COVER & BOTTOM

353 mm

142 mm

286.9 mm

2022-2023 2022-2023 2022-2023

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Kolesar • Vermeulen

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Jill M. Kolesar • Lee C. Vermeulen

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- Off-Label Use
- Contraindications
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- Drug Interactions
- Monitoring Parameters
- Medication Safety Issues and Black Box Warnings
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COVER & TOP

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PHARMACY

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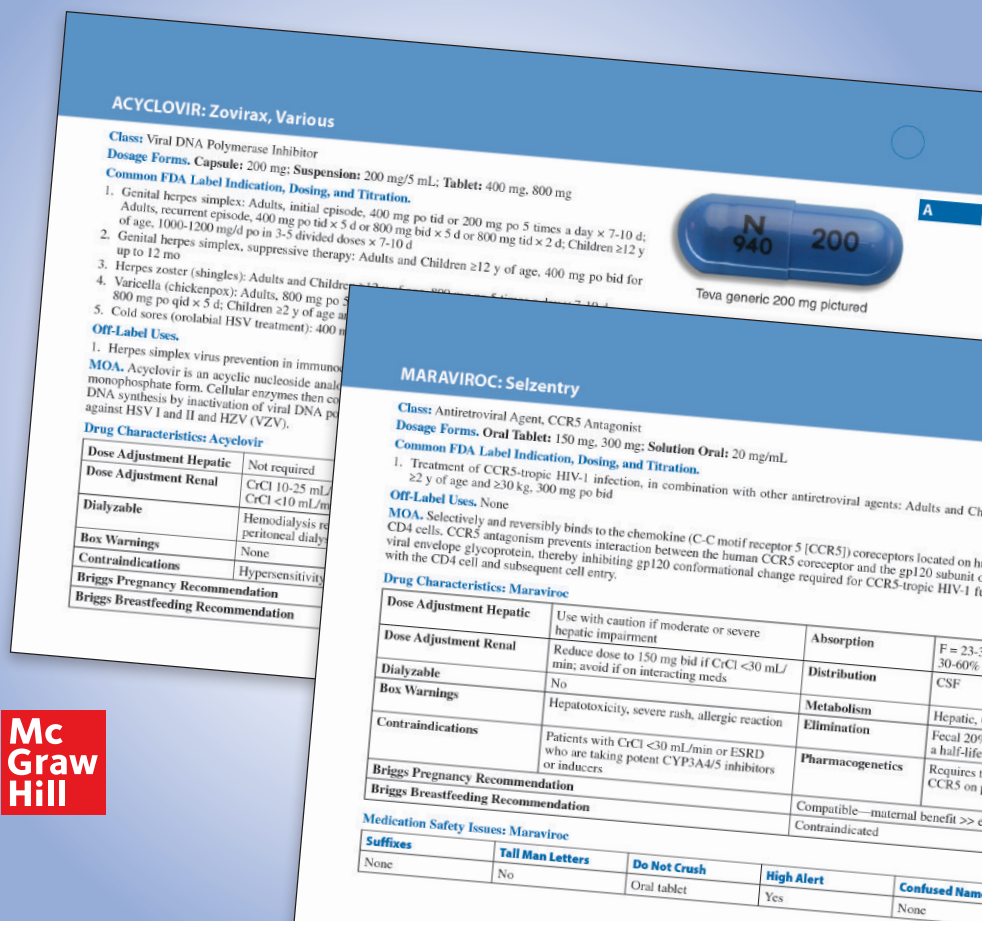

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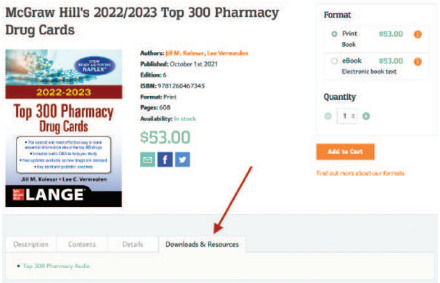
For additional Q&A Audio and drug card PDFs, included only with the purchase of *Top 300 Pharmacy Drug Cards*, go to: www.Top300DrugCards.com and click on "Downloads and Resources" tab as shown below.



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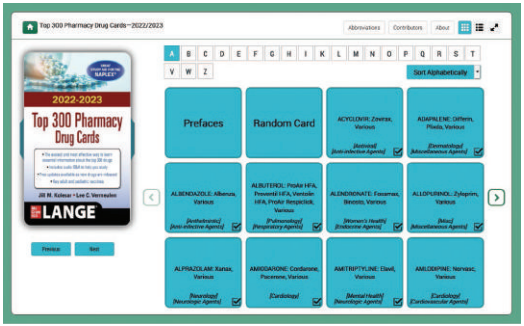

Top 300 Pharmacy Drug Cards—2022/2023

Jill M. Kolesar, PharmD, MS, BCPS, FCCP
University Research Professor, Colleges of Pharmacy and Medicine
Director, Precision Medicine Initiatives
Markey Cancer Center
University of Kentucky
Lexington, Kentucky

Lee C. Vermeulen, BSPharm, MS, FCCP, FFIP
Chief Efficiency Officer
UK HealthCare
Professor of Medicine and Pharmacy
University of Kentucky
Lexington, Kentucky

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

Notice

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Top 300 Pharmacy Drug Cards—2022/2023

1 2 3 4 5 6 7 8 9 DSS 26 25 24 23 22 21

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The editors were Michael Weitz and Kim J. Davis.
The production supervisor was Catherine Saggese.
Project management was provided by Mansi Agarwal, KnowledgeWorks Global Ltd.

Contents

Contributors

Editors
Jill M. Kolesar, PharmD, MS, BCPS, FCCP
University Research Professor, Colleges of Pharmacy and Medicine
Director, Precision Medicine Initiatives
Markey Cancer Center
University of Kentucky
Lexington, Kentucky

Lee C. Vermeulen, BSPharm, MS, FCCP, FFIP
Chief Efficiency Officer
UK HealthCare
Professor of Medicine and Pharmacy
University of Kentucky
Lexington, Kentucky

Contributing Authors
David S. Burgess, PharmD, FCCP, FIDP
Professor and Chair, Department of Pharmacy Practice and Science
University of Kentucky College of Pharmacy
Lexington, Kentucky

Donna R. Burgess, BSPharm, BCIDP
Clinical Pharmacy Coordinator, Infectious Diseases
Medication Safety, Utilization and Value
UK HealthCare
Lexington, Kentucky

Collin M. Clark, PharmD, BCPS, BCGP
Clinical Assistant Professor
Department of Pharmacy Practice
University at Buffalo School of Pharmacy and Pharmaceutical Sciences
Clinical Pharmacist—Transitions of Care
Buffalo General Medical Center
Buffalo, New York

Christopher J. Daly, PharmD, MBA, BCACP
Clinical Assistant Professor
Department of Pharmacy Practice
University at Buffalo School of Pharmacy and Pharmaceutical Sciences
Ambulatory Care Pharmacist – UBMD Family Medicine Outpatient Practice
Buffalo, New York

Fred Doloresco, PharmD, MS
Clinical Associate Professor
Director of Assessment
University at Buffalo
Consultant Pharmacist
Erie County Medical Center
Buffalo, New York

Introduction

The selection of the most commonly prescribed medications was based on a report evaluating medication use based on the number of prescriptions filled in the United States and the cost of those prescriptions.[1] Many estimates rely on data from IQVIA (formerly 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, Target Pharmacy in Madison, Wisconsin, and at the Kentucky Clinic, UK HealthCare, in Lexington, Kentucky. 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.

These cards represent over 300 of the most frequently prescribed medications and join the Top 200 Injectable Drug Cards and the Top 100 Nonprescription Drug Cards as essential learning tools for students. As with all flash cards, these cards focus on the most critical facts about each medication. They have value as a learning tool, helping to familiarize students and others with key information. They should not be considered an exhaustive reference—other reference databases should be consulted when seeking a complete resource on individual medications. 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.

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[1]Tichy EM, Schumock GT, Hoffman JM, et al. National trends in prescription drug expenditures and projections for 2020. *Am J Health Syst Pharm.* 2020;77(15):1213-1230. doi: 10.1093/ajhp/zxaa116

Acknowledgments

The editors would like to acknowledge the valuable assistance of our contributing authors, David Burgess, Donna Burgess, Collin Clark, Chris Daly, and Fred Doloresco for their outstanding work on this edition. We also wish to recognize Sheryl Krato for her assistance securing permission to reprint content from the *Briggs' Drugs in Pregnancy and Lactation* text in these cards. Special thanks to Aaron Webb, PharmD, MS, from the University of Wisconsin and UW Health, for his assistance with photographs in this edition. Finally, we would like to acknowledge Michael Weitz and the rest of the McGraw Hill team who have also been incredibly helpful for over 10 years with the development and production of this product and our other flash card products—we are grateful for their help and guidance.

Preface Card Summary

1. Preface A: Anatomy of a Flash Card
2. Preface B: Weight and Measure Equivalents
3. Preface C: Supplemental Content Related to Oral Contraceptives
4. Preface D: Guide to Cytochrome P450 (CYP) and UGT1A1 Metabolism
5. Preface E: Guide to Transporters
6. Preface F: Drugs That Affect Cardiac Rhythm
7. Preface G: Drugs Affected by Gastric pH
8. Preface H: Abbreviations

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, pharmacologic, 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. 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, including parenteral formulations (some of which may be included in the Top 200 Injectable Drug Card product), 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 1 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 1 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, regardless of whether the FDA has approved the indication or not. 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. Please note that in the interest of brevity, many off-label uses are not listed in the cards—tertiary drug information reference sources should be consulted for more information on uncommon uses of approved medications.

MOA (Mechanism of Action)

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

Drug Characteristics

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

Dose Adjustments

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 3 times a day to daily dosing). The degree of renal or hepatic 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.

Dose Adjustments Hepatic

A Child-Pugh score can be used to assess hepatic dysfunction. The score employs 5 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.

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

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.

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 website: https://www.fda.gov/drugs/scienceresearch/ucm572698.htm.

Box Warnings

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

Pregnancy Recommendations

The FDA published a final rule for revisions to the pregnancy and lactation labeling (PLLR) for medications in 2014, and those changes were scheduled to be phased in over several years, starting in 2015. Previously, product labels used a categorical system (A, B, C, D, and X) to describe the level of risk of fetal harm that medications pose when taken by pregnant women. While these categories were discrete, they were of limited clinical value in evaluating or managing fetal risk. The new PLLR now contains information from pregnancy exposure registries if available. Additional information on the FDA labeling guidance can be found at https://www.fda.gov/drugs/labeling-information-drug-products/pregnancy-and-lactation-labeling-drugs-final-rule.

While FDA product labels now contain more clinically valuable information on pregnancy and fetal risk, the most common and definitive resource on this topic is *Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk* edited by Gerald Briggs and colleagues. Since its first publication in 1983, this text has provided guidance on the extent of risks associated with various medications, but also recommendations on the most appropriate management of those risks. Permission has been granted by the publisher of this reference to reprint pregnancy recommendations from the 12th edition of the Briggs text. (Gerald G. Briggs, Craig V. Towers, Alicia B. Forinash: *Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk,* Twelfth Edition: Copyright © Wolters Kluwer. All rights reserved.)

Note: While most medications included in this card set have recommendations reprinted from the Briggs text, some are not included in that resource. In those cases, the category title on the card does not mention Briggs, and the recommendations in those cases have been prepared by the card editors, drawing information from various sources, including the product label.

COMPATIBLE

The human pregnancy experience, either for the drug itself or drugs in the same class or with similar mechanisms of action, is adequate to demonstrate that the embryo–fetal risk is very low or nonexistent. Animal reproduction data are not relevant.

NO (LIMITED) HUMAN DATA—PROBABLY COMPATIBLE

There may or may not be human pregnancy experience, but the characteristics of the drug suggest that it does not represent a significant risk to the embryo–fetus. For example, other drugs in the same class or with similar mechanisms are compatible or the drug does not obtain significant systemic concentrations. Any animal reproduction data are not relevant.

COMPATIBLE—MATERNAL BENEFIT >> EMBRYO–FETAL RISK

There may or may not be human pregnancy experience, but the potential maternal benefit far outweighs the known or unknown embryo–fetal risk. Animal reproduction data are not relevant.

HUMAN DATA SUGGEST LOW RISK

There is limited human pregnancy experience, either for the drug itself or drugs in the same class or with similar mechanisms of action, including the 1st trimester, suggesting that the drug does not represent a significant risk of developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death) at any time in pregnancy. The limited human pregnancy data outweighs any animal reproduction data.

NO (LIMITED) HUMAN DATA—ANIMAL DATA SUGGEST LOW RISK

Either there is no human pregnancy experience or the few pregnancy exposures have not been associated with developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death). The drug does not cause

developmental toxicity (at doses that did not cause maternal toxicity) in all animal species studied at doses ≤10 times the human dose based on body surface area (BSA) or AUC.

NO (LIMITED) HUMAN DATA—ANIMAL DATA SUGGEST MODERATE RISK

Either there is no human pregnancy experience or the few pregnancy exposures have not been associated with developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death). The drug causes developmental toxicity (at doses that did not cause maternal toxicity) in one animal species at doses ≤10 times the human dose based on body surface area (BSA) or AUC.

NO (LIMITED) HUMAN DATA—ANIMAL DATA SUGGEST RISK

Either there is no human pregnancy experience or the few pregnancy exposures have not been associated with developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death). The drug causes developmental toxicity (at doses that did not cause maternal toxicity) in two animal species at doses ≤10 times the human dose based on body surface area (BSA) or AUC.

NO (LIMITED) HUMAN DATA—ANIMAL DATA SUGGEST HIGH RISK

Either there is no human pregnancy experience or the few pregnancy exposures have not been associated with developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death). The drug causes developmental toxicity (at doses that did not cause maternal toxicity) in three or more animal species at doses ≤10 times the human dose based on body surface area (BSA) or AUC.

CONTRAINDICATED—1ST TRIMESTER

Human exposures in the 1st trimester, either to the drug itself or to drugs in the same class or with similar mechanisms of action, have been associated with developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death). The drug should not be used in the 1st trimester.

CONTRAINDICATED—2ND AND 3RD TRIMESTERS

Human exposures in the 2nd and 3rd trimesters, either to the drug itself or to drugs in the same class or with similar mechanisms of action, have been associated with developmental toxicity (growth restriction, structural anomalies, functional/behavior deficits, or death). The drug should not be used in the 2nd and 3rd trimesters.

CONTRAINDICATED

Human exposures at any time in pregnancy, either to the drug itself or to drugs in the same class or with similar mechanisms of action, have been associated with developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death). Animal reproduction data, if available, confirm the risk. The drug should not be used in pregnancy.

NO (LIMITED) HUMAN DATA—NO RELEVANT ANIMAL DATA

There are no human pregnancy data or relevant data in animals, or the human pregnancy experience, that may or may not include the 1st trimester, is limited. The risk in pregnancy cannot be assessed.

HUMAN DATA SUGGEST RISK IN 1ST TRIMESTER

Evidence (for the drug or similar drugs) suggests that there may be an embryo–fetal risk for developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death) in the 1st trimester but not in the 2nd and 3rd trimesters. The human pregnancy data outweigh any animal reproduction data.

HUMAN DATA SUGGEST RISK IN 1ST AND 3RD TRIMESTERS

Evidence (for the drug or similar drugs) suggests that there may be an embryo–fetal risk for developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death) in the 1st and 3rd trimesters but not in the 2nd trimester. The human pregnancy data outweigh any animal reproduction data.

HUMAN DATA SUGGEST RISK IN 2ND AND 3RD TRIMESTERS

Evidence (for the drug or similar drugs) suggests that there may be a fetal risk for developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death) in the 2nd and 3rd trimesters but not in the 1st trimester. The human pregnancy data outweigh any animal reproduction data.

HUMAN DATA SUGGEST RISK IN 3RD TRIMESTER

Evidence (for the drug or similar drugs) suggests that there may be a fetal risk for developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death) in the 3rd trimester, or close to delivery but not in the 1st or 2nd trimesters. The human pregnancy data outweigh any animal reproduction data.

HUMAN (AND ANIMAL) DATA SUGGEST RISK

The human data for the drug or drugs in the same class or with the same mechanism of action, and animal reproduction data if available, suggest that there may be a risk for developmental toxicity (growth restriction, structural anomalies, functional/behavioral deficits, or death) throughout pregnancy. Usually, pregnancy exposure should be avoided, but the risk may be acceptable if the maternal condition requires the drug.

Breastfeeding

As with the pregnancy risk information, the changes to the pregnancy and lactation labeling (PLLR) by the FDA in 2014 have provided some additional clinical guidance regarding the management of care when medications are used by patients who are breastfeeding. 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. The most common and definitive resource on this topic is *Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk* edited by Gerald Briggs and colleagues. Permission has been granted by the publisher of this reference to reprint breastfeeding recommendations from the 12th edition of the Briggs text. (Gerald G. Briggs, Craig V. Towers, Alicia B. Forinash: *Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk,* Twelfth Edition: Copyright © Wolters Kluwer. All rights reserved.)

Note: While most medications included in this card set have recommendations reprinted from the Briggs text, some are not included in that resource. In those cases, the category title on the card does not mention Briggs, and the recommendations in those cases have been prepared by the card editors, drawing information from various sources, including the product label.

For those products where Briggs recommendations are provided, each standardized recommendation is defined in their text as follows:

COMPATIBLE

Either the drug is not excreted in clinically significant amounts into human breast milk or its use during lactation does not, or is not expected to, cause toxicity in a nursing infant.

HOLD BREASTFEEDING

The drug may or may not be excreted into human breast milk, but the maternal benefit of therapy far outweighs the benefits of breast milk to an infant. Breastfeeding should be held until maternal therapy is completed and the drug has been eliminated (or reaches a low concentration) from her system.

NO (LIMITED) HUMAN DATA—PROBABLY COMPATIBLE

Either there is no human data or the human data are limited. The available data suggest that the drug does not represent a significant risk to a nursing infant.

NO (LIMITED) HUMAN DATA—POTENTIAL TOXICITY

Either there is no human data or the human data are limited. The characteristics of the drug suggest that it could represent a clinically significant risk to a nursing infant. Breastfeeding is not recommended.

HUMAN DATA SUGGEST POTENTIAL TOXICITY

Human data suggest a risk to a nursing infant. The drug is best avoided during breastfeeding. Depending on the drug, short-term use by the mother may be possible, but the infant should be closely monitored for potential adverse effects.

NO (LIMITED) HUMAN DATA—POTENTIAL TOXICITY (MOTHER)

Either there are no human data or the human data are limited. The characteristics of the drug suggest that breastfeeding could represent a clinically significant risk to the mother such as further loss of essential vitamins or nutrients. Breastfeeding is not recommended.

CONTRAINDICATED

There may or may not be human experience, but the combined data suggest that the drug may cause severe toxicity in a nursing infant, or breastfeeding is contraindicated because of the maternal condition for which the drug is indicated. Women should not breastfeed if they are taking the drug or have the condition.

Medication Safety Issues

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

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 or prefixes that are 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 website 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 Beers Criteria is a guideline maintained by the American Geriatrics Society identifying medications that should be avoided or used with caution in older patients. The guideline 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 2019 (2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2019. DOI: 10.111/jgs.15767. [Epub ahead of print]). The Beers Criteria® contains multiple tables categorizing drugs to be avoided in the elderly and those warranting caution. In these Drug Cards, those agents listed in Tables 2 and 3 of the Beers Criteria® (agents inappropriate for all older adults and agents inappropriate for some adults with specific diseases or syndromes) are highlighted. In addition, agents with strong anticholinergic properties (as shown in Table 7 of the Beers Criteria®) are highlighted. The Beers Criteria® also includes information about drug-drug interactions of particular concern in the elderly, and drugs that should be avoided in older patients with renal dysfunction; however, those warnings are not noted in these Drug Cards. Readers are encouraged to review the Beers Criteria® article referenced above for more information.

Drug Interactions

Concurrent use of multiple medications (polypharmacy) 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 D, E, F, and G. 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. 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 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.

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 (℥)
1 ounce (℥)	= 480 grains (gr)
16 ounces	= 1 pound (lb)

Apothecary Volume Equivalents

60 minims (♏)	= 1 fluidram (fl ʒ)
8 fluidrams (fl ʒ)	= 1 fluid ounce (fl ℥)
1 fluid ounce (fl ℥)	= 480 minims (♏)
16 fluid ounces (fl ℥)	= 1 pint (pt)

Avoirdupois Equivalents

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

Weight/Volume Equivalents

1 mg/dL	= 10 mcg/mL
1 mg/dL	= 1 mg%
1 ppm	= 1 mg/L

Conversion Equivalents

1 gram (g)	= 15.43 grains (gr)
1 grain (gr)	= 64.8 milligrams (mg)
1 ounce (℥)	= 31.1 grams (g)
1 ounce (oz)	= 28.35 grams (g)
1 pound (lb)	= 453.6 grams (g)
1 kilogram (kg)	= 2.2 pounds (lb)
1 milliliter (mL)	= 16.23 minims (♏)
1 minim (♏)	= 0.06 milliliter (mL)
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

Pharmacokinetics of Progestins

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

Monophasic Oral Contraceptive Contents

Estrogen Component	Progestin Component	Example Brand Names
Ethinyl estradiol 20 mcg	Drospirenone 3 mg	Beyaz, Gianvi, Loryna, Nikki, Yaz
Ethinyl estradiol 20 mcg	Levonorgestrel 0.1 mg	Aviane, Falmina, Larissia, Lessina, Lutera
Ethinyl estradiol 20 mcg	Norethindrone 1 mg	Gemmily, Junel Fe 1/20, Loestrin Fe 1/20, Microgestin Fe 1/20

Estrogen Component	Progestin Component	Example Brand Names
Ethinyl estradiol 30 mcg	Desogestrel 0.15 mg	Apri, Emoquette, Juleber, Reclipsen
Ethinyl estradiol 30 mcg	Drospirenone 3 mg	Ocella, Safyral, Tydemi, Yasmin, Zarah
Ethinyl estradiol 30 mcg	Levonorgestrel 0.15 mg	Chateal, Kurvelo, Levora, Marlissa, Portia
Ethinyl estradiol 30 mcg	Norethindrone 1.5 mg	Blisovi FE 1.5/30, Larin FE 1.5/30, Loestrin Fe 1.5/30, Junel Fe 1.5/30
Ethinyl estradiol 30 mcg	Norgestrel 0.3 mg	Cryselle, Elinest, Low-Ogestrel
Ethinyl estradiol 35 mcg	Ethynodiol 1 mg	Kelnor, Pirmella, Zovia
Ethinyl estradiol 35 mcg	Norethindrone 0.4 mg	Balziva, Briellyn, Philith, Vyfemla
Ethinyl estradiol 35 mcg	Norethindrone 0.5 mg	Brevicon, Necon, Nortrel, Wera
Ethinyl estradiol 35 mcg	Norethindrone 1 mg	Alyacen 1/35, Cyclafem 1/35, Dasetta 1/35, Nortrel 1/35, Ortho-Novum 1/35
Ethinyl estradiol 35 mcg	Norgestimate 0.25 mg	Femynor, Milia, MonoNessa, Ortho-Cyclen, Previfem, Sprintec
Ethinyl estradiol 50 mcg	Norgestrel 0.5 mg	Ogestrel 0.5/50 (Note: Not indicated for routine contraception due to risk of cardiovascular adverse effects.)

Note: Various monophasic products are available packaged with 21 active tablets and 7 inactive tablets (iron or placebo) or packaged with 24 active tablets and 4 inactive tablets (iron or placebo). Any 21-d monophasic product can also be used for continuous therapy by omitting the inactive tablets, starting the next pack of active tablets the day after the previous pack of active tablets are finished.

Multiphasic Oral Contraceptive Contents

Estrogen Component and Dose (Duration in Each Phase)	Progestin Component and Dose (Duration in Each Phase)	Example Brand Names
Ethinyl estradiol 10 mcg (d 1-26)	Norethindrone 1 mg (d 1-24)	Lo Loestrin Fe
Ethinyl estradiol 20 mcg (d 1-21, d 24-28)	Desogestrel 0.15 mg (d 1-21)	Azurette, Bekyree, Kariva, Mircette, Viorele, Volnea
Ethinyl estradiol 20 mcg (d 1-5), 30 mcg (d 6-12), 35 mcg (d 13-21)	Norethindrone 1 mg (d 1-21)	Estrostep Fe, Tilia Fe, Tri-Legest Fe
Ethinyl estradiol 25 mcg (d 1-21)	Norgestimate 0.18 mg (d 1-7), 0.215 mg (d 8-14), 0.25 mg (d 15-21)	Ortho Tri-Cyclen Lo, Tri-Lo-Marzia, Tri-Lo-Sprintec, TriNessa Lo
Ethinyl estradiol 25 mcg (d 1-21)	Desogestrel 0.1 mg (d 1-7), 0.125 mg (d 8-14), 0.15 mg (d 15-21)	Caziant, Cyclessa, Velivet
Ethinyl estradiol 30 mcg (d 1-6), 40 mcg (d 7-11), 30 mcg (d 12-21)	Levonorgestrel 0.05 mg (d 1-6), 0.075 mg (d 7-11), 0.125 mg (d 12-21)	Enpresse, Levonest, Myzilra, Trivora
Ethinyl estradiol 35 mcg (d 1-21)	Norgestimate 0.18 mg (d 1-7), 0.215 mg (d 8-14), 0.25 mg (d 15-21)	Ortho Tri-Cyclen, Tri-Femynor, Tri-Linyah, Tri-Previfem, Tri-Sprintec, TriNessa
Ethinyl estradiol 35 mcg (d 1-21)	Norethindrone 0.5 mg (d 1-7), 0.75 mg (d 8-14), 1 mg (d 15-21)	Alyacen 7/7/7, Cyclafem 7/7/7, Dasetta 7/7/7, Nortrel 7/7/7, Ortho-Novum 7/7/7
Ethinyl estradiol 35 mcg (d 1-21)	Norethindrone 0.5 mg (d 1-7), 1 mg (d 8-14), 0.5 mg (d 15-21)	Aranelle 7/9/5, Leena 7/9/5

Extended Dosing Oral Contraceptive Contents

Estrogen Component and Dose (Duration in Each Phase)	Progestin Component and Dose (Duration in Each Phase)	Example Brand Names
Ethinyl estradiol 20 mcg (d 1-84), 10 mcg (d 85-91)	Levonorgestrel 0.1 mg (d 1-84)	Amethia Lo, Camrese, LoJaimiess, LoSeasonique
Ethinyl estradiol 20 mcg (d 1-42), 25 mcg (d 43-63), 30 mcg (d 64-84), 10 mcg (d 85-91)	Levonorgestrel 0.15 mg (d 1-84)	Fayosim, Rivelsa, QuarteSe
Ethinyl estradiol 30 mcg (d 1-84), 10 mcg (d 85-91)	Levonorgestrel 0.15 mg (d 1-84)	Amethia, Ashlyna, Camrese, Jaimiess, Seasonique
Ethinyl estradiol 30 mcg (d 1-84)	Levonorgestrel 0.15 mg (d 1-84)	Introvale, Jolessa, Quasense

Drug Interactions: Oral Contraceptives - See Preface C for critical information on drug interactions with 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	Carefully monitor INR

Preface D: 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.
- *Nonsensitive 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 an 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 or reduce amiodarone dose. 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). Ciprofloxacin, fluvoxamine, ketoconazole, lidocaine, methoxsalen, mexiletine, norfloxacin, ofloxacin, primaquine, thiabendazole

Inhibitors (Moderate). Amiodarone, amlodipine, cimetidine, diclofenac, fluoxetine, fospropofol, gemfibrozil, miconazole, nifedipine, propofol, zileuton

Inducers. Aminoglutethimide, carbamazepine, phenobarbital, primidone, rifampin

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

CYP2A6

Inhibitors (Strong). Letrozole, methoxsalen, miconazole, tranylcypromine

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

Inducers. Amobarbital, pentobarbital, phenobarbital, rifampin, secobarbital

Substrates (Sensitive). Dexmedetomidine

CYP2B6

Inhibitors (Strong). None

Inhibitors (Moderate). Doxorubicin, paroxetine, sorafenib

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, primidone, rifampin, secobarbital

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

CYP2C9

Inhibitors (Strong). Delavirdine, fluconazole, flurbiprofen, 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, primidone, rifampin, rifapentine, secobarbital

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

CYP2C19

Inhibitors (Strong). Delavirdine, 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, pentamidine, pantoprazole, phenobarbital, phenytoin, progesterone, rabeprazole, ranitidine, sertraline, siponimod, trimipramine, voriconazole

CYP2D6

Inhibitors (Strong). Chlorpromazine, cinacalcet, cocaine, delavirdine, dexmedetomidine, dextromethorphan, fluoxetine, miconazole, paroxetine, pergolide, quinidine, quinine, ritonavir, ropinirole, terbinafine

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, trazodone

Inducers. None

Substrates (Sensitive).

- *Antibiotics:* Chloroquine, doxycycline
- *Cardiovascular:* Atorvastatin, betaxolol, captopril, carvedilol, flecainide, lidocaine, metoprolol, mexiletine, pindolol, propafenone, propranolol, timolol
- *CNS:* Amitriptyline, amoxapine, amphetamine, 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, tamsulosin

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, delavirdine, 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/primidone, 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, cerivastatin, chlorpheniramine
- *Cardiovascular:* Amiodarone, bosentan, budesonide, cilostazol, diltiazem, disopyramide, enalapril, felodipine, isosorbide, isradipine, lidocaine, losartan, lovastatin, moricizine, nicardipine, nifedipine, nimodipine, nisoldipine, quinidine, simvastatin, ticlopidine
- *CNS:* Alprazolam, amoxapine, benztropine, buprenorphine, buspirone, carisoprodol, chlordiazepoxide, clobazam, clonazepam, clorazepate, cocaine, dantrolene, diazepam, dihydroergotamine, doxepin, eletriptan, escitalopram, ethosuximide, felbamate,

flurazepam, haloperidol, istradefylline, mirtazapine, modafinil, pergolide, phencyclidine, pimozide, pitolisant, quetiapine, ranolazine, tiagabine, trazodone, triazolam, ubrogepant

- *Hematology:* Voxelotor
- *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:* Avapritinib, bortezomib, busulfan, cyclophosphamide (activated to acrolein by CYP3A4/5), docetaxel, doxorubicin, entrectinib, etoposide, ifosfamide (activated to acrolein by CYP3A4/5), imatinib, irinotecan, paclitaxel, sorafenib, sunitinib, tazemetostat, teniposide, zanubrutinib
- *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

Preface E: Guide to Transporters

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 P-glycoprotein (P-gp) can assist with managing drug interactions. For example, adding carbamazepine (a P-gp inducer) to digoxin (a P-gp 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 (P-gp) is a membrane-bound, active transport protein located in a number of 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 P-gp 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, P-gp transports substrate drugs out of the brain. Inducers may decrease concentrations in the CSF, because there is increased amount of P-gp 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

Preface F: Drugs That Affect Cardiac Rhythm

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

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

Alfuzosin, amiodarone, amisulpride, anagrelide, apomorphine, arformoterol, aripiprazole, arsenic trioxide, 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, 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