globulin or blood product |

**Adverse Reactions: Varicella Vaccine, Live**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Injection site reactions, including erythema and soreness. Headache, irritability, and somnolence | Fever, rash, GI symptoms, lymphadenopathy | Thrombocytopenia, anaphylaxis, herpes zoster, febrile seizure |

**Efficacy Monitoring Parameters.** Prevention of varicella infection, although antibody concentrations might be measured; routine measurement for vaccine response is not recommended.

**Toxicity Monitoring Parameters.** Monitor for fever and rash.

**Key Patient Counseling Points.** Some children may experience mild fever and rash 7-10 d after vaccine administration.

**Clinical Pearls.** Varicella vaccine contains the same vaccine virus as zoster vaccine, but the doses are dramatically different and are not interchangeable. Indicators of varicella immunity include birth in the United States before 1980, physician-documented history of disease, laboratory evidence of immunity, or 2 doses of varicella vaccine after 12 mo of age. Individuals born in the United States before 1980 can be considered immune to varicella unless health-care personnel, immunocompromised, or pregnant woman. Transmission of the vaccine virus to susceptible individuals without serious lasting consequences has been documented. If not administered simultaneously, varicella vaccine must be separated by at least 4 wk from other live vaccines. Febrile seizure is more common with the combination measles-mumps-rubella-varicella vaccine compared to MMR and varicella vaccines given as separate injections. Pregnant women exposed to varicella should not receive vaccine; instead, should receive varicella zoster immune globulin.

# VENLAFAXINE: Effexor, Effexor XR, Various

**Class:** Antidepressant, Serotonin/Norepinephrine Reuptake Inhibitor

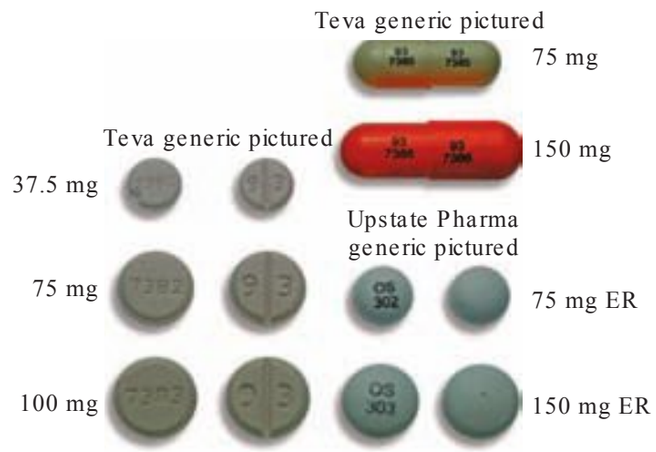
**Dosage Forms.** **Oral Capsule, Extended Release:** 37.5 mg, 75 mg, 150 mg; **Oral Tablet:** 25 mg, 37.5 mg, 50 mg, 75 mg, 100 mg; **Oral Tablet, Extended Release:** 37.5 mg, 75 mg 150 mg, 225 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Generalized anxiety disorder: Extended release, 37.5-75 mg po daily, may titrate to 225 mg/d
2. Depression: Immediate release, 75 mg po daily in 2-3 divided doses, may titrate to 225 mg/d; extended release, 37.5-75 mg po daily, may titrate to 225 mg/d
3. Panic disorder: Extended release, 37.5 mg po daily × 7 d, then 75 mg po daily, then may titrate to 225 mg/d
4. Social anxiety disorder: Extended release, 75 mg po daily

**Off-Label Uses.**

1. OCD: Immediate release, 25 mg po tid, may titrate to 300 mg/d
2. Hot flashes: 37.5-75 mg po daily




**MOA.** Potent reuptake inhibitor of serotonin and norepinephrine but lacks effects on muscarinic, α-adrenergic, or histamine receptors.

**Drug Characteristics: Venlafaxine**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Mild-moderate liver impairment, decrease dose by 25-50%; severe impairment, avoid | **Absorption** | F = 12.6% (immediate release), 45% (extended release); no effect of food on absorption |
| **Dose Adjustment Renal** | Mild-moderate renal impairment, decrease dose by 25-50%; dialysis, decrease dose by 50% | **Distribution** | Vd = 7.5 L; 27-30% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | 87% hepatic, CYP2D6 and CYP3A4/5 substrate |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 87% (82% as metabolites, 5% unchanged) with a half-life of 5 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | Venlafaxine metabolized to an active metabolite by CYP2D6. Poor CYP2D6 metabolizers have higher concentrations of venlafaxine, but similar clinical effects. |
| **Contraindications** | Hypersensitivity; MAOIs | **Black Box Warnings** | Suicidal ideation |

## Medication Safety Issues: Venlafaxine

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| XR | No | Do not crush, chew ER formulations. Capsule may be sprinkled on food | No | No | No |

## Drug Interactions: Venlafaxine

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Agents that prolong the QT interval | Increased risk of cardiotoxicity | Avoid concurrent use |
| Anticoagulants, antiplatelet drugs, NSAIDs | Increased risk of bleeding | Monitor for bleeding, avoid concurrent use if possible |
| CYP3A4/5, CYP2D6 inhibitors | Decreased venlafaxine metabolism increases risk of venlafaxine toxicity | Avoid concurrent use or monitor for adverse effects; consider dose decrease |
| CYP3A4/5 inducers | Increased venlafaxine metabolism reduces venlafaxine efficacy | Monitor for efficacy and consider dose increase |
| Dextroamphetamine, SSRIs, sumatriptan, tramadol, trazodone, zolmitriptan, linezolid | Increased risk of serotonin syndrome | Monitor closely for symptoms of serotonin syndrome, linezolid contraindicated |

## Adverse Reactions: Venlafaxine

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Dizziness, headache, insomnia, nausea, somnolence, xerostomia | Anxiety, asthenia, bleeding, blurred vision, diaphoresis, hypertension, hyponatremia, hypercholesterolemia, sexual dysfunction, tremor, vomiting, weight loss, sexual dysfunction | GI hemorrhage, hepatotoxicity, serotonin syndrome, suicidal thoughts |

**Efficacy Monitoring Parameters.** Improvement in depression, anxiety, and panic symptoms.

**Toxicity Monitoring Parameters.** Worsening of depression, suicidality, or unusual changes in behavior, especially at the initiation of therapy or with dosage increases or decreases; signs/symptoms of abnormal bleeding; signs/symptoms of serotonin syndrome; monitor BP, LFT, serum cholesterol levels, in case of severe impairment at baseline and periodically during therapy; signs/symptoms of hyponatremia, especially in patients on concomitant diuretics, volume-depleted patients, and elderly.

**Key Patient Counseling Points.** Take venlafaxine with food, but avoid alcohol. Extended-release capsules and tablets should be swallowed whole. Contents of extended-release capsules may be sprinkled on food and swallowed without chewing, followed by water. Symptomatic improvement may not be evident for a few weeks. Do not discontinue drug abruptly, as this may precipitate withdrawal symptoms such as dysphoric mood, irritability, and agitation. Avoid activities requiring mental alertness; may cause dizziness or somnolence.

**Clinical Pearls.** May convert to extended-release capsules or tablets based on nearest equivalent dose (mg/d) of stable immediate-release dose.

# VERAPAMIL: Calan, Calan SR, Isoptin SR, Various

**Class:** Calcium Channel Blocker

**Dosage Forms. Oral Tablet:** 40 mg, 80 mg, 120 mg; **Oral Tablet, Extended Release:** 120 mg, 180 mg, 240 mg; **Oral Capsule, Extended Release:** 100 mg, 120 mg, 180 mg, 200 mg, 240 mg, 300 mg, 360 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Angina: Immediate release, 80-120 mg po tid; extended release, 180 mg po daily hs, may titrate to 480 mg po daily
2. Atrial arrhythmia or paroxysmal supraventricular tachycardia prophylaxis: Immediate release, 240-320 mg/d in 3-4 divided doses, may titrate to 480 mg/d in nondigitalized patients
3. Hypertension: Immediate release, 80 mg po tid, may titrate to 360-480 mg/d; extended release, 180-200 mg po daily hs, may titrate to 400-480 mg po daily; sustained release 180 mg po daily in am, may titrate to 240-480 mg/d

**Off-Label Uses.** None

**MOA.** Inhibits calcium "slow channels" on vascular smooth muscle and myocardium producing relaxation of muscle and vasodilation. Increases myocardial oxygen delivery and slow conduction through the AV node.

Mylan generic pictured

Mylan generic 120 mg pictured

Teva generic 240 mg pictured

**Drug Characteristics: Verapamil**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Reduce dose by 20-50% | **Absorption** | F = 13-65%; no affect of food on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 3.89 L/kg; 86-94% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | 70% and occurs by CYP3A4/5, moderate inhibitor of CYP3A4/5 |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 70% (3-4% unchanged) and 9-16% in feces, with a half-life of 4-12 h |
| **Lactation** | Compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to verapamil; symptomatic hypotension (systolic BP <90 mm Hg); 2nd- or 3rd-degree AV heart block, sick sinus syndrome; severe left ventricular dysfunction (ejection fraction <30%) | **Black Box Warnings** | None |

### Medication Safety Issues: Verapamil

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| SR, PM | No | Do not crush or chew sustained or extended-release products | Yes (IV only) | Colace | No |

### Drug Interactions: Verapamil

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Amiodarone, beta-blockers | Increased risk of bradycardia, heart block (amiodarone), sinus arrest, AV conduction disturbances (beta-blockers) | Avoid concurrent use in patients with sick sinus syndrome or AV block or monitor BP and HR |
| CYP3A4/5 inhibitors | Decreased verapamil metabolism increases the risk of verapamil toxicity | Avoid concurrent use or monitor for adverse effects |
| CYP3A4/5 inducers | Increased verapamil metabolism decreases verapamil efficacy | Monitor for efficacy; consider dose increase |
| CYP3A4/5 substrates | Increased substrate concentration and increased substrate toxicity via inhibition of CYP3A4/5 by verapamil | Avoid narrow therapeutic index concurrent medications; otherwise monitor and consider dose reductions |
| Disopyramide | May aggravate or precipitate heart failure | Avoid giving disopyramide 48 h before or for 24 h after verapamil |

### Adverse Reactions: Verapamil

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Gingival hyperplasia | Bradyarrhythmia, constipation, dizziness, fatigue, headache, hypotension, indigestion, nausea, palpitations, peripheral edema, rash, syncope, elevated liver enzymes | Congestive heart failure, heart block, hepatotoxicity, pulmonary edema |

**Efficacy Monitoring Parameters.** Decreased BP, improvement in HR and rhythm, reduction in chest pain, decreased number of weekly angina attacks, reduction in use of nitroglycerin for chest pain.

**Toxicity Monitoring Parameters.** Signs/symptoms of heart failure, decreased HR, signs/symptoms of liver toxicity. Exacerbations of angina pectoris or acute coronary insufficiency; while tapering chronic therapy, especially in patients with ischemic heart disease. Monitor LFTs, ECG, and vital signs.

**Key Patient Counseling Points.** Do not crush or chew extended-release products. Contents of extended-release capsules may be sprinkled on food and swallowed without chewing, followed by water. Instruct patient to report symptomatic hypotension, bradyarrhythmia, peripheral edema, or syncope. Advise patients against sudden discontinuation of drug, as this may precipitate hypertensive rebound/crisis. Rise slowly from a sitting or lying position to avoid dizziness.

**Clinical Pearls.** Not approved in children <18 y of age.

# VILAZODONE: Viibryd

**Class:** Antidepressant, SSRI/5-$HT_{1A}$ Receptor Partial Agonist

**Dosage Forms. Oral Tablet:** 10 mg, 20 mg, 40 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Depression: Adults, 10 mg po once daily × 7 d, then 20 mg po once daily × 7 d, then 40 mg po daily

**Off-Label Uses.** None

**MOA.** Vilazodone inhibits CNS neuron serotonin uptake, with minimal or no effect on reuptake of norepinephrine or dopamine. It binds selectively with high affinity to 5-$HT_{1A}$ receptors (altered in depression and anxiety patients) and is a 5-$HT_{1A}$ receptor partial agonist.

**Drug Characteristics: Vilazodone**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 72% with food; food increases AUC 50% |
| **Dose Adjustment Renal** | Not required | **Distribution** | Widely distributed; 96-99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | Hepatic, CYP3A4/5 substrate |
| **Pregnancy Category** | C | **Elimination** | Renal elimination (primarily as metabolites), with a half-life of 25 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity; concurrent use of MAOI | **Black Box Warnings** | Suicidal thinking and suicidal behavior |



**Medication Safety Issues: Vilazodone**

| Suf xes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Lurasidone, paliperidone, risperidone, ziprasidone | No |

### Drug Interactions: Vilazodone

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| CYP3A4/5 inducers | Increased vilazodone metabolism reduces vilazodone effectiveness | Monitor and consider dose increases of vilazodone |
| CYP3A4/5 inhibitors | Decreased vilazodone metabolism increases risk of vilazodone toxicity | Monitor and consider dose decreases of vilazodone |
| Triptans, SSRIs, dextroamphetamine, tramadol, MAOIs | Increased risk of serotonin syndrome | Monitor closely for symptoms of serotonin syndrome (restlessness, hyperthermia, hyperref exia, incoordination) |

### Adverse Reactions: Vilazodone

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Diarrhea, nausea | Palpitations, dizziness, insomnia, fatigue, drowsiness, restlessness, migraine, sedation, xerostomia, arthralgia, sexual dysfunction | Hyponatremia, serotonin syndrome |

**Efficacy Monitoring Parameters.** Reduction in symptoms of depression.

**Toxicity Monitoring Parameters.** Signs and symptoms of withdrawal upon abrupt dose reduction or discontinuation. Signs and symptoms of serotonin syndrome or akatheisia. Monitor for suicidal ideation.

**Key Patient Counseling Points.** Patient should avoid activities requiring mental alertness or coordination until drug effects are realized. Advise patient that symptomatic improvement may not be seen for a few weeks. Advise patient against sudden discontinuation of drug. Patient may take with or without food, but should always take drug consistently. Patient should not drink alcohol or large amounts of grapefruit juice while taking this drug. Avoid concomitant use with MAO inhibitors.

**Clinical Pearls.** Safety and efficacy not established in pediatric patients <18 y of age.

# WARFARIN: Coumadin, Various

**Class:** Anticoagulant, Vitamin K Antagonist

**Dosage Forms. Oral Tablet:** 1 mg, 2 mg, 2.5 mg, 3 mg, 4 mg, 5 mg, 6 mg, 7.5 mg, 10 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Multiple FDA-labeled indications, all dosed similarly, including atrial fibrillation; myocardial infarction; prosthetic cardiac valve component embolism; pulmonary embolism; thrombosis, postmyocardial infarction; venous thromboembolism: Initial, 2-5 mg po daily, adjust dose based on INR; usual maintenance 2-10 mg po daily

**Off-Label Uses.**

1. Prevention of transient ischemic attacks: Initial, 2-5 mg po daily, adjust dose based on INR; usual maintenance 2-10 mg po daily

**MOA.** Warfarin prevents the conversion of vitamin K back to its active form from vitamin K epoxide. This impairs formation of the vitamin K–dependent clotting factors II, VII, IX, and X (prothrombin) and proteins C and S (physiologic anticoagulants).

Taro generic pictured

**Drug Characteristics: Warfarin**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Initial dose should be <5 mg po daily, adjust dose based on INR | **Absorption** | F = 100%; no effect of food on absorption |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 0.14 L/kg; protein binding 99% |
| **Dialyzable** | Not dialyzable | **Metabolism** | >90% hepatic, CYP2C9 substrate |
| **Pregnancy Category** | X | **Elimination** | Renal elimination of metabolites is 92% with a half-life of 20-60 h |
| **Lactation** | Compatible | **Pharmacogenetics** | CYP2C9 and VKORC1 genetic variation may be useful in initial dosing of warfarin |
| **Contraindications** | Hypersensitivity, bleeding tendencies recent or potential surgery, uncontrolled hypertension; pericarditis or pericardial effusion; bacterial endocarditis; noncompliant patients, eclampsia/preeclampsia, threatened abortion, pregnancy | **Black Box Warnings** | Bleeding |

### Medication Safety Issues: Warfarin

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | Yes | Avandia | No |

### Drug Interactions: Warfarin

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Agents with a risk of bleeding, antiplatelet agents, direct thrombin inhibitors, NSAIDs, acetaminophen, others | Additive effects and increased risk of bleeding | Monitor for signs/symptoms of bleeding; measure INR and avoid concurrent use if possible |
| CYP2C9 inhibitors | Decreased warfarin metabolism increases risk of warfarin toxicity | Use caution with concomitant therapy; monitor INR and adjust warfarin dose |
| CYP2C9 inducers | Increased warfarin metabolism decreases warfarin efficacy | Use caution with concomitant therapy; monitor INR and adjust warfarin dose |
| Sucralfate | Inhibits warfarin absorption | Separate administration by 1-2 h |

### Adverse Reactions: Warfarin

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Bleeding | Anemia, epistaxis, rash | Hemorrhage (particularly GI tract), purple toe syndrome, tissue necrosis |

**Efficacy Monitoring Parameters.** Measure initial INR after the first 2-3 doses and subsequently at intervals no longer than every 4 wk, once stable dose has been achieved; may monitor every 12 wk in stable patients, use clinical judgment; patients at high risk of bleeding require more frequent monitoring. INR target and therapeutic range depend on indication. Atrial fibrillation/atrial flutter: target 2.5 (range 2-3); prosthetic heart valves: target 2.5 (range 2-3); mechanical mitral or aortic valve: target 3 (range 2.5-3.5); myocardial infarction, ST segment elevation: target 3 (2.5-3.5, with aspirin); venous thromboembolism, prophylaxis and treatment (including pulmonary embolism, DVT, hip/knee arthroplasty): target 2.5 (range 2-3).

**Toxicity Monitoring Parameters.** Signs/symptoms of bleeding, CBC, LFT, stool guaiac test.

**Key Patient Counseling Points.** Report signs/symptoms of hemorrhage, skin and tissue necrosis. Avoid situations/activities in which cuts, bruising, or injury is likely to occur. Many significant drug-drug interactions, consult health-care professional prior to new prescription or OTC use. Avoid alcohol, cranberry products, and drastic changes in vitamin K consumption from diet (cruciferous vegetables).

**Clinical Pearls.** Patients often managed in pharmacist-run anticoagulation clinics. Consult local protocols. Excessive anticoagulation with warfarin can be corrected with vitamin K. Pharmacogenetic testing for initial dosing of warfarin decreases the time required to achieve a therapeutic INR, but improved clinical efficacy and decreased adverse effects have not been achieved; therefore pharmacogenetic testing is not routine.

# ZIPRASIDONE: Geodon

**Class:** Second-Generation Antipsychotic

**Dosage Forms.** **Oral Capsule:** 20 mg, 40 mg, 60 mg, 80 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Bipolar disorder, acute manic or mixed episodes, monotherapy, or adjunct to lithium or valproate: 40-80 mg po bid
2. Schizophrenia: 20 mg po bid, may titrate to 40-100 mg bid

Pfizer 60 mg pictured

**Off-Label Uses.**

1. Psychosis and agitation related to Alzheimer dementia: 20-80 mg po bid

**MOA.** Ziprasidone is an atypical antipsychotic drug with a very high ratio of 5-$HT_{2A}$ to dopamine-2 blockade, suggesting a very low risk of extrapyramidal effects. In addition, it is a 5-$HT_{1A}$ agonist and inhibits reuptake of both serotonin and norepinephrine like antidepressants. The clinical value of the latter 2 effects is not established.

**Drug Characteristics: Ziprasidone**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F = 60%; food increases absorption twofold |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 1.5 L/kg; >99% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | >95% and occurs by aldehyde oxidase |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is 20% (<1% unchanged) and 66% in feces (<4% unchanged), with a half-life of 7 h |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to ziprasidone; acute or recent myocardial infarction; uncompensated heart failure; QT prolongation, including congenital long QT syndrome; concomitant administration of other drugs that cause QT prolongation | **Black Box Warnings** | Elderly patients with dementia are at increased risk of death |

### Medication Safety Issues: Ziprasidone

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | TraZODone | Avoid use for behavioral problems of dementia unless nonpharmacologic options have failed and patient is threat to self or others |

### Drug Interactions: Ziprasidone

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Agents that increase QT interval | Increased risk of cardiotoxicity (QT prolongation, torsades de pointes, cardiac arrest) | Concomitant use contraindicated |
| Carbamazepine | Decreased ziprasidone concentrations | Use with caution; monitor ziprasidone efficacy |

### Adverse Reactions: Ziprasidone

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Dizziness, extrapyramidal disease, headache, nausea, somnolence | Abnormal vision, akathisia, anxiety, asthenia, constipation, diarrhea, indigestion, rash, spasmodic movement, tremor, weight gain, vomiting, xerostomia | Bone marrow depression, diabetes, neuroleptic malignant syndrome, prolonged QT interval, syncope, tardive dyskinesia, torsades de pointes |

**Efficacy Monitoring Parameters.** Improvement in signs and symptoms of schizophrenia or manic or mixed episodes associated with bipolar disorder.

**Toxicity Monitoring Parameters.** FPG and CBC at baseline and periodically during therapy; patients at high risk for suicide should be closely supervised during therapy. Monitor vital signs, including temperature.

**Key Patient Counseling Points.** Take with food but avoid alcohol. Avoid activities requiring mental alertness or coordination, as this medicine may cause dizziness and somnolence. Use caution with activities leading to an increased core temperature, such as strenuous exercise, exposure to extreme heat, or dehydration. Rise slowly from a sitting/supine position, as drug may cause orthostatic hypotension. Report signs/symptoms of bradycardia, arrhythmia, tardive dyskinesia, or neuroleptic malignant syndrome.

**Clinical Pearls.** Safety and effectiveness in pediatric patients have not been established. Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Not approved for dementia-related psychosis.

# ZOLPIDEM: Ambien, Various

**Class:** Nonbarbiturate Hypnotic

**C-IV**

**Dosage Forms.** **Oral Tablet:** 5 mg, 10 mg; **Oral Tablet, Extended Release:** 6.25 mg, 12.5 mg; **Sublingual Tablet:** 1.75 mg, 3.5 mg, 5 mg, 10 mg; **Oromucosal Spray:** 5 mg/actuation

**Common FDA Label Indication, Dosing, and Titration.**

1. Insomnia, short-term treatment: Immediate release, spray or sublingual, 1.75-5 mg (females), 3.5-10 mg (males) po daily hs; extended release, 6.25 mg (females), 6.25-12.5 mg (males) po daily hs

**Off-Label Uses.** None

**MOA.** Zolpidem binds the benzodiazepine receptor but is structurally different from a benzodiazepine. Sedative and hypnotic effects due to increased chloride conductance, neuronal hyperpolarization, inhibition of action potential, and decrease in neuronal excitability.

Wockhardt generic 5 mg pictured

**Drug Characteristics: Zolpidem**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Moderate or severe hepatic failure: reduce dose by 50% | **Absorption** | F = 70%, food decreases absorption; Cmax and AUC increased ~45% in females |
| **Dose Adjustment Renal** | Not required | **Distribution** | Vd = 0.54 L/kg; 93% protein bound |
| **Dialyzable** | Not dialyzable | **Metabolism** | >99% hepatic, CYP3A4/5 (60%) and CYP2C9 (20%) substrate, other CYPs with small contributions |
| **Pregnancy Category** | C | **Elimination** | Renal elimination is <1% with a half-life of 3 h |
| **Lactation** | Usually compatible | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity | **Black Box Warnings** | None |

**Medication Safety Issues: Zolpidem**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| CR | No | Do not crush or chew ER tablets or SL tablet | No | Abilify, Ativan | Avoid chronic use (>90 d) |

### Drug Interactions: Zolpidem

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Benzodiazepines, CNS depressants, TCAs | Additive CNS depression | Avoid if possible and consider dose reductions of both agents |
| Bupropion, desipramine, sertraline, venlafaxine | Increased risk of hallucinations | Avoid if possible and consider dose reductions of both agents |
| CYP3A4/5 inhibitors | Decreased zolpidem metabolism increases risk of zolpidem toxicity | Avoid concurrent use or consider dose reductions |
| CYP3A4/5 inducers | Increased zolpidem metabolism decreases efficacy | Avoid concurrent use or consider dose increases |

### Adverse Reactions: Zolpidem

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Dizziness, drowsiness, headache | Chest pain, blurred vision, nausea, diarrhea, confusion, impaired motor coordination, somnolence | Tachycardia, complex behavior, abnormal thinking, behavior changes, anaphylaxis, worsening of depression, angioedema, drug dependence |

**Efficacy Monitoring Parameters.** Improved ability to fall asleep and sleep through the night. Increased daytime alertness.

**Toxicity Monitoring Parameters.** Seek medical attention if severe drowsiness, thoughts of suicide, allergic reaction, irregular respiratory rate, fast or irregular heartbeat.

**Key Patient Counseling Points.** Take on an empty stomach. May cause drowsiness; avoid driving or other tasks requiring motor coordination. Avoid alcohol. Take immediately prior to bedtime. May interfere with complex behaviors (driving, talking on phone, etc, while not fully awake); bed partner should monitor irregular respiratory rate for abnormalities.

**Clinical Pearls.** Not for long-term use (usually 7-10 d only). Use caution in elderly, appear more sensitive to the effects; dose reductions of 50% have been recommended. Use of CNS depressants with caution, may have additive effects. Recommended dose for immediate-release products was recently lowered from 10 to 5 mg and from 12.5 to 6.25 mg for extended-release products in women to reduce risk of morning somnolence. Dispense with medication safety guide.

# ZOSTER VACCINE, LIVE: Zostavax

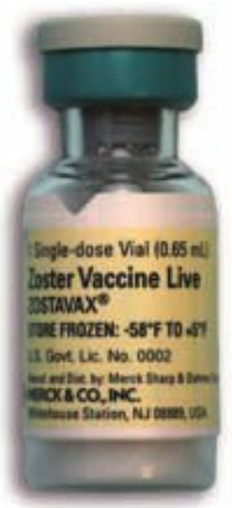
**Class:** Vaccine, Live, Viral

**Dosage Forms. Suspension for Subcutaneous Injection:** 0.65 mL after reconstitution

**Common FDA Label Indication, Dosing, and Titration.**

1. Prevention of herpes zoster (zoster, shingles): Adults, single dose for adults ≥50 y of age

**Off-Label Uses.** None



Merck pictured

**Drug Characteristics: Zoster Vaccine, Live**

| | | | |
|---|---|---|---|
| **Pregnancy Category** | Contraindicated | **ADME** | None known |
| **Lactation** | Weigh risks and benefits | **Pharmacogenetics** | None known |
| **Contraindications** | Hypersensitivity to zoster vaccine or a component of the vaccine; immunosuppression; pregnancy | **Black Box Warnings** | None |

**Medication Safety Issues: Zoster Vaccine, Live**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | Zovirax | No |

**Drug Interactions: Zoster Vaccine, Live**

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| Moderate- to high-dose corticosteroids | Immunosuppression and increased risk of infection by vaccine virus | Delay zoster vaccine administration until corticosteroid therapy has been discontinued |
| Immunosuppressing agents; azathioprine, chemotherapy, cyclosporine | Immunosuppression and increased risk of infection by vaccine virus | Delay zoster vaccine administration until immunosuppressive therapy has been discontinued |
| Pneumococcal polysaccharide vaccine (PPSV23) | Immunological interference | Concomitant administration with PPSV23 lowers antibody concentrations to zoster vaccine; clinical consequences are unknown and no change in efficacy observed if administered simultaneously; separate vaccines by 4 wk if follow-up assured |
| Antiviral agents | Neutralization of the vaccine virus; theoretical | Hold antiviral therapy for 1 d prior to and 14 d following zoster vaccine administration |

**Adverse Reactions: Zoster Vaccine, Live**

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Injection site reactions, including erythema and soreness | Headache, f u-like symptoms | Anaphylaxis, Guillain-Barré syndrome |

**Efficacy Monitoring Parameters.** Prevention of herpes zoster (shingles).

**Toxicity Monitoring Parameters.** None.

**Key Patient Counseling Points.** About 1 in 3 individuals develops a rash at the injection site, which resolves after a few days with no treatment. The zoster vaccine is not 100% effective in preventing zoster. However, the disease and its consequences are less severe in immunized individuals who develop zoster.

**Clinical Pearls.** A history of chicken pox need not be obtained prior to zoster vaccine administration as birth before 1980 is considered evidence of varicella immunity. Consider administering the vaccine to 50-59-year-olds who are anticipating immunosuppressive therapy and those with HIV. Single dose recommended for all adults aged ≥60 y without regard to history of shingles; zoster vaccine may be administered to individuals on inhaled, topical, or intra-articular steroids or low-dose oral steroids; treated with low-dose methotrexate (<0.4 mg/kg/wk) or 6-mercaptopurine (<1.5 mg/kg/d), anticipating immunosuppressive therapy if vaccine can be administered at least 14 d prior or on antiviral therapy if it is stopped 1 d prior to vaccine administration and held for 14 d. Zoster vaccine can be administered to individuals with HIV if no manifestations of AIDS and CD4 count >200/$mm^3$.

# SOFOSBUVIR: Sovaldi

**Class:** Polymerase Inhibitor (Anti-HCV)

**Dosage Forms. Oral Tablet:** 400 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. Chronic hepatitis C (CHC) infection in monoinfected (HCV) or coinfected (HCV/HIV-1) patients: 400 mg po daily with concomitant ribavirin and/or peginterferon alfa (treatment regimen and duration based on HCV genotype and/or clinical scenario); HCV genotype 1 or 4, treat for 12 wk with ribavirin and peginterferon alfa; HCV genotype 2, treat for 12 wk with concomitant ribavirin; HCV genotype 3, treat for 24 wk with concomitant ribavirin
2. Patients with hepatocellular carcinoma awaiting liver transplantation: 400 mg po daily with concomitant ribavirin for 48 wk or until the time of liver transplantation, whichever occurs first

**Off-Label Uses.** None

**MOA.** A direct-acting antiviral agent against the hepatitis C virus. It inhibits HCV NS5B RNA-dependent RNA polymerase, essential for viral replication, and acts as a chain terminator.

**Drug Characteristics: Sofosbuvir**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F is unknown; food has no effect on Cmax or AUC |
| **Dose Adjustment Renal** | Primary metabolite accumulates in renal dysfunction, but no dose adjustments are required | **Distribution** | Protein binding 61-65% |
| **Dialyzable** | Yes, hemodialysis | **Metabolism** | Hepatic, P-glycoprotein substrate |
| **Pregnancy Category** | B (X in combination with ribavirin) | **Elimination** | Renal, 78% as active metabolite; half-life of parent compound, 0.4 h; half-life of active metabolite, 27 h |
| **Lactation** | Not recommended | **Pharmacogenetics** | HCV genotype determines treatment regimen |
| **Contraindications** | Because of ribavirin risk, do not use in pregnant women, or men whose female partners are pregnant | **Black Box Warnings** | None |

### Medication Safety Issues: Sofosbuvir

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | No | No | No | No |

### Drug Interactions: Sofosbuvir

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| P-glycoprotein inhibitors | Decreased sofosbuvir transport increases risk of sofosbuvir toxicity | Monitor carefully and consider sofosbuvir dose reduction |
| P-glycoprotein inducers | Increased sofosbuvir transport decreases sofosbuvir efficacy | Avoid concurrent use, or monitor carefully and consider sofosbuvir dose increases |

### Adverse Reactions: Sofosbuvir

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Fatigue, headache, insomnia, chills, pruritus, rash, nausea, anemia | Diarrhea, thrombocytopenia increased LFTs | Pancytopenia, depression, suicidality |

**Efficacy Monitoring Parameters.** Improvement in signs and symptoms of hepatitis C infection. Monitor SCr and LFTs. Serum hepatitis C viral RNA levels prior and during treatment.

**Toxicity Monitoring Parameters.** In female patients and female partners of male patients, pregnancy tests should be done prior to and during treatment.

**Key Patient Counseling Points.** Must be taken with ribavirin, and depending on viral genotype, peginterferon alfa. Pregnancy warnings (due to ribavirin risk) for female patients and female partners of male patients.

**Clinical Pearls.** Astronomically expensive (approximately $80,000 per 12-wk course of therapy). Must be used in combination with other treatments based on the viral genetic category (not the patient's genetic make-up). In patients who cannot tolerate interferon, off-label regimens have been recommended that include sofosbuvir and ribavirin alone. Off-label regimens are also recommended in patients with HCV genotype 5 and 6, and those patients who fail on treatments with sofosbuvir and/or ribavirin and peginterferon alfa.

# SIMEPREVIR: Olysio

**Class:** Polymerase Inhibitor (Anti-HCV)

**Dosage Forms. Oral Capsule:** 150 mg

**Common FDA Label Indication, Dosing, and Titration.**

1. CHC infection in patients with HCV genotype 1a: 150 mg po daily with food as part of combination regimen with concomitant ribavirin and peginterferon alfa (duration 12 wk, followed by 12 or 36 additional weeks of peginterferon alfa and ribavirin alone depending on prior response status), or with sofosbuvir (duration 12 wk in patients without cirrhosis, or 24 wk in patients with cirrhosis; screening patients with HCV genotype 1a infection for the presence of virus with the NS3 Q80K polymorphism at baseline is strongly recommended, and alternative therapy should be considered for patients infected with HCV genotype 1a containing the Q80K polymorphism

**Off-Label Uses.** None

**MOA.** A direct-acting antiviral agent against the hepatitis C virus. It inhibits HCV NS3/4A protease, essential for viral replication, and acts as a chain terminator.

**Drug Characteristics: Simeprevir**

| | | | |
|---|---|---|---|
| **Dose Adjustment Hepatic** | Not required | **Absorption** | F is unknown; food enhances AUC |
| **Dose Adjustment Renal** | Not required | **Distribution** | Protein binding >99% |
| **Dialyzable** | Unknown | **Metabolism** | Hepatic, CYP3A4/5 and P-glycoprotein substrate |
| **Pregnancy Category** | C (X in combination with ribavirin) | **Elimination** | Feces, 91%; <1% eliminated renally; half-life is 10-13 h |
| **Lactation** | Not recommended | **Pharmacogenetics** | HCV genotype determines treatment regimen |
| **Contraindications** | Because of ribavirin risk, do not use in pregnant women, or men whose female partners are pregnant | **Black Box Warnings** | None |

**Medication Safety Issues: Simeprevir**

| Suffixes | Tall Man Letters | Do Not Crush | High Alert | Confused Names | Beers Criteria |
|---|---|---|---|---|---|
| No | No | Do not chew or open capsules | No | No | No |

### Drug Interactions: Simeprevir

| Typical Agents | Mechanism | Clinical Management |
|---|---|---|
| P-glycoprotein inhibitors | Decreased simeprevir transport increases risk of simeprevir toxicity | Monitor carefully and consider simeprevir dose reduction |
| P-glycoprotein inducers | Increased simeprevir transport decreases simeprevir eff cacy | Avoid concurrent use, or monitor carefully and consider simeprevir dose increases |
| CYP3A4/5 inhibitors | Decreased simeprevir metabolism and increased risk of simeprevir toxicity | Avoid concurrent use or consider dose increases of simeprevir |
| CYP3A4/5 inducers | Increased simeprevir metabolism and decreased simeprevir eff cacy | Avoid concurrent use or consider dose decreases of simeprevir |

### Adverse Reactions: Simeprevir

| Common (>10%) | Less Common (1-10%) | Rare but Serious (<1%) |
|---|---|---|
| Fatigue, headache, dizziness, insomnia, pruritus, rash, nausea, diarrhea, increased bilirubin, myalgia, dyspnea | Photosensitivity | None |

**Efficacy Monitoring Parameters.** Improvement in signs and symptoms of hepatitis C infection. Monitor LFTs. Serum hepatitis C viral RNA levels prior and during treatment.

**Toxicity Monitoring Parameters.** In female patients and female partners of male patients, pregnancy tests should be done prior to and during treatment.

**Key Patient Counseling Points.** Must be taken in combination with other antiviral products, cannot be taken alone. Pregnancy warnings (due to ribavirin risk) for female patients and female partners of male patients. Avoid excessive sunlight and take precautions if exposed to sun. Take particular caution in patients of East Asian descent (higher risk of phototoxicity and rash).

**Clinical Pearls.** Astronomically expensive (approximately $80,000 per 12-wk course of therapy). Genetic category of HCV virus must be considered to determine appropriateness of treatment. Complicated stopping rules utilizing serum hepatitis C viral RNA levels (viral loads) used to determine overall length of treatment. Not recommended in patients who have failed simeprevir or other HCV protease inhibitor therapy in the past. Off-label dosing regimen for treatment of patients with HCV genotype 1 and 4 available.