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.

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.

- *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.

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

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.

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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

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

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.

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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.

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 Captopril Enalapril Fosinopril Lisinopril Moexipril Perindopril Quinapril Ramipril Trandolapril
Aldosterone antagonists	Eplerenone Spironolactone
α_1-Blockers	Doxazosin Prazosin Terazosin
Angiotensin receptor blockers	Candesartan Eprosartan Irbesartan Losartan Olmesartan Telmisartan Valsartan

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

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

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 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 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 Pravastatin 10-20 mg Lovastatin 20 mg Fluvastatin 20-40 mg Pitavastatin 1 mg	Atorvastatin 10-20 mg Rosuvastatin 5-10 mg Simvastatin 20-40 mg Pravastatin 40-80 mg Lovastatin 40 mg Fluvastatin XL 80 mg Fluvastatin 40 mg bid Pitavastatin 2-4 mg	Atorvastatin 40-80 mg Rosuvastatin 20-40 mg

Cholesterol-Lowering Drugs

Class	Drugs	Average Effects on Lipoproteins	Adverse Effects
Bile acid sequestrants	Cholestyramine Colesevelam Colestipol	HDL-C ↑ 3-5% TG No change to ↑ 9% LDL-C ↓ 15-30%	Abdominal discomfort and cramping, constipation, flatulence, nausea/vomiting, vitamin deficiency
Cholesterol absorption inhibitor	Ezetimibe	HDL-C ↑ 1% TG ↓ 8% LDL-C ↓ 18%	Arthralgia, diarrhea, myalgia
Fibric acid	Fenofibric acid Fenofibrate Gemfibrozil	HDL-C ↑ 10-20% TG ↓ 20-50% LDL-C ↓ 5-20%	Abdominal pain, arthralgia, constipation, diarrhea, headache, increased liver enzymes, indigestion, myalgia, myopathy, nausea, rhabdomyolysis
HMG-CoA reductase inhibitors (statins)	Atorvastatin Fluvastatin Fluvastatin XL Lovastatin Pitavastatin Pravastatin Rosuvastatin Simvastatin	HDL-C ↑ 5-15% TG ↓ 7-30% LDL-C ↓ 18-55%	Arthralgia, diarrhea, headache, increased liver enzymes, indigestion, insomnia, myalgia, myopathy, nausea, rhabdomyolysis
Nicotinic acid	Niaspan	HDL-C ↑ 15-35% TG ↓ 20-50% 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% TG ↓ 45% 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

Hypertension

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

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

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) Spironolactone-HCTZ (25/25, 50/50) Triamterene-HCTZ (37.5/25, 75/50)	Moduretic Aldactazide 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) Ezetimibe-simvastatin (10/10, 10/20, 10/40, 10/80)	Liptruzet Vytorin
Statin and nicotinic acid	Lovastatin-niacin (20/500, 20/750, 20/1000, 40/1000) Niacin-simvastatin (500/20, 500/40, 750/20, 1000/20, 1000/40)	Advicor 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

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Preface G: Guide to Combination Vaccines

Vaccine	Trade Name	Type	Route	Comments
DTaP	Daptacel Infanrix 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 Adacel	Inactivated bacterial, toxoid	IM	Tetanus and diphtheria toxoids and pertussis vaccine; ≥10 y of age Tetanus and diphtheria toxoids and pertussis vaccine; 11-64 y of age

IM = intramuscular
SC = subcutaneous

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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

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

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

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.

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

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Preface K: Drugs Affected by Gastric pH

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)

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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

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