MEDfacts

POCKET GUIDE OF DRUG INTERACTIONS

Second Edition

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This drug interactions pocket guide was written on behalf of Nephrology Pharmacy Associates, Inc. (NPA) by George R. Bailie, PharmD, PhD, Curtis A. Johnson, PharmD, Nancy A. Mason, PharmD, and Wendy L. St. Peter, PharmD, BCPS.

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Disclaimer

These drug interaction guidelines are offered as a general summary of information for physicians, pharmacists, nurses and other health professionals. Inappropriate administration of interacting drugs to patients can result in severe injury or death. These guidelines cannot identify medical risks specific to an individual patient or recommend patient treatment. These guidelines are not to be used as a substitute for professional training. The absence of typographical errors is not guaranteed. These guidelines are not necessarily all-inclusive. Use of these guidelines indicates acknowledgement that neither Nephrology Pharmacy Associates, Inc. (NPA), Bone Care International, Inc. nor the authors will be responsible for any loss or injury, including death, sustained in connection with, or as a result of, the use of these guidelines. Readers should consult the complete information available in the package insert for each agent indicated before prescribing medications.

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Preface

Patients with acute renal failure, chronic kidney disease (CKD) or those treated with dialysis or kidney transplantation are frequently prescribed numerous medications. Drugs of many therapeutic classes are used to treat the underlying diseases leading to CKD, such as diabetes mellitus and hypertension, while others are used to control or treat the common complications of CKD, such as anemia, renal bone disease and lipid disorders. Dialysis patients often are prescribed 10 to 12 medications. With such a large number of medications, there is an increased risk for drug interactions. The accompanying table has been prepared as a reference regarding the most clinically significant drug interactions that might occur, together with an indication of the possible consequence. This table should be used as a general guideline.

Sometimes information is known about one specific drug within a certain drug class, while additional information is not known about other agents within the same therapeutic category. Clinicians must be aware of this possibility and use their best judgement when prescribing or assessing drug therapy.

Types of Drug Interactions

Drug interactions are often classified as either pharmacodynamic or pharmacokinetic interactions. Pharmacodynamic interactions include those that result in additive or antagonistic pharmacological effects. Pharmacokinetic interactions involve induction or inhibition of metabolizing enzymes in the liver or elsewhere, displacement of drug from plasma protein binding sites, alterations in gastrointestinal absorption, or competition for active renal secretion.

The frequency and prevalence of interactions is dependent upon the number of concomitant medications and the complexity of the regimens. The prevalence is also dependent upon other variables, such as patient adherence, hydration and nutritional status, degree of renal or hepatic impairment, smoking and alcohol use, genetics and drug dosing. Additionally, some patients may exhibit evidence of a particular drug interaction, while others with the same drug combination do not.

Pharmacodynamic interactions

This type of interaction will not be addressed in this reference, since these should be reasonably easy to predict, knowing the pharmacology of any given drug.

Pharmacokinetic interactions

Interactions Resulting from Alterations in Gastrointestinal Absorption
The rate and extent of drug absorption after oral administration may be grossly altered by other agents. Absorption of a drug is a function of the drug's ability to diffuse from the lumen of the gastrointestinal tract into the systemic circulation. Changes in intestinal pH may profoundly affect drug diffusion as well as dissolution of the dosage form. For example, the absorption of ketoconazole is reduced by the co-administration of antacids or H_2-blockers (e.g. ranitidine, famotidine) that reduce the extent to which the ketoconazole tablet is dissolved. Formation of insoluble complexes by a process known as chelation is another mechanism by which a drug interaction may lead to reduced oral absorption. For example, fluoroquinolones (e.g. ciprofloxacin) and divalent metal ions (such as calcium and iron) form an insoluble complex that results in reduced absorption of both the antibiotic and the metal ion. Interactions that decrease the rate of drug absorption may be of little importance, since the overall extent of absorption may remain unaltered.

Interactions Resulting from Alterations in Metabolizing Enzymes
The liver is the major, though not exclusive, site for drug metabolism. Other sites include the kidney and the lining of the gastrointestinal tract. The two main types of hepatic drug metabolism are phase I and phase II reactions. Phase I oxidative reactions are the initial step in drug biotransformation, and are mediated by the cytochrome P-450 (CYP) system. This complex superfamily of enzymes has been subclassified into numerous enzymatic subfamilies. The most common CYP subfamilies include CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP2E1, and CYP3A4. These enzymes may be induced or inhibited by other agents, thereby leading to an increase or decrease in the metabolism of the primary drug. Phase II reactions occur following Phase I reactions. In this process, drug metabolites are converted into more water-soluble compounds that can be more easily eliminated by the kidneys.

Enzyme induction may result in increased CYP enzyme synthesis, faster drug metabolism, subtherapeutic drug concentrations and the risk for ineffective drug therapy. The rapidity of the enzyme induction is dependent upon the half-life of the inducing drug as well as the rate of synthesis of new enzymes. Examples of drugs that cause enzyme induction are the barbiturates, some anticonvulsants and rifampin.

Enzyme inhibition may result from noncompetitive or competitive inhibition of CYP enzymes by a second drug, an effect that may occur rapidly. Examples of hepatic enzyme inhibitors include cimetidine, fluconazole and erythromycin. The result of noncompetitive enzyme inhibition by addition of a second agent is slower metabolism of the first drug, higher plasma drug concentrations, and a risk for toxicity. In the case of competitive inhibition, the metabolism of both drugs can be reduced, resulting in higher than expected concentrations of each drug.

A few drugs are metabolized by enzymes found in cells lining the gastrointestinal tract. One of these drugs is cyclosporine. Some foods and other preparations such as grapefruit juice contain certain substances that may inhibit those specific enzymes, resulting in elevated serum cyclosporine concentrations.

Interactions Resulting from Alterations in Protein Binding

Drugs may exist in plasma either reversibly bound to plasma proteins or in the free (unbound) state. The primary drug-binding plasma proteins are albumin and α_1-acid glycoprotein. It is free drug that exerts the pharmacological effect. Drugs may compete with each other for plasma protein binding sites, and when this occurs, one drug may displace another that was previously bound to the protein. Displacement of a drug from its binding sites will therefore increase that agent's unbound concentrations, perhaps resulting in toxicity.

Some drugs normally exist in a state of high protein binding, often exceeding 90%. Thus, even a small decrease in protein binding could significantly increase the free concentrations. Drugs which are normally highly protein bound, and which might participate in binding interactions, include anticonvulsants and warfarin.

Interactions Resulting from Changes in Renal Excretion

The majority of renally eliminated drugs are excreted via passive glomerular filtration. Some drugs are eliminated via active tubular secretion, such as penicillins, cephalosporins, and most diuretics. The active secretion may be inhibited by secondary agents, such as cimetidine, nonsteroidal anti-inflammatory agents and probenecid, with resulting elevations in the serum drug concentrations and reduced urinary drug concentrations. In some cases, the interaction is desirable, while others may lead to adverse therapeutic outcomes.

Risk Factors and Management of Drug Interactions

In general, the more complex a patient's drug regimen, the higher the risk for interactions. CKD patients often take numerous medications. The average age of a dialysis patient is over 60 years and as a group, elderly patients are more prone to experience drug interactions because of reduced hepatic and renal function. Identification of the potential for interactions may enable the clinician to avoid its occurrence. Drugs that require careful dose titration to maintain efficacy and avoid toxicity must be monitored particularly carefully for drug interactions. Most drug interactions can be avoided or managed by substitution of one or more agents or more intense monitoring for the potential result. Other management strategies include separation of doses of interacting agents (e.g. ciprofloxacin and calcium) or prospective adjustment of doses.

Clinical Significance of Interactions

This guide lists only those interactions that have been previously rated as having a moderate or high level of clinical significance by the *Drug Interaction Facts* (see References). This rating scale requires that a potential interaction has a moderate to major severity. The effects of a *moderate* interaction may cause a deterioration in the patient's clinical status, resulting in additional treatment, hospitalization, and/or an extended hospital stay. The effects of a *major* interaction are potentially life-threatening or can lead to permanent damage. In addition to being clinically significant, the interaction must be reasonably documented in the literature (suspected, probable, or established). Therefore, the accompanying table is NOT an all-inclusive list of every possible drug interaction.

Key to the Table

The accompanying table contains four columns. The first is titled "Drug," and lists the primary drugs and drug classes, by generic name, which may have a significant interaction. The drugs are listed according to therapeutic classes.

The second column is titled "Interacting Drug," and lists drugs or drug classes that have potential clinically significant interactions with the primary listed drugs. These two columns are cross-referenced, as appropriate.

The third column, "Potential Effect," gives a short description of the possible clinical outcome of the interaction. The outcomes listed are possible, not definite, events. Clinicians must be aware that not all patients will manifest these interactions.

The last column, "Management," indicates suggested strategies for prevention, monitoring, and managing any potential interactions. If combination therapy of interacting drugs cannot be avoided, the patient should be advised of any potential adverse effects. Always monitor the patient for any changes in clinical response when starting, stopping, or changing the dose of interacting drugs. Also monitor for any signs/symptoms of known toxicities. Appropriate clinical intervention should be taken when necessary.

References and Additional Reading

Further information about the listings in the table may be found in reference number 1. Additional readings are listed for the convenience of the reader.

1. Tatro DS (ed). Drug Interaction Facts 2004. Facts and Comparisons, St. Louis, MO, 2004.

2. Stockley IH, Drug Interactions, 5th ed. London: Pharmaceutical Press; 1999.

3. Landrum EL. Update: clinically significant cytochrome P-450 drug interactions. *Pharmacotherapy* 1998; 18:84-112.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
ANEMIA AGENTS			
Androgens			
Nandrolone decanoate	Warfarin, see *Anticoagulants/Thrombolytic Agents—Androgens*		
Methyltestosterone/ Testosterone	Cyclosporine, see *Transplant Immunosuppressants—Androgens*		
	Warfarin, see *Anticoagulants/Thrombolytic Agents—Androgens*		
Epoetin Alfa	**No interactions noted.**		
Iron Products			
Iron Salts (IV) [iron dextran, ferric gluconate, iron sucrose]	Chloramphenicol	Increased concentrations of iron.	Use alternative antibiotic if possible. Otherwise, monitor iron stores and adjust iron replacement as needed.
Iron Salts (Oral) [ferrous fumarate, ferrous gluconate, ferrous sulfate, iron polysaccharide]	Chloramphenicol	Increased concentrations. of iron.	Use alternative antibiotic if possible. Otherwise monitor iron stores and adjust iron replacement as needed.
	Levodopa, see *Antiparkinson Agents*		
	Levothyroxine, see *Miscellaneous Agents*		
	Mycophenolate mofetil, see *Transplant Immunosuppressants*		
	Penicillamine	Decreased GI absorption of penicillamine.	Administer penicillamine on an empty stomach. Separate administration times.
	Phosphate Binders/Antacids [aluminum hydroxide, aluminum-magnesium hydroxide, calcium acetate, calcium carbonate, magnesium hydroxide]	Decreased GI absorption of iron.	Separate administration times.
	Quinolones, see *Antimicrobial Agents (Antibacterial Antibiotics)*		
	Tetracyclines, see *Antimicrobial Agents (Antibacterial Antibiotics)*		
ANTIHYPERTENSIVE AND CARDIOVASCULAR AGENTS			
Adrenergic Modifiers			
Clonidine	Beta-Blockers [acebutolol, atenolol, betaxolol, carteolol, esmolol, metoprolol, nadolol, penbutolol, pindolol, propranolol, timolol]	Increased blood pressure.	Monitor blood pressure when starting or stopping either drug. Discontinue either drug gradually.
	Tricyclic Antidepressants [amitriptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine, nortriptyline, protriptyline, trimipramine]	Loss of blood pressure control. Increased risk of hypertensive crisis.	Avoid combination.
Methyldopa	Sympathomimetics [dobutamine, dopamine, ephedrine, epinephrine, mephentermine, metaraminol, methoxamine, norepinephrine, phenylephrine, pseudoephedrine]	Increased blood pressure.	Monitor blood pressure. Discontinue sympathomimetic or administer phentolamine if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
Prazosin	Beta-Blockers [acebutolol, atenolol, betaxolol, bisoprolol, carteolol, esmolol, metoprolol, nadolol, penbutolol, pindolol, propranolol, sotalol, timolol]	Increased postural hypotension.	Monitor for symptoms of postural hypotension.
	Verapamil	Increased postural hypotension.	Monitor for symptoms of postural hypotension.
Angiotensin Converting Enzyme Inhibitors (ACEIs)	**Benazepril, Captopril, Enalapril, Fosinopril, Lisinopril, Moexipril, Perindopril, Quinapril, Trandolapril**		
Angiotensin Converting Enzyme Inhibitors-class	Indomethacin	Decreased effects of angiotensin converting enzyme inhibitor.	Monitor blood pressure. Discontinue indomethacin or use alternative antihypertensive.
	Lithium, see *Sedative/Hypnotics/Agents used in Psychiatry, Antidepressants (Miscellaneous Antidepressants)*		
	Potassium-Sparing Diuretics [amiloride, spironolactone, triamterene]	Elevated serum potassium.	Monitor serum potassium.
Captopril *(see also Angiotensin Converting Enzyme Inhibitors-class)*	Food	Decreased GI absorption of captopril.	Administer captopril 1 hour before meals.
Angiotensin II Receptor Blockers (ARBs)	**Candesartan, Eprosartan, Irbesartan, Losartan, Olmesartan, Telmisartan, Valsartan**		
Angiotensin II Receptor Blockers-class	Lithium, see *Sedative/Hypnotics/Agents used in Psychiatry, Antidepressants (Miscellaneous Antidepressants)*		
Beta-Blockers	**Cardio-Selective [Acebutolol, Atenolol, Betaxolol, Bisoprolol, Esmolol, Metoprolol, Nadolol]; Noncardio-Selective [Carteolol, Carvedilol, Labetalol, Penbutolol, Pindolol, Propranolol, Sotalol, Timolol]**		
Cardio-Selective and Noncardio-Selective Beta-Blockers-class	Barbiturates [amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital]	Decreased bioavailability of beta-blocker.	Increase beta-blocker dose if necessary.
	Cimetidine	Increased concentrations of beta-blocker.	Monitor cardiovascular status. Decrease beta-blocker dose if necessary.
	Clonidine, see *Antihypertensive and Cardiovascular Agents (Adrenergic Modifiers)*		
	Hydralazine	Increased concentrations of both drugs (metoprolol, propranolol).	Decrease dose of one or both drugs if necessary.
	NSAIDs [ibuprofen, indomethacin, naproxen, piroxicam]	Decreased effects of beta-blocker.	Use noninteracting NSAID if possible (eg, sulindac). Monitor blood pressure. Increase beta-blocker dose if necessary.
	Prazosin, see *Antihypertensive and Cardiovascular Agents (Adrenergic Modifiers)*		

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Propafenone	Increased effects of beta-blocker (metoprolol, propanolol).	Monitor cardiovascular status. Decrease beta-blocker dose if necessary.
	Quinidine	Increased effects of beta-blocker (atenolol, propranolol, metoprolol, timolol).	Monitor cardiovascular status. Decrease beta-blocker dose if necessary.
	Rifamycins [rifabutin, rifampin]	Decreased effects of beta-blocker (atenolol, bisoprolol, metoprolol, propranolol).	Monitor cardiovascular status. Increase beta-blocker dose if necessary.
	Verapamil	Increased effects of both drugs.	Monitor cardiovascular status. Decrease dose of one or both drugs if necessary.
Noncardio-Selective Beta-Blockers-class	Epinephrine, see *Antihypertensive and Cardiovascular Agents (Miscellaneous Antihypertensive and Cardiovascular Agents)*		
	Ergot Alkaloids, see *Miscellaneous Agents*		
	Insulin, see *Hypoglycemic Agents*		
	Prazosin, see *Antihypertensive and Cardiovascular Agents (Adrenergic Modifiers)*		
	Theophylline, see *Bronchodilators*		
Atenolol *(see also Cardio-Selective and Noncardio-Selective Beta-Blockers-class)*	Ampicillin	Decreased effects of atenolol.	Separate administration times. Monitor blood pressure. Increase atenolol. dose if necessary.
Carvedilol *(see also Cardio-Selective and Noncardio-Selective Beta-Blockers-class)*	Cyclosporine, see *Transplant Immunosuppressants*		
Labetalol *(see also Cardio-Selective and Noncardio-Selective Beta-Blockers-class)*	Inhalation Anesthetics [desflurane, enflurane, halothane, isoflurane, sevoflurane]	Excessive hypotension.	Monitor blood pressure. Use combination with caution. Halothane concentration should not exceed 3%.
Metoprolol *(see also Cardio-Selective and Noncardio-Selective Beta-Blockers-class)*	Lidocaine, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		
	Thioamines [methimazole, propylthiouracil]	Increased effects of metoprolol.	Monitor cardiovascular status. Decrease metoprolol dose if necessary as patient becomes euthyroid. Use alternative beta-blocker (eg, atenolol, nadolol).
Nadolol *(see also Cardio-Selective and Noncardio-Selective Beta-Blockers-class)*	Lidocaine, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		
Pindolol *(see also Cardio-Selective and Noncardio-Selective Beta-Blockers-class)*	Lidocaine, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		
	Phenothiazines [chlorpromazine, thioridazine]	Increased effects of one or both drugs.	Decrease dose of one or both drugs if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
Propranolol *(see also Cardio-Selective and Noncardio-Selective Beta-Blockers-class)*	Lidocaine, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		
	Phenothiazines [chlorpromazine, thioridazine]	Increased effects of one or both drugs.	Decrease dose of one or both drugs if necessary.
	Thioamines [methimazole, propylthiouracil]	Increased effects of propranolol.	Monitor cardiovascular status. Decrease propranolol dose if necessary as patient becomes euthyroid. Use alternative beta-blocker (eg, atenolol, nadolol).
Sotalol *(see also Cardio-Selective and Noncardio-Selective Beta-Blockers-class)*	Quinolones [gatifloxacin, moxifloxacin, sparfloxacin]	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination. Use alternative quinolones (eg, ciprofloxacin, levofloxacin).
Calcium-Channel Blockers (CCBs)	**Amlodipine, Bepridil, Diltiazem, Felodipine, Isradipine, Nicardipine, Nifedipine, Nimodipine, Nisoldipine, Verapamil**		
Bepridil	Digoxin, see *Antihypertensive and Cardiovascular Agents (Miscellaneous Antihypertensive and Cardiovascular Agents)*		
	Quinolones [gatifloxacin, moxifloxacin, sparfloxacin]	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination. Use alternative quinolones (eg, ciprofloxacin, levofloxacin).
	Ritonavir	Increased concentrations of bepridil.	Avoid combination.
Diltiazem	Benzodiazepines, see *Sedatives/Hypnotics/Agents used in Psychiatry (Sedatives)*		
	Carbamazepine	Increased concentrations of carbamazepine.	Monitor carbamazepine concentrations. Adjust dose as needed when starting or stopping diltiazem.
	Cyclosporine, see *Transplant Immunosuppressants*		
	HMG-CoA Reductase Inhibitors, see *Hypolipidemic Agents*		
	Moricizine	Increased concentrations of moricizine. Decreased concentrations of diltiazem.	Adjust dose of one or both drugs as needed.
	Quinidine, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		
	Sirolimus, see *Transplant Immunosuppressants*		
	Tacrolimus, see *Transplant Immunosuppressants*		
	Theophyllines [aminophylline, oxtriphylline, theophylline]	Increased concentrations of theophylline.	Monitor theophylline concentrations. Adjust theophylline dose as needed when starting or stopping diltiazem.
Felodipine	Barbiturates [amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital]	Decreased effects of felodipine.	Monitor cardiovascular status. Increase felodipine dose if necessary.
	Carbamazepine	Decreased effects of felodipine.	Monitor cardiovascular status. Increase felodipine dose if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Erythromycin	Increased effects of felodipine.	Monitor cardiovascular status. Decrease felodipine dose if necessary.
	Grapefruit Juice	Increased effects of felodipine.	Avoid combination.
	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased effects of felodipine.	Monitor cardiovascular status Increase felodipine dose if necessary.
	Itraconazole	Increased effects of felodipine.	Monitor cardiovascular status Decrease felodipine dose if necessary.
Nicardipine	Cyclosporine, see *Transplant Immunosuppressants*		
Nifedipine	Barbiturates [amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital]	Decreased effects of nifedipine.	Monitor cardiovascular status. Increase nifedipine dose if necessary.
	Cimetidine	Increased effects of nifedipine.	Adjust nifedipine dose as needed when starting, stopping, or changing dose of cimetidine. Use alternative histamine H_2-antagonist (eg, ranitidine).
	Rifampin	Decreased effects of nifedipine.	Monitor cardiovascular status. Adjust nifedipine dose as needed when starting or stopping rifampin.
	Tacrolimus, see *Transplant Immunosuppressants*		
Nisoldipine	Grapefruit Juice	Increased effects of nisoldipine.	Avoid combination.
	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased effects of nisoldipine.	Monitor cardiovascular status. Adjust nisoldipine dose when starting, stopping, or changing dose of hydantoin.
Verapamil	Beta-Blockers, see *Antihypertensive and Cardiovascular Agents (Cardio-Selective and Noncardio-Selective Beta-Blockers)*		
	Calcium Salts [calcium acetate, calcium carbonate, calcium chloride, calcium citrate, calcium glubionate, calcium gluconate, calcium glycerophosphate, calcium lactate, calcium levulinate, tricalcium phosphate]	Reverse clinical effects and toxicities of verapamil.	Monitor cardiovascular status. Calcium may be used to reverse verapamil toxicities.
	Carbamazepine, see *Anticonvulsants*		
	Cyclosporine, see *Transplant Immunosuppressants*		
	Digoxin	Increased concentrations of digoxin.	Monitor cardiovascular status and digoxin concentrations. Decrease digoxin dose if necessary.
	Ethanol, see *Miscellaneous Agents*		
	HMG-CoA Reductase Inhibitors, see *Hypolipidemic Agents*		

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Nondepolarizing Muscle Relaxants [atracurium, doxacurium, mivacurium, pancuronium, pipecuronium, tubocurarine, vecuronium]	Increased nondepolarizing muscle relaxant effects (prolonged respiratory depression).	Avoid combination if possible. Monitor respiratory function. Adjust nondepolarizing muscle relaxant dose as needed.
	Prazosin, see *Antihypertensive and Cardiovascular Agents (Adrenergic Modifiers)*		
	Quinidine, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		
	Rifampin	Decreased effects of oral verapamil.	Use intravenous verapamil or alternative drug. Adjust verapamil dose as needed when starting or stopping rifampin.
Antiarrhythmic Agents			
Amiodarone	Cyclosporine, see *Transplant Immunosuppressants*		
	Digoxin, see *Antihypertensive and Cardiovascular Agents (Miscellaneous Antihypertensive and Cardiovascular Agents)*		
	Fentanyl	Increased risk of profound bradycardia, sinus arrest, and hypotension.	Avoid combination if possible. Otherwise, monitor hemodynamic status and manage with supportive treatment as needed.
	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Increased concentrations of hydantoin. Decreased concentrations of amiodarone.	Monitor cardiovascular status and for signs/symptoms of hydantoin toxicity. Adjust dose of one or both drugs as needed.
	Procainamide, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		
	Protease Inhibitors [indinavir, ritonavir]	Increased concentrations of amiodarone.	Avoid combination.
	Quinidine, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		
	Quinolones [gatifloxacin, moxifloxacin, sparfloxacin]	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination. Use alternative quinolones (eg, ciprofloxacin, levofloxacin).
	Warfarin, see *Anticoagulants/Thrombolytic Agents*		
Disopyramide	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased concentrations of disopyramide. Increased risk of anticholinergic effects.	Monitor cardiovascular status and anticholinergic effects. Increase disopyramide dose if necessary.
	Quinolones [gatifloxacin, moxifloxacin, sparfloxacin]	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination. Use alternative quinolones (eg, ciprofloxacin, levofloxacin).
	Rifampin	Decreased concentrations of disopyramide.	Monitor cardiovascular status. Increase disopyramide dose if necessary.
Flecainide	Ritonavir	Increased concentrations of flecainide.	Avoid combination.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
Lidocaine	Beta-Blockers [atenolol, metoprolol, nadolol, pindolol, propranolol]	Increased concentrations of lidocaine.	Administer bolus lidocaine at a slow rate to avoid high peak concentrations and toxicity. Monitor lidocaine concentrations. Decrease lidocaine dose if necessary.
	Cimetidine	Increased concentrations of lidocaine.	Monitor lidocaine concentrations. Decrease lidocaine dose if necessary. Use alternative histamine H_2-antagonist (eg, ranitidine).
Mexiletine	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased concentrations of mexiletine.	Monitor cardiovascular status. Increase mexiletine dose if necessary.
	Theophylline, see *Bronchodilators*		
Moricizine	Cimetidine	Increased concentrations of moricizine.	Monitor ECG when starting, stopping, or changing dose of cimetidine. Decrease moricizine dose if necessary. Use alternative histamine H_2-antagonist (eg, ranitidine).
Procainamide	Amiodarone	Increased concentrations of procainamide and N-acetylprocainamide.	Monitor serum procainamide and N-acetylprocainamide concentrations. Decrease procainamide dose if necessary.
	Cimetidine	Increased concentrations of procainamide and N-acetylprocainamide	Avoid combination if possible. Otherwise, decrease procainamide dose if necessary.
	Ofloxacin	Increased concentrations of procainamide.	Monitor serum procainamide concentrations. Decrease procainamide dose if necessary.
	Quinolones [gatifloxacin, moxifloxacin, sparfloxacin]	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination. Use alternative quinolones (eg, ciprofloxacin, levofloxacin).
	Trimethoprim	Increased concentrations of procainamide and N-acetylprocainamide.	Monitor serum procainamide and N-acetylprocainamide concentrations. Decrease procainamide dose if necessary.
Propafenone	Quinidine	Increased concentrations of propafenone.	Monitor cardiovascular status. Decrease propafenone dose or extend dosing interval if necessary.
	Ritonavir	Increased concentrations of propafenone.	Avoid combination.
Quinidine	Amiloride	Increased risk of cardiac arrhythmias and reversal of quinidine effects.	Avoid combination if possible. Otherwise, closely monitor ECG.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Amiodarone	Increased concentrations of quinidine. Increased risk of cardiac arrhythimas.	Avoid combination if possible. Otherwise, monitor quinidine concentrations and decrease quinidine dose if necessary.
	Barbiturates [amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital]	Decreased concentrations of quinidine	Monitor quinidine concentrations. Adjust quinidine dose as needed when starting, stopping, or changing dose of barbiturate.
	Cimetidine	Increased concentrations of quinidine.	Avoid combination. if possible. Otherwise, monitor quinidine concentrations and decrease quinidine dose if necessary.
	Codeine, see *Pain Medications (Narcotic)*		
	Digoxin, see *Antihypertensive and Cardiovascular Agents (Miscellaneous Antihypertensive and Cardiovascular Agents)*		
	Diltiazem	Increased concentrations of quinidine.	Monitor cardiovascular status and quinidine concentrations. Adjust quinidine dose as needed when starting or stopping diltiazem.
	Hydantoins [fosphenytoin, phenytoin]	Decreased concentrations of quinidine.	Monitor quinidine concentrations. Increase quinidine dose if necessary.
	Itraconazole	Increased concentrations of quinidine.	Monitor quinidine concentrations. Decrease quinidine dose if necessary.
	Phosphate Binders/Antacids [aluminum hydroxide, aluminum-magnesium hydroxide, magnesium hydroxide, sodium bicarbonate]	Increased concentrations of quinidine.	Monitor quinidine concentrations. Decrease quinidine dose if necessary.
	Propafenone, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		
	Quinolones [gatifloxacin, moxifloxacin, sparfloxacin]	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination. Use alternative quinolones (eg, ciprofloxacin, levofloxacin).
	Rifamycins [rifabutin, rifampin]	Decreased concentrations of quinidine.	Monitor quinidine concentrations when starting, stopping, or changing dose of rifamycin. Adjust quinidine dose as needed.
	Ritonavir	Increased concentrations of quinidine.	Avoid combination.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Verapamil	Increased concentrations of quinidine. Increased risk of cardiac arrhythimas and hypotension.	Avoid combination if possible. Otherwise, monitor cardiovascular status and quinidine concentrations. Stop one or both drugs if interaction develops and treat symptomatically.
	Warfarin, see *Anticoagulants/Thrombolytic Agents*		
Nitrates	**Amyl Nitrite, Isosorbide Dinitrate, Isosorbide Mononitrate, Nitroglycerin**		
Nitrates-class	Ergot Alkaloids, see *Miscellaneous Agents*		
	Phosphodiesterase-5 Enzyme Inhibitors [sildenafil, tradalafil, vardenafil]	Severe hypotension.	Avoid combination.
Nitroglycerin	Alteplase (tPA)	Decreased effects of tPA.	Avoid combination.
Miscellaneous Antihypertensive and Cardiovascular Agents			
Digoxin	Aminoglycosides [kanamycin, neomycin, paromomycin]	Decreased concentrations of digoxin.	Monitor digoxin concentrations. Increase digoxin dose if necessary.
	Amiodarone	Increased concentrations of digoxin.	Monitor digoxin concentrations and for signs/symptoms of digoxin toxicity. Decrease digoxin dose if necessary.
	Antineoplastic Agents [bleomycin, carmustine, cyclophosphamide, cytarabine, doxorubicin, methotrexate, vincristine]	Decreased concentrations of digoxin.	Monitor digoxin concentrations. Increase digoxin dose if necessary.
	Bepridil	Increased concentrations of digoxin. Increased negative chronotropic effects.	Monitor cardiovascular status. Decrease digoxin dose if necessary.
	Cholestyramine	Decreased concentrations of digoxin.	Separate administration times. Monitor for decreased digoxin effects. Increase digoxin dose if necessary.
	Cyclosporine	Increased concentrations of digoxin.	Monitor digoxin concentrations and for signs/symptoms of digoxin toxicity. Decrease digoxin dose if necessary.
	Indomethacin	Increased concentrations of digoxin in premature infants.	Monitor digoxin concentrations and for signs/symptoms of digoxin toxicity. Decrease digoxin dose if necessary.
	Itraconazole	Increased concentrations of digoxin in premature infants.	Monitor digoxin concentrations and for signs/symptoms of digoxin toxicity. Decrease digoxin dose if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Loop Diuretics [bumetanide, ethacrynic acid, furosemide]	Increased risk of arrhythmias.	Monitor serum potassium and magnesium concentrations. Supplement electrolytes if necessary. Restrict dietary and sodium intake or use potassium-sparing diuretics.
	Macrolide Antibiotics [clarithromycin, erythromycin]	Increased concentrations of digoxin.	Monitor digoxin concentrations and for signs/symptoms of digoxin toxicity. Decrease digoxin dose if necessary.
	Metoclopramide	Decreased concentrations of digoxin.	Monitor for decreased digoxin effects. Increase digoxin dose if necessary.
	Penicillamine	Decreased concentrations of digoxin.	Monitor digoxin concentrations and for signs/symptoms of digoxin toxicity. Increase digoxin dose if necessary.
	Propafenone	Increased concentrations of digoxin.	Monitor digoxin concentrations and for signs/symptoms of digoxin toxicity. Decrease digoxin dose if necessary.
	Quinidine	Increased concentrations of digoxin.	Monitor digoxin concentrations and for signs/symptoms of digoxin toxicity. Decrease digoxin dose if necessary.
	Quinine	Increased concentrations of digoxin.	Monitor digoxin concentrations and for signs/symptoms of digoxin toxicity. Decrease digoxin dose if necessary.
	Spironolactone	Decreased inotropic effects.	Monitor for decreased digoxin effects. Increase digoxin dose if necessary.
	Tetracyclines [demeclocycline, doxycycline, minocycline, oxytetracycline, tetracycline]	Increased concentrations of digoxin.	Monitor digoxin concentrations and for signs/symptoms of digoxin toxicity. Decrease digoxin dose if necessary.
	Thiazide Diuretics [bendroflumethiazide, chlorothiazide, chlorthalidone, hydrochlorothiazide, hydroflumethiazide, indapamide, methyclothiazide, metolazone, polythiazide, trichlormethiazide]	Increased risk of arrhythmias.	Monitor serum potassium and magnesium concentrations. Supplement electrolytes if necessary. Restrict dietary and sodium intake or use potassium-sparing diuretics.
	Thioamines [methimazole, propylthiouracil]	Increased concentrations of digoxin.	Monitor digoxin concentrations and for signs/symptoms of digoxin toxicity. Decrease digoxin dose if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Thyroid Hormones [levothyroxine, liothyronine, liotrix, thyroid]	Decreased concentrations of digoxin	Increase digoxin dose if necessary in hypothyroid patients if they become euthyroid.
	Verapamil	Increased concentrations of digoxin	Monitor digoxin concentrations and for signs/symptoms of digoxin toxicity. Decrease digoxin dose if necessary.
Epinephrine	Beta-Blockers [carteolol, nadolol, penbutolol, pindolol, propranolol, timolol]	Initial hypertensive episode, followed by reflex bradycardia.	Avoid combination if possible. Discontinue beta-blocker 3 days prior to epinephrine use if possible. Otherwise, monitor vital signs and use IV chlorpromazine, IV hydralazine, IV aminophylline, and/or IV atropine if necessary.
Hydralazine	Beta-Blockers, see *Antihypertensive and Cardiovascular Agents (Cardio-Selective and Noncardio-Selective Beta-Blockers)*		

ANTIMICROBIAL AGENTS

ANTIBACTERIAL ANTIBIOTICS

Aminoglycosides — **Amikacin, Gentamicin, Kanamycin, Neomycin, Streptomycin, Tobramycin**

Aminoglycosides-class	Cephalosporins [cefamandole, cefazolin, cefonicid, cefoperazone, cefotaxime, cefotetan, cefoxitin, ceftazidime, ceftizoxime, ceftriaxone, cefuroxime, cephalothin, cephapirin, cephradine]	Increased risk of nephrotoxicity.	Monitor aminoglycoside concentrations and kidney function.
	Digoxin, see *Antihypertensive and Cardiovascular Agents (Miscellaneous Antihypertensive and Cardiovascular Agents)*		
	Loop Diuretics [bumetanide, ethacrynic acid, furosemide, torsemide]	Increased risk of auditory toxicity.	Avoid excessive doses of either drug. Monitor aminoglycoside concentrations. Use alternative antibiotic if possible.
	NSAIDs [diclofenac, etodolac, fenoprofen, flubiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, mefenamic acid, nabumetone, naproxen, oxaprozin, piroxicam, sulindac, tolmetin]	Increased concentrations of aminoglycoside in premature infants.	Avoid combination if possible. Otherwise, decrease aminoglycoside dose before starting NSAID. Monitor aminoglycoside concentrations and renal function.
	Penicillins [ampicillin, methicillin, mezlocillin, nafcillin, oxacillin, penicillin G, piperacillin, ticarcillin]	Inactivation of aminoglycoside.	Do not mix drugs in same solution. Separate administration times by at least 2 hours.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
Cephalosporins	**Cefamandole, Cefazolin, Cefonicid, Cefoperazone, Cefotaxime, Cefotetan, Cefoxitin, Ceftazidime, Ceftizoxime, Ceftriaxone, Cefuroxime, Cephalothin, Cephapirin, Cephradine**		
Cephalosporins-class	Aminoglycosides, see *Antimicrobial Agents (Antibacterial Antibiotics)*		
	Warfarin, see *Anticoagulants/Thrombolytic Agents*		
Cefamandol *(see also Cephalosporins-class)*	Ethanol, see *Miscellaneous Agents*		
Cefonicid *(see also Cephalosporins-class)*	Ethanol, see *Miscellaneous Agents*		
Cefoperazone *(see also Cephalosporins-class)*	Ethanol, see *Miscellaneous Agents*		
Ceforanide *(see also Cephalosporins-class)*	Ethanol, see *Miscellaneous Agents*		
Cefotetan *(see also Cephalosporins-class)*	Ethanol, see *Miscellaneous Agents*		
Moxalactam *(see also Cephalosporins-class)*	Ethanol, see *Miscellaneous Agents*		
Macrolide Antibiotics	**Azithromycin, Clarithromycin, Erythromycin, Troleandomycin**		
Macrolide Antibiotics-class	Cyclosporine, see *Transplant Immunosuppressants*		
	HMG-CoA Reductase Inhibitors, see *Hypolipidemic Agents*		
	Theophylline, see *Bronchodilators*		
Clarithromycin *(see also Macrolide Antibiotics-class)*	Buspirone, see *Sedatives/Hypnotics/Agents used in Psychiatry (Miscellaneous Sedatives)*		
	Carbamazepine, see *Anticonvulsants*		
	Digoxin, see *Antihypertensive and Cardiovascular Agents (Miscellaneous Antihypertensive and Cardiovascular Agents)—Macrolide Antibiotics*		
	Ergot Alkaloids, see *Miscellaneous Agents— Macrolide Antibiotics*		
	Rifamycins [rifabutin, rifampin, rifapentine]	Decreased effects of clarithromycin. Increased adverse effects of rifamycin.	Monitor for increased rifamycin adverse effects and decreased response to macrolide antibiotic. Use alternative antibiotic (eg, azithromycin, dirithromycin).
	Tacrolimus, see *Transplant Immunosuppressants— Macrolide Antibiotics*		
	Warfarin, see *Anticoagulants/Thrombolytic Agents—Macrolide Antibiotics*		
Erythromycin *(see also Macrolide Antibiotics-class)*	Benzodiazepines, see *Sedatives/Hypnotics/Agents used in Psychiatry (Sedatives)*		
	Bromocriptine	Increased concentrations of bromocriptine.	Monitor for signs/symptoms of bromocriptine toxicity. Decrease bromocriptine dose if necessary.
	Buspirone, see *Sedatives/Hypnotics/Agents used in Psychiatry (Miscellaneous Sedatives)—Macrolide Antibiotics*		
	Carbamazepine, see *Anticonvulsants—Macrolide Antibiotics*		

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Digoxin, see *Antihypertensive and Cardiovascular Agents (Miscellaneous Antihypertensive and Cardiovascular Agents)—Macrolide Antibiotics*		
	Ergot Alkaloids, see *Miscellaneous Agents—Macrolide Antibiotics*		
	Felodipine, see *Antihypertensive and Cardiovascular Agents (Calcium-Channel Blockers)*		
	Food	Decreased GI absorption of erythromycin.	Administer erythromycin stearate and non-enteric tablets at least 2 hours before or after a meal.
	Grapefruit Juice	Increased concentrations of erythromycin.	Avoid combination.
	Methylprednisolone, see *Corticosteroids*		
	Quinolones [gatifloxacin, moxifloxacin, sparfloxacin]	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination. Use alternative quinolones (eg, ciprofloxacin, levofloxacin).
	Rifamycins [rifabutin, rifampin]	Decreased effects of erythromycin Increased adverse effects of rifamycin.	Monitor for increased rifamycin adverse effects and decreased response to macrolide antibiotic. Use alternative antibiotic (eg, azithromycin, dirithromycin).
	Tacrolimus, see *Transplant Immunosuppressants—Macrolide Antibiotics*		
	Warfarin, see *Anticoagulants/Thrombolytic Agents—Macrolide Antibiotics*		
Penicillins	**Amoxicillin, Ampicillin, Bacampicillin, Carbenicillin, Cloxacillin, Dicloxacillin, Methicillin, Mezlocillin, Penicillin G, Penicillin V, Piperacillin, Ticarcillin**		
Penicillins-class	Aminoglycosides, see *Antimicrobial Agents (Antibacterial Antibiotics)*		
	Food	Decreased or delayed GI absorption of oral penicillins.	Administer penicillin at least 2 hours before or after a meal.
	Methotrexate, see *Antineoplastic Agents*		
	Tetracyclines [demeclocycline, doxycycline, minocycline, oxytetracycline, tetracycline]	Decreased effects of penicillins.	Avoid combination.
	Warfarin, see *Anticoagulants/Thrombolytic Agents*		
Ampicillin *(see also Penicillins-class)*	Allopurinol	Increased rate of ampicillin-associated skin rash.	Decrease allopurinol dose or use alternative drug if rash develops.
	Atenolol	Decreased effects of atenolol.	Separate administration times. Monitor blood pressure. Increase atenolol dose if necessary.
Quinolones	**Ciprofloxacin, Gatifloxacin, Gemifloxacin, Levofloxacin, Lomefloxacin, Moxifloxacin, Nalidixic Acid, Norfloxacin, Ofloxacin, Sparfloxacin, Trovafloxacin**		
Quinolones-class	Didanosine	Decreased GI absorption of quinolone.	Administer didanosine at least 6 hours before or 2 hours after quinolone

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Iron Salts (Oral) [ferrous fumarate, ferrous gluconate, ferrous sulfate, iron polysaccharide]	Decreased GI absorption of quinolone.	Avoid combination.
	Phosphate Binders/Antacids [aluminum hydroxide, aluminum-magnesium hydroxide, calcium acetate, calcium carbonate, magnesium hydroxide]	Decreased GI absorption of quinolone.	Separate administration times by at least 2 hours.
	Sucralfate	Decreased GI absorption of quinolone.	Administer sucralfate at least 6 hours after quinolone.
Ciprofloxacin *(see also Quinolones-class)*	Cyclosporine, see *Transplant Immunosuppressants—Quinolones*		
	Food [milk]	Decreased GI absorption of ciprofloxacin.	Avoid combination.
	Theophylline, see *Bronchodilators—Quinolones*		
Norfloxacin *(see also Quinolones-class)*	Cyclosporine, see *Transplant Immunosuppressants—Quinolones*		
	Food [milk]	Decreased GI absorption of norfloxacin.	Avoid combination.
	Theophylline, see *Bronchodilators—Quinolones*		
Ofloxacin *(see also Quinolones-class)*	Procainamide, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		
Sparfloxacin *(see also Quinolones-class)*	Amiodarone, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		
	Bepridil	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination.
	Disopyramide, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		
	Erythromycin, see *Antimicrobial Agents, Antibacterial Antibiotics (Macrolide Antibiotics)*		
	Phenothiazines, see *Sedatives/Hypnotics/Agents used in Psychiatry (Antipsychotic Agents)*		
	Procainamide, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		
	Quinidine, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		
	Sotalol, see *Antihypertensive and Cardiovascular Agents (Beta-Blockers)*		
	Tricyclic Antidepressants, see *Sedatives/Hypnotics/Agents used in Psychiatry (Tricyclic Antidepressants)*		
Tetracyclines	**Demeclocycline, Doxycycline, Methacycline, Minocycline, Oxytetracycline, Tetracycline**		
Tetracyclines-class	Bismuth Salts [bismuth subgallate, bismuth subsalicylate]	Decreased GI absorption of tetracycline.	Separate administration times by at least 2 hours.
	Iron Salts (Oral) [ferrous fumarate, ferrous gluconate, ferrous sulfate, iron polysaccharide]	Decreased GI absorption of tetracycline.	Separate administration times by at least 3-4 hours. Use enteric-coated or sustained-release formulation of iron salt.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Phosphate Binders/Antacids (aluminum carbonate, aluminum hydroxide, calcium acetate, calcium carbonate, calcium citrate, calcium glubionate, calcium gluconate, calcium lactate, tricalcium phosphate, magaldrate, magnesium carbonate, magnesium gluconate, magnesium hydroxide, magnesium oxide, magnesium sulfate, magnesium trisilicate)	Decreased GI absorption of tetracycline.	Separate administration times by at least 3-4 hours.
	Urinary Alkalinizers [potassium citrate, sodium acetate, sodium bicarbonate, sodium citrate, sodium lactate, tromethamine]	Decreased concentrations of tetracycline.	Separate administration times by at least 3-4 hours. Increase tetracycline dose if necessary.
	Zinc Salts [zinc gluconate, zinc sulfate]	Decreased GI absorption of tetracycline.	Separate administration times by at least 3-4 hours.
Doxycycline *(see also Tetracyclines-class)*	Barbiturates [amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, metharbital, pentobarbital, phenobarbital, primidone, secobarbital]	Decreased concentrations of doxycycline.	Increase doxycycline dose if necessary. Use alternative tetracycline.
	Carbamazepine	Decreased concentrations of doxycycline.	Increase doxycycline dose if necessary. Use alternative tetracycline.
	Digoxin, see *Antihypertensive and Cardiovascular Agents (Miscellaneous Antihypertensive and Cardiovascular Agents)—Tetracyclines*		
	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased concentrations of doxycycline.	Increase doxycycline dose if necessary. Use alternative tetracycline.
	Penicillins, see *Antimicrobial Agents (Antibacterial Antibiotics)—Tetracyclines*		
	Rifamycins [rifabutin, rifampin]	Decreased concentrations of doxycycline.	Increase doxycycline dose if necessary. Use alternative tetracycline.
Minocycline *(see also Tetracyclines-class)*	Digoxin, see *Antihypertensive and Cardiovascular Agents (Miscellaneous Antihypertensive and Cardiovascular Agents)—Tetracyclines*		
	Penicillins, see *Antimicrobial Agents (Antibacterial Antibiotics)—Tetracyclines*		
Tetracycline *(see also Tetracyclines-class)*	Penicillins, see *Antimicrobial Agents (Antibacterial Antibiotics)—Tetracyclines*		
Miscellaneous Antibacterial Antibiotics			
Chloramphenicol	Iron Products, see *Anemia Agents*		
	Phenytoin, see *Anticonvulsants (Hydantoins)*		
	Sulfonylureas, see *Hypoglycemic Agents*		
	Warfarin, see *Anticoagulants/Thrombolytic Agents*		

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
Clindamycin	Aluminum Salts [aluminum carbonate, aluminum hydroxide, aluminum phosphate, attapulgite, kaolin, magaldrate]	Delayed GI absorption of clindamycin.	Administer aluminum salts at least 2 hours before clindamycin.
Dapsone	Trimethoprim	Increased concentrations of both drugs.	Monitor for methemoglobinemia.
Imipenem/Cilastatin	Cyclosporine, see *Transplant Immunosuppressants*		
Metronidazole	Barbiturates [amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital]	Therapeutic failure of metronidazole.	Monitor for metronidazole treatment failure. Increase metronidazole dose if necessary. Use higher initial metronidazole dose.
	Disulfiram	Acute psychosis or confusion.	Avoid combination.
	Ethanol, see *Miscellaneous Agents*		
	Warfarin, see *Anticoagulants/Thrombolytic Agents*		
Trimethoprim/ Sulfamethoxazole	Cyclosporine, see *Transplant Immunosuppressants—Sulfonamides*		
	Dapsone, see *Antimicrobial Agents (Miscellaneous Antibacterial Antibiotics)*		
	Methotrexate, see *Antineoplastic Agents—Sulfonamides*		
	Phenytoin, see *Anticonvulsants—Sulfonamides*		
	Procainamide, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		
	Sulfonylureas, see *Hypoglycemic Agents*		
	Warfarin, see *Anticoagulants/Thrombolytic Agents—Sulfonamides*		
Vancomycin	Nondepolarizing Muscle Relaxants [atracurium, gallamine triethiodide, metocurine iodide, pancuronium, pipecuronium, tubocurarine, vecuronium]	Increased effects of nondepolarizing muscle relaxant (prolonged respiratory depression).	Avoid combination if possible. Otherwise, monitor respiratory function and adjust nondepolarizing muscle relaxant dose as needed.
Azole Antifungals	**Fluconazole, Itraconazole, Ketoconazole, Miconazole, Voriconazole**		
Azole Antifungals-class	Benzodiazepines, see *Sedatives/Hypnotics/Agents used in Psychiatry (Sedatives)*		
	Buspirone, see *Sedatives/Hypnotics/Agents used in Psychiatry (Miscellaneous Sedatives)*		
	Cyclosporine, see *Transplant Immunosuppressants*		
	Dexamethasone, see *Corticosteroids*		
	Grapefruit Juice	Decreased GI absorption of azole antifungal.	Avoid combination.
	Haloperidol, see *Sedatives/Hypnotics/Agents used in Psychiatry (Antipsychotic Agents)*		
	HMG-CoA Reductase Inhibitors, see *Hypolipidemic Agents*		
	Indinavir, see *Antimicrobial Agents (Antiviral Agents)*		
	Methylprednisolone, see *Corticosteroids*		
	Nelfinavir, see *Antimicrobial Agents (Antiviral Agents)*		
	Prednisolone and Prednisone, see *Corticosteroids*		
	Rifamycins [rifabutin, rifampin]	Decreased concentrations of azole antifungal.	Avoid combination if possible. Otherwise, increase azole antifungal dose if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Ritonavir, see *Antimicrobial Agents (Antiviral Agents)*		
	Saquinavir, see *Antimicrobial Agents (Antiviral Agents)*		
	Tacrolimus, see *Transplant Immunosuppressants*		
	Warfarin, see *Anticoagulants/Thrombolytic Agents*		
Fluconazole *(see also Azole Antifungals-class)*	Glimepride, see *Hypoglycemic Agents (Sulfonylureas)*		
	Phenytoin, see *Anticonvulsants*		
	Tolbutamide, see *Hypoglycemic Agents (Sulfonylureas)*		
Itraconazole *(see also Azole Antifungals-class)*	Didanosine	Decreased GI absorption of itraconazole.	Separate administration by at least 2 hours.
	Digoxin, see *Antihypertensive and Cardiovascular Agents (Miscellaneous Antihypertensive and Cardiovascular Agents)*		
	Felodipine, see *Antihypertensive and Cardiovascular Agents (Calcium-Channel Blockers)*		
	Food/Cola	Increased GI absorption of itraconazole.	Administer drug immediately after meals.
	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased effects of itraconazole. Increased effects of hydantoin.	Avoid combination.
	Proton Pump Inhibitors [esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole]	Decreased GI absorption of itraconazole.	Avoid combination if possible. Otherwise, administer itraconazole with an acidic beverage (cola).
	Quinidine, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmia Agents)*		
Ketoconazole *(see also Azole Antifungals-class)*	Didanosine	Decreased GI absorption of ketoconazole.	Separate administration by at least 2 hours.
	Histamine H_2-Antagonists [cimetidine, famotidine, nizatidine, ranitidine]	Decreased GI absorption of ketoconazole.	Avoid combination if possible. Otherwise, administer glutamic acid hydrochloride 680 mg 15 minutes before ketoconazole.
	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased effects of ketoconazole.	Avoid combination.
	Indinavir, see *Antimicrobial Agents (Antiviral Agents)*		
	Proton Pump Inhibitors [esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole]	Decreased GI absorption of itraconazole (ketoconazole).	Avoid combination if possible. Otherwise, administer ketoconazole with an acidic beverage (cola).
Voriconazole *(see also Azole Antifungals-class)*	Barbiturates [mephobarbital, phenobarbital]	Decreased concentrations of voriconazole.	Avoid combination.
	Carbamazepine	Decreased concentrations of voriconazole.	Avoid combination.
	Ergot Alkaloids, see *Miscellaneous Agents*		
	Pimozide	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Quinidine	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination.
Miscellaneous Antifungal Agents			
Griseofulvin	Barbiturates [amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital]	Decreased concentrations of griseofulvin	Separate administration times. Increase griseofulvin dose if necessary.
	Warfarin, see *Anticoagulants/Thrombolytic Agents*		
Caspofungin	Cyclosporine, see *Transplant Immunosuppressants*		
	Tacrolimus, see *Transplant Immunosuppressants*		
ANTIMYCOBACTERIAL AGENTS			
Aminosalicylic acid (PAS)	Rifampin, see *Antimicrobial Agents (Rifamycins)—Rifampin*		
Isoniazid	Carbamazepine, see *Anticonvulsants*		
	Phenytoin, see *Anticonvulsants (Hydantoins)*		
	Rifampin	Increased risk of hepatotoxicity.	Monitor liver function tests. Discontinue one or both drugs if necessary.
Rifamycins	**Rifabutin, Rifampin, Rifapentine**		
Rifamycins-class	Azole Antifungals, see *Antimicrobial Agents (Azole Antifungals)*		
	Bisoprolol	Decreased effects of bisoprolol.	Monitor cardiovascular status. Increase bisoprolol dose if necessary.
	Buspirone, see *Sedatives/Hypnotics/Agents used in Psychiatry (Miscellaneous Sedatives)*		
	Clarithromycin, see *Antimicrobial Agents, Antibacterial Antibiotics (Macrolide Antibiotics)*		
	Corticosteroids , see *Corticosteroids*		
	Cyclosporine, see *Transplant Immunosuppressants*		
	Delavirdine, see *Antimicrobial Agents (Antiviral Agents)*		
	Doxycycline, see *Antimicrobial Agents, Antibacterial Antibiotics (Tetracyclines)*		
	Erythromycin, see *Antimicrobial Agents, Antibacterial Antibiotics (Macrolide Antibiotics)*		
	Estrogens, see *Miscellaneous Agents*		
	Haloperidol, see *Sedatives/Hypnotics/Agents used in Psychiatry (Antipsychotic Agents)*		
	HMG-CoA Reductase Inhibitors, see *Hypolipidemic Agents*		
	Indinavir, see *Antimicrobial Agents (Antiviral Agents)*		
	Methadone, see *Pain Medications (Narcotic)*		
	Metoprolol	Decreased effects of metoprolol.	Monitor cardiovascular status. Increase metoprolol dose if necessary.
	Morphine, see *Pain Medications (Narcotic)*		
	Nelfinavir, see *Antimicrobial Agents (Antiviral Agents)*		
	Phenytoin, see *Anticonvulsants (Hydantoins)*		

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Propranolol	Decreased effects of propranolol.	Monitor cardiovascular status. Increase propranolol dose if necessary.
	Quinidine, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		
	Quinine, see *Miscellaneous Agents*		
	Ritonavir, see *Antimicrobial Agents (Antiviral Agents)*		
	Sulfonylureas, see *Hypoglycemic Agents*		
	Tacrolimus, see *Transplant Immunosuppressants*		
	Theophyllines, see *Bronchodilators*		
	Tricyclic Antidepressants, see *Sedatives/Hypnotics/Agents used in Psychiatry (Antidepressants)*		
	Warfarin, see *Anticoagulants/Thrombolytic Agents*		
Rifampin *(see also Rifamycins-class)*	Disopyramide, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		
	Isoniazid, see *Antimicrobial Agents (Antimycobacterial Agents)*		
	Nifedipine, see *Antihypertensive and Cardiovascular Agents (Calcium-Channel Blockers)*		
	Verapamil, *see Antihypertensive and Cardiovascular Agents (Calcium-Channel Blockers)*		
ANTIVIRAL AGENTS			
Acyclovir	Theophyllines, see *Bronchodilators*		
Delavirdine	Ergot Alkaloids, see *Miscellaneous Agents-NNRT Inhibitors*		
	Rifamycins [rifabutin, rifampin]	Decreased concentrations of delavirdine.	Avoid combination.
Didanosine	Food	Decreased GI absorption of didanosine.	Administer didanosine on an empty stomach.
	Indinavir, see *Antimicrobial Agents (Antiviral Agents)*		
	Itraconazole, see *Antimicrobial Agents (Azole Antifungals)*		
	Ketoconazole, see *Antimicrobial Agents (Azole Antifungals)*		
	Quinolones, see *Antimicrobial Agents (Antibacterial Antibiotics)*		
Foscarnet	Cyclosporine	Increased risk of renal failure.	Avoid combination if possible. Otherwise, monitor renal function and discontinue foscarnet if necessary.
Ganciclovir	Zidovudine	Increased risk of life-threatening hematologic toxicity.	Avoid combination. Use foscarnet instead.
Indinavir	Azole Antifungals [fluconazole, itraconazole, ketoconazole]	Increased concentrations of protease inhibitor.	Decrease protease inhibitor dose if necessary.
	Benzodiazepines, see *Sedatives/Hypnotics/Agents used in Psychiatry (Sedatives)-Protease Inhibitor*		
	Didanosine	Decreased GI absorption of indinavir.	Separate administration times by at least 1 hour on an empty stomach.
	Ergot Alkaloids, see *Miscellaneous Agents-Protease Inhibitors*		
	Methadone, see *Pain Medications (Narcotic)-Protease Inhibitors*		
	Rifamycins [rifabutin, rifampin, rifapentine]	Decreased concentrations of in dinavir. Increased concentrations of rifamycin.	Avoid combination if possible. Otherwise, decrease rifabutin dose by 50%. Increase indinvair dose if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
Nelfinavir	Azole Antifungals [fluconazole, itraconazole, ketoconazole]	Increased concentrations of protease inhibitor.	Decrease protease inhibitor dose if necessary.
	Ergot Alkaloids, see *Miscellaneous Agents-Protease Inhibitors*		
	Ethinyl Estradiol	Loss of contraceptive efficacy of ethinyl estradiol.	Use alternative nonhormonal or additional method of contraception. Use alternative protease inhibitor (eg, indinavir).
	Methadone, see *Pain Medications (Narcotic)-Protease Inhibitors*		
	Rifamycins [rifabutin, rifampin]	Decreased concentrations of nelfinavir.	Avoid combination if possible. Otherwise, decrease rifabutin dose by 50%. Increase nelfinavir dose if necessary.
Ritonavir	Amiodarone, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		
	Azole Antifungals [fluconazole, itraconazole, ketoconazole]	Increased concentrations of protease inhibitor.	Decrease protease inhibitor dose if necessary.
	Benzodiazepines, see *Sedatives/Hypnotics/Agents used in Psychiatry (Sedatives)-Protease Inhibitor*		
	Buproprion, see *Sedatives/Hypnotics/Agents used in Psychiatry, Antidepressants (Miscellaneous Antidepressants)*		
	Clozapine, see *Sedatives/Hypnotics/Agents used in Psychiatry (Antipsychotic Agents)*		
	Encainide	Increased concentrations of encainide.	Avoid combination.
	Ergot Alkaloids, see *Miscellaneous Agents-Protease Inhibitors*		
	Ethinyl Estradiol	Loss of contraceptive efficacy of ethinyl estradiol.	Use alternative nonhormonal or additional method of contraception. Use alternative protease inhibitor (eg, indinavir).
	Flecainide	Increased concentrations of flecainide.	Avoid combination.
	Meperidine, see *Pain Medications (Narcotic)*		
	Piroxicam, see *Arthritis and Gout Agents (NSAIDs)*		
	Propafenone	Increased concentrations of propafenone.	Avoid combination.
	Propoxyphene, see *Pain Medications (Narcotic)*		
	Quinidine	Increased concentrations of quinidine.	Avoid combination.
	Rifamycins [rifabutin, rifampin]	Decreased concentrations of ritonavir. Increased concentrations of rifabutin.	Avoid combination if possible. Otherwise, decrease rifabutin dose by 50%. Increase ritonavir dose if necessary.
Saquinavir	Benzodiazepines, see *Sedatives/Hypnotics/Agents used in Psychiatry (Sedatives)-Protease Inhibitor*		
	Ergot Alkaloids, see *Miscellaneous Agents-Protease Inhibitors*		
	Grapefruit Juice	Increased concentrations of saquinavir.	Avoid combination.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
Zidovudine	Atovaquone	Increased concentrations of zidovuine.	Monitor for signs/symptoms of toxicity. Decrease zidovudine dose if necessary.
	Ganciclovir, see *Antimicrobial Agents (Antiviral Agents)*		
	Probenecid	Rash, malaise, myalgia, and fever.	Monitor for signs/symptoms of toxicity.
ANTICOAGULANTS/THROMBOLYTIC AGENTS			
Alteplase	Nitroglycerin, see *Antihypertensive and Cardiovascular Agents (Nitrates)*		
Dipyridamole	Adenosine	Increased effects of adenosine (profound bradycardia).	No special precautions needed when using adenosine to terminate SVT due to its short half-life. Decrease initial infusion rate of adenosine when using it to simulate exercise during cardiac imaging.
Heparin	Salicylates [aspirin]	Increased risk of bleeding.	Monitor for signs/symptoms of bleeding. Treat symptomatically.
Ticlopidine	Phenytoin, see *Anticonvulsants*		
	Theophylline, see *Bronchodilators*		
Warfarin	Acetaminophen	Increased effects of warfarin.	Limit acetaminophen use. Monitor INR more frequently with chronic or high doses of acetaminophen.
	Aminoglutethimide	Decreased effects of warfarin.	Monitor INR. Adjust warfarin dose as needed when starting or stopping aminoglutethimide.
	Amiodarone	Increased effects of warfarin.	Monitor INR. Decrease warfarin dose empirically and adjust warfarin dose as needed.
	Androgens [danazol, fluoxymesterone, methyltestosterone, nandrolone decanoate, oxandrolone, oxymetholone, stanozolol, testosterone]	Increased effects of warfarin.	Avoid combination if possible. Otherwise, monitor INR and decrease warfarin dose if necessary.
	Azole Antifungals [fluconazole, itraconazole, ketoconazole, miconazole]	Increased effects of warfarin.	Monitor INR. Adjust warfarin dose as needed when starting or stopping azole antifungal.
	Barbiturates [amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital,	Decreased effects of warfarin.	Monitor INR. Adjust warfarin dose as needed when starting or stopping barbiturate. Use benzodiazepine instead.
	Carbamazepine	Decreased effects of warfarin.	Monitor INR. Adjust warfarin dose as needed when starting or stopping carbamazepine.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Cephalosporins [cefamandole, cefazolin, cefoperazone, cefotetan, cefoxitin, ceftriaxone]	Increased effects of warfarin.	Monitor INR . Adjust warfarin dose as needed when starting or stopping cephalosporin.
	Chloramphenicol	Increased effects of warfarin.	Monitor INR. Decrease warfarin dose if necessary.
	Cholestyramine	Decreased effects of warfarin.	Separate administration times by at least 3 hours. Monitor INR. Increase warfarin dose if necessary.
	Cimetidine	Increased effects of warfarin.	Avoid combination if possible. Otherwise, monitor INR and decrease warfarin dose if necessary. Use alternative histamine H_2-antagonist (eg, ranitidine).
	Dextrothyroxine	Increased effects of warfarin.	Monitor INR. Decrease warfarin dose if necessary.
	Disulfiram	Increased effects of warfarin.	Monitor INR. Decrease warfarin dose if necessary.
	Ethchlorvynol	Decreased effects of warfarin.	Monitor INR. Increase warfarin dose if necessary. Use benzodiazepine instead.
	Fibric Acids [clofibrate, fenofibrate, gemfibrozil]	Increased effects of warfarin.	Avoid combination.
	Glucagon	Increased effects of warfarin with prolonged glucagon dosing.	Monitor INR. Decrease warfarin dose if necessary.
	Glutethimide	Decreased effects of warfarin.	Monitor INR. Adjust warfarin dose as needed when starting or stopping glutethimide. Use benzodiazepine instead.
	Griseofulvin	Decreased effects of warfarin.	Monitor INR. Adjust warfarin dose as needed when starting, stopping, or changing dose of griseofulvin.
	HMG-CoA Reductase Inhibitors [fluvastatin, lovastatin, simvastatin]	Increased effects of warfarin.	Monitor INR. Adjust warfarin dose as needed when starting or stopping HMG-CoA reductase inhibitor.
	Levamisole	Increased effects of warfarin.	Monitor INR when starting or stopping levamisole. Adjust warfarin dose as needed.
	Macrolide Antibiotics [azithromycin, clarithromycin, erythromycin]	Increased effects of warfarin.	Monitor INR. Decrease warfarin dose if necessary.
	Metronidazole	Increased effects of warfarin.	Monitor INR. Decrease warfarin dose if necessary.
	Nalidixic Acid	Increased effects of warfarin.	Monitor INR. Decrease warfarin dose if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	NSAIDs [diclofenac, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, nabumetone, naproxen, oxaprozin, piroxicam, sulindac, tolmetin]	Increased effects of warfarin. Increased risk of bleeding.	Monitor INR and for signs/ symptoms of bleeding. Treat symptomatically.
	Penicillins [ampicillin, dicloxacillin, methicillin, mezlocillin, nafcillin, oxacillin, penicillin G, piperacillin, ticarcillin]	Increased effects of warfarin with large doses of IV penicillin. Nafcillin and dicloxacillin can cause warfarin resistance.	Monitor INR. Decrease warfarin dose if necessary.
	Quinine Derivatives [quinidine, quinine]	Increased effects of warfarin.	Monitor INR. Decrease warfarin dose if necessary.
	Rifamycins [rifabutin, rifampin, rifapentine]	Decreased effects of warfarin.	Monitor INR. Adjust warfarin dose as needed when starting or stopping rifamycin.
	Salicylates [aspirin, methylsalicylate]	Increased effects of warfarin with large doses of salicylate. Increased risk of bleeding with any aspirin dose.	Avoid large doses of aspirin. Monitor INR and for signs/symptoms of bleeding. Treat symptomatically.
	Sulfinpyrazone	Increased effects of warfarin.	Monitor INR. Decrease warfarin dose if necessary.
	Sulfonamides [sulfamethizole, sulfamethoxazole, sulfasalazine, sulfisoxazole, trimethoprim/ sulfamethoxazole]	Increased effects of warfarin.	Monitor INR. Decrease warfarin dose if necessary.
	Thioamines [methimazole, propylthiouracil]	Various effects on warfarin activity.	Monitor INR. Adjust warfarin dose as needed.
	Thyroid Hormones [levothyroxine, liothyronine, liotrix, thyroid]	Increased effects of warfarin.	Monitor INR. Adjust warfarin dose as needed when starting, stopping, or changing dose of thyroid hormone.
	Vitamin E (Tocopherol)	Increased effects of warfarin.	Monitor INR. Decrease warfarin dose if necessary.
	Vitamin K (Phytonadione)	Decreased or reversed effects of warfarin.	Avoid or minimize intake of foods with high vitamin K. Monitor INR. Adjust warfarin dose as needed.

ANTICONVULSANTS

Carbamazepine	Bupropion, see *Sedatives/Hypnotics/Agents used in Psychiatry (Miscellaneous Sedatives)*		
	Cimetidine	Increased concentrations of carbamazepine.	Avoid combination if possible. Otherwise, monitor carbamazepine concentrations. Decrease dose if necessary. Use alternative histamine H_2-antagonist (eg, ranitidine).
	Cyclosporine, see *Transplant Immunosuppressants*		

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Danazol	Increased concentrations of carbamazepine.	Avoid combination if possible. Otherwise, monitor carbamazepine concentrations. Decrease dose if necessary.
	Diltiazem	Increased concentrations of carbamazepine.	Monitor carbamazepine concentrations. Decrease carbamazepine dose if necessary.
	Doxycycline, see *Antimicrobial Agents, Antibacterial Antibiotics (Tetracyclines)*		
	Felodipine, see *Antihypertensive and Cardiovascular Agents (Calcium-Channel Blockers)*		
	Fluoxetine	Increased concentrations of carbamazepine.	Monitor carbamazepine concentrations. Decrease carbamazepine dose if necessary.
	Grapefruit Juice	Increased concentrations of carbamazepine.	Avoid combination.
	Haloperidol, see *Sedatives/Hypnotics/Agents used in Psychiatry (Antipsychotic Agents)*		
	Isoniazid	Increased risk of carbamazepine toxicity and isoniazid hepatotoxicity.	Monitor liver function tests. Monitor carbamazepine concentrations. Decrease carbamazepine dose if necessary.
	Lamotrigine, see *Anticonvulsants*		
	Lithium, see *Sedative/Hypnotics/Agents used in Psychiatry, Antidepressants (Miscellaneous Antidepressants)*		
	Macrolide Antibiotics [clarithromycin, erythromycin, troleandomycin]	Increased concentrations of carbamazepine.	Avoid combination if possible. Otherwise, monitor carbamazepine concentrations and decrease dose if necessary.
	MAO Inhibitors [isocarboxazid, phenelzine, tranylcypromine]	Increased risk of severe adverse effects (hyperpyrexia, hyperexcitability, muscle rigidity, seizures).	Avoid combination. Discontinue MAO inhibitor at least 14 days prior to starting carbamazepine.
	Nefazodone	Increased concentrations of carbamazepine. Decreased concentrations of nefazodone.	Avoid combination.
	Phenytoin, see *Anticonvulsants (Hydantoins)*		
	Primidone	Decreased concentrations of carbamazepine, primidone, and phenobarbital (metabolite of primidone).	Monitor carbamazepine and primidone concentrations. Adjust dose of one or both drugs as needed.
	Propoxyphene	Increased concentrations of carbamazepine.	Avoid combination if possible. Otherwise, monitor carbamazepine concentrations and decrease dose if necessary.
	Tricyclic Antidepressants [amitriptyline, desipramine, doxepin, imipramine, nortriptyline]	Increased concentrations of carbamazepine. Decreased concentrations of tricyclic antidepressant.	Monitor carbamazepine and tricyclic antidepressant concentrations. Adjust dose of one or both drugs as needed.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Valproic acid, see *Anticonvulsants*		
	Verapamil	Increased concentrations of carbamazepine.	Monitor carbamazepine concentrations. Decrease carbamazepine dose if necessary.
	Warfarin, see *Anticoagulants/Thrombolytic Agents*		
Lamotrigine	Carbamazepine	Decreased concentrations of lamotrigine. Increased risk of carbamazepine toxicity.	Adjust dose of lamotrigine as needed when starting, stopping, or changing dose of carbamazepine.
	Valproic Acid [divalproex sodium, valproic acid, valproate sodium]	Increased concentrations of lamotrigine. Decreased concentrations of valproic acid.	Adjust dose of one or both drugs as needed.
Phenobarbital	Beta-Blockers [metoprolol, propranolol]	Decreased bioavailability of beta-blocker.	Increase beta-blocker dose if necessary.
	Corticosteroids, see *Corticosteroids—Barbiturates*		
	Doxycycline, see *Antimicrobial Agents, Antibacterial Antibiotics (Tetracyclines)—Barbiturates*		
	Estrogens, see *Miscellaneous Agents—Barbiturates*		
	Ethanol, see *Miscellaneous Agents—Barbiturates*		
	Felodipine, see *Antihypertensive and Cardiovascular Agents (Calcium-Channel Blockers)—Barbiturates*		
	Griseofulvin, see *Antimicrobial Agents (Miscellaneous Antifungals)—Barbiturates*		
	Methadone, see *Pain Medications (Narcotic)—Barbiturates*		
	Metronidazole, see *Antimicrobial Agents (Miscellaneous Antibacterial Antibiotics)—Barbiturates*		
	Nifedipine, see *Antihypertensive and Cardiovascular Agents (Calcium-Channel Blockers)—Barbiturates*		
	Quinidine, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)—Barbiturates*		
	Theophylline, see *Bronchodilators—Barbiturates*		
	Valproic Acid	Increased concentrations of phenobarbital.	Decrease phenobarbital dose if necessary.
	Voriconazole, see *Antimicrobial Agents (Azole Antifungals)—Barbiturates*		
	Warfarin, see *Anticoagulants/Thrombolytic Agents—Barbiturates*		
Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin] ***Monitor free (unbound) phenytoin concentrations in patients with renal insufficiency or failure.**	Amiodarone	Increased concentrations of phenytoin. Decreased concentrations of amiodarone.	Monitor phenytoin concentrations* and signs/symptoms of phenytoin toxicity. Monitor for loss of amiodarone effect. Adjust doses of one or both drugs as needed.
	Anticoagulants [anisidione, dicumarol, warfarin]	Increased concentrations of phenytoin. Increased INR and risk of bleeding.	Monitor for altered response to phenytoin or anticoagulant. Monitor phenytoin concentrations* and INR. Adjust dose of one or both drugs as needed.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Antineoplastic Agents [bleomycin, carboplatin, carmustine, cisplatin, methotrexate, vinblastine]	Decreased concentrations of phenytoin.	Monitor phenytoin concentrations.* Increase phenytoin dose if necessary.
	Carbamazepine	Decreased concentrations of carbamazepine. Variable effects on concentrations of phenytoin.	Monitor carbamazepine and phenytoin concentrations*. Adjust dose of one or both drugs as needed.
	Chloramphenicol	Increased concentrations of phenytoin. Variable effects on concentrations of chloramphenicol.	Monitor phenytoin concentrations.* Adjust dose of one or both drugs as needed.
	Cimetidine	Increased concentrations of phenytoin.	Avoid combination. Use alternative histamine H_2-antagonist (eg, ranitidine).
	Corticosteroids, see *Corticosteroids—Hydantoins*		
	Cyclosporine, see *Transplant Immunosuppressants—Hydantoins*		
	Diazoxide	Decreased concentrations of phenytoin.	Monitor phenytoin concentrations.* Increase phenytoin dose if necessary.
	Disopyramide, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)—Hydantoins*		
	Disulfiram	Increased concentrations of phenytoin.	Monitor phenytoin concentrations.* Decrease phenytoin dose if necessary.
	Dopamine	Increased risk of profound hypotension and cardiac arrest.	Monitor blood pressure. Discontinue phenytoin if hypotension occurs.
	Doxycycline, see *Antimicrobial Agents, Antibacterial Antibiotics (Tetracyclines)—Hydantoins*		
	Estrogens, see *Miscellaneous Agents—Hydantoins*		
	Felbamate	Increased concentrations of phenytoin. Decreased concentrations of felbamate.	Monitor felbamate and phenytoin concentrations.* Adjust dose of one or both drugs as needed.
	Felodipine, see *Antihypertensive and Cardiovascular Agents (Calcium-Channel Blockers)—Hydantoins*		
	Fluconazole	Increased concentrations of phenytoin.	Monitor phenytoin concentrations.* Decrease phenytoin dose if necessary.
	Fluoxetine	Increased concentrations of phenytoin.	Monitor phenytoin concentrations.* Decrease phenytoin dose if necessary.
	Folic acid	Decreased concentrations of phenytoin.	Monitor phenytoin concentrations.* Increase phenytoin dose if necessary.
	Isoniazid	Increased concentrations of phenytoin.	Monitor phenytoin concentrations.* Decrease phenytoin dose if necessary.
	Itraconazole, see *Antimicrobial Agents (Azole Antifungals)—Hydantoins*		
	Ketoconazole, see *Antimicrobial Agents (Azole Antifungals)—Hydantoins*		
	Levodopa, see *Antiparkinson Agents—Hydantoins*		

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Methadone, see *Pain Medications (Narcotic)—Hydantoins*		
	Metyrapone, see *Miscellaneous Agents—Hydantoins*		
	Mexiletine, see *Antihypertensive and Cardiovascular Agents, (Antiarrhythmic Agents)—Hydantoins*		
	Nisoldipine, *see Antihypertensive Agents and Cardiovascular Agents (Calcium-Channel Blockers)—Hydantoins*		
	Phenacemide	Increased concentrations of phenytoin.	Monitor phenytoin concentrations.* Decrease phenytoin dose if necessary.
	Phenylbutazones [oxyphenbutazone, phenylbutazone]	Increased concentrations of phenytoin.	Monitor phenytoin concentrations.* Decrease phenytoin dose if necessary.
	Primidone	Increased concentrations of primidone and primidone-metabolite.	Monitor primidone and primidone-metabolite concentrations. Decrease primidone dose if necessary.
	Quinidine, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)—Hydantoins*		
	Rifamycins [rifabutin, rifampin]	Decreased concentrations of phenytoin.	Monitor phenytoin concentrations.* Increase phenytoin dose if necessary.
	Sertraline	Increased concentrations of phenytoin.	Monitor phenytoin concentrations.* Decrease phenytoin dose if necessary.
	Sucralfate	Decreased GI absorption of phenytoin.	Monitor phenytoin concentrations.* Increase phenytoin dose if necessary.
	Sulfonamides [sulfadiazine, sulfamethizole]	Increased concentrations of phenytoin.	Monitor phenytoin concentrations.* Decrease phenytoin dose if necessary.
	Tacrolimus, see *Transplant Immunosuppressants*		
	Theophylline, see *Bronchodilators*		
	Ticlopidine	Increased concentrations of phenytoin.	Monitor phenytoin concentrations.* Decrease phenytoin dose if necessary.
	Trimethoprim	Increased concentrations of phenytoin.	Monitor phenytoin concentrations.* Decrease phenytoin dose if necessary.
	Valproic Acid [divalproex sodium, valproic acid]	Increased concentrations of phenytoin. Decreased concentrations of valproic acid.	Monitor free phenytoin and valproic acid concentrations. Adjust dose of one or both both drugs as needed.
Valproic Acid [divalproex sodium, sodium valproate, valproic acid]	Barbiturates [phenobarbital, primidone]	Increased concentrations of barbiturate.	Increase barbiturate dose if necessary.
	Carbamazepine	Decreased concentrations of valproic acid.	Monitor valproic acid concentrations, seizure activity, and signs/symptoms of toxicity for at least a month after starting or stopping either drug. Increase valproic acid dose if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Cholestyramine	Decreased GI absorption of valproic acid.	Separate administration times by at least 3 hours. Monitor valproic acid concentrations. Increase valproic acid dose if necessary.
	Felbamate	Increased concentrations of valproic acid.	Monitor valproic acid concentrations. Decrease valproic acid dose if necessary.
	Lamotrigine, see *Anticonvulsants*		
	Phenytoin, see *Anticonvulsants*		
	Salicylates [aspirin, bismuth subsalicylate, choline salicylate, magnesium salicylate, salsalate, sodium salicylate, sodium thiosalicylate]	Increased free (unbound) concentrations of valproic acid.	Monitor free valproic acid concentrations. Decrease valproic acid dose if necessary.
	Tricyclic Antidepressants, see *Sedatives/Hypnotics/Agents used in Psychiatry (Antidepressants)*		
ANTINEOPLASTIC AGENTS			
Azathioprine	Allopurinol, see *Arthritis and Gout Agents (Miscellaneous Arthritis and Gout Agents)—Thiopurines*		
Methotrexate	NSAIDs [diclofenac, etodolac, fenoprofen, flubiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, mefenamic acid, nabumetone, naproxen, oxaprozin, piroxicam, sulindac, tolmetin]	Increased risk of methotrexate toxicity.	Monitor for renal impairment and signs/symptoms of toxicity. Monitor methotrexate concentrations. Consider extended leucovorin rescue therapy.
	Penicillins [amoxicillin, ampicillin, bacampicillin, carbenicillin, cloxacillin, dicloxacillin, methicillin, mezlocillin, penicillin G, penicillin V, piperacillin, ticarcillin]	Increased concentrations of methotrexate. Increased risk of methotrexate toxicity.	Monitor for signs/symptoms of toxicity. Monitor methotrexate concentrations. Consider extended leucovorin rescue therapy. Use alternative anbiotic if possible (eg, ceftazidime).
	Probenecid	Increased concentrations of methotrexate. Increased risk of methotrexate toxicity.	Decrease methotrexate dose. Monitor for signs/symptoms of toxicity. Monitor methotrexate concentrations. Consider extended leucovorin rescue therapy.
	Salicylates [aspirin, bismuth subsalicylate, choline magnesium salicylate, choline salicylate, magnesium salicylate, salsalate, sodium salicylate, sodium thiosalicylate]	Increased risk of methotrexate toxicity.	Decrease methotrexate dose. Monitor for signs/symptoms of toxicity. Monitor methotrexate concentrations. Consider extended leucovorin rescue therapy.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Sulfonamides [sulfadiazine, sulfamethizole, sulfamethoxazole, sulfasalazine, sulfisoxazole, trimethoprim/ sulfamethoxazole]	Increased risk of bone marrow suppression and megaloblastic anemia.	Avoid combination if possible. Otherwise, monitor for signs/symptoms of hematologic toxicity. Administer leucovorin if necessary.
ANTIPARKINSON AGENTS			
Levodopa	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased effects of levodopa.	Avoid combination.
	Iron Salts (Oral) [ferrous fumarate, ferrous gluconate, ferrous sulfate, iron polysaccharide]	Decreased effects of levodopa.	Separate administration times. Monitor clincial response and increase levodopa dose if necessary.
	MAO Inhibitors [phenelzine, tranylcypromine]	Increased risk of hypertensive reactions.	Avoid combination. Use alternative MAOI (eg, selegiline).
	Pyridoxine	Decreased effects of levodopa.	Avoid combination if possible in patients treated with levodopa alone.
ARTHRITIS AND GOUT AGENTS			
Allopurinol	Ampicillin, see *Antimicrobial Agents (Penicillins)*		
	Thiopurines [azathioprine, mercaptopurine]	Increased effects of thiopurine.	Decrease thiopurine dose by 25-33%. Monitor hematologic function (bone marrow suppression).
Colchicine	Cyclosporine, see *Transplant Immunosuppressants*		
Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)	**Diclofenac, Diflunisal, Etodolac, Fenoprofen, Flubiprofen, Ibuprofen, Indomethacin, Ketoprofen, Ketorolac, Meclofenamate, Mefenamic Acid, Nabumetone, Naproxen, Piroxicam, Sulindac, Tolmetin**		
Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)-class	Aminoglycosides, see *Antimicrobial Agents (Antibacterial Antibiotics)*		
	Beta-Blockers, see *Antihypertensive and Cardiovascular Agents (Cardio-Selective and Noncardio-Selective Beta-Blockers)*		
	Lithium, see *Sedatives/Hypnotics/Agents used in Psychiatry, Antidepressants (Miscellaneous Antidepressants)*		
	Methotrexate, see *Antineoplastic Agents*		
	Warfarin, see *Anticoagulants/Thrombolytic Agents*		
Diflunisal *(see also Nonsteroidal Anti-Inflammatory Drugs-class)*	Probenecid	Increased effects of diflunisal.	Monitor for diflunisal toxicity.
Ibuprofen *(see also Nonsteroidal Anti-Inflammatory Drugs-class)*	Beta-Blockers, see *Antihypertensive and Cardiovascular Agents (Cardio-Selective and Noncardio-Selective Beta-Blockers) — NSAIDs*		
Indomethacin *(see also Nonsteroidal Anti-Inflammatory Drugs-class)*	Beta-Blockers, see *Antihypertensive and Cardiovascular Agents (Cardio-Selective and Noncardio-Selective Beta-Blockers) — NSAIDs*		

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Digoxin, see *Antihypertensive and Cardiovascular Agents (Miscellaneous Antihypertensive and Cardiovascular Agents)*		
Ketorolac *(see also Nonsteroidal Anti-Inflammatory Drugs-class)*	Probenecid	Increased risk of ketorolac toxicity.	Avoid combination.
	Salicylates [aspirin]	Increased risk of ketorolac adverse effects.	Avoid combination.
Naproxen *(see also Nonsteroidal Anti-Inflammatory Drugs-class)*	Beta-Blockers, see *Antihypertensive and Cardiovascular Agents (Cardio-Selective and Noncardio-Selective Beta-Blockers) — NSAIDs*		
Piroxicam *(see also Nonsteroidal Anti-Inflammatory Drugs-class)*	Beta-Blockers, see *Antihypertensive and Cardiovascular Agents (Cardio-Selective and Noncardio-Selective Beta-Blockers) — NSAIDs*		
	Ritonavir	Increased risk of piroxicam toxicity.	Avoid combination.

BRONCHODILATORS

Theophyllines	**Aminophylline, Dyphylline, Oxtriphylline, Theophylline**		
Theophyllines-class	Acyclovir	Increased concentrations of theophylline.	Monitor theophylline concentrations. Decrease theophylline dose if necessary.
	Barbiturates [amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital]	Decreased concentrations of theophylline.	Monitor theophylline concentrations. Increase theophylline dose if necessary.
	Beta-Blockers, noncardio-selective [carteolol, penbutolol, pindolol, propranolol, timolol]	Increased concentrations of theophylline. Pharmacologic antagonism may decrease effects of one or both drugs.	Monitor theophylline concentrations. Use cardio-selective beta-blockers.
	Cimetidine	Increased concentrations of theophylline.	Monitor theophylline concentrations. Decrease theophylline dose by 20-40% when starting cimetidine. Use alternative histamine H_2-antagonist (eg, ranitidine).
	Contraceptives, Oral	Increased concentrations of theophylline.	Monitor theophylline concentrations. Decrease theophylline dose if necessary.
	Diltiazem	Increased concentrations of theophylline.	Monitor theophylline concentrations. Decrease theophylline dose if necessary.
	Disulfiram	Increased concentrations of theophylline.	Monitor theophylline concentrations. Decrease theophylline dose if necessary.
	Food	Increased or decreased absorption or clearance of various theophylline products.	Refer to package insert for specific management.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Halothane	Increased risk of arrhythmias.	Avoid combination. Use alternative anesthetic (eg, enflurane).
	Hydantoins [fosphenytoin, phenytoin]	Decreased concentrations of theophylline and phenytoin.	Monitor theophylline and phenytoin concentrations. Adjust dose of one or both drugs as needed.
	Macrolide Antibiotics [azithromycin, clarithromycin, dirithromycin, erythromycin, troleandomycin]	Increased concentrations of theophylline.	Monitor theophylline concentrations. Decrease theophylline dose if necessary. Use alternative antibiotic.
	Mexiletine	Increased concentrations of theophylline.	Monitor theophylline concentrations. Decrease theophylline dose if necessary.
	Quinolones [ciprofloxacin, enoxacin, norfloxacin]	Increased concentrations of theophylline.	Monitor theophylline concentrations. Decrease theophylline dose if necessary.
	Rifamycins [rifabutin, rifampin, rifapentine]	Decreased concentrations of theophylline.	Monitor theophylline concentrations. Increase theophylline dose if necessary.
	Thiabendazole	Increased concentrations of theophylline.	Monitor theophylline concentrations. Decrease theophylline dose if necessary.
	Thioamines [methimazole, propylthiouracil]	Decreased theophylline concentrations in hyperthyroid patients; returns to normal once euthyroid state achieved.	Monitor theophylline concentrations. Adjust theophylline dose as needed. Achieve euthyroid state as soon as possible.
	Thyroid Hormones [dextrothyroxine, levothyroxine, liothyronine, liotrix, thyroglobulin, thyroid]	Decreased theophylline concentrations in hyperthyroid patients; returns to normal once euthyroid state achieved.	Monitor theophylline concentrations. Adjust theophylline dose as needed. Achieve euthyroid state as soon as possible.
	Ticlopidine	Increased concentrations of theophylline.	Monitor theophylline concentrations. Decrease theophylline dose if necessary.
	Zileuton	Increased concentrations of theophylline.	Monitor theophylline concentrations. Decrease theophylline dose by 50% when starting zileuton.
Leukotriene Inhibitors			
Zileuton	Theophylline, see *Bronchodilators*		

CORTICOSTEROIDS

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
Corticosteroids	**Betamethasone, Corticotropin, Cortisone, Cosyntropin, Dexamethasone, Fludrocortisone, Hydrocortisone, Methylprednisolone, Prednisolone, Prednisone, Triamcinolone**		
Corticosteroids-class	Anticholinesterases [ambenonium, edrophonium, neostigmine, pyridostigmine]	Corticosteroids antagonize effect of anticholinesterases in myasthenia gravis.	Monitor clinical response.
	Aspirin, see *Pain Medications (Non-Narcotic)*		
	Barbiturates [amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital]	Decreased effects of corticosteroid.	Avoid combination if possible. Otherwise, increase corticosteroid dose if necessary.
	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased effects of corticosteroid.	Increase corticosteroid dose if necessary.
	Rifamycins [rifabutin, rifampin, rifapentine]	Decreased effects of corticosteroid.	Avoid combination if possible. Otherwise, increase corticosteroid dose if necessary.
Dexamethasone *(see also Corticosteroids-class)*	Aminoglutethimide	Decreased effects of dexamethasone.	Increase dexamethasone dose if necessary. Use alternative corticosteroid (eg, hyrdrocortisone).
	Azole Antifungals [fluconazole, itraconazole, ketoconazole]	Increased effects of dexamethasone.	Decrease dexamethasone dose if necessary.
Hydrocortisone *(see also Corticosteroids-class)*	Azole Antifungals [fluconazole, itraconazole, ketoconazole]	Increased effects of hydrocortisone.	Decrease hydrocortisone dose if necessary.
	Bile Acid Sequestrants [cholestyramine, colestipol]	Decreased GI absorption of hydrocortisone.	Separate administration times. Use alternative lipid-lowering drug.
	Estrogens [chlorotrianisene, conjugated estrogens, diethylstilbesterol, esterified estrogens, estradiol, estrone, estropipate, ethinyl estradiol, quinestrol]	Increased effects of hydrocortisone.	Decrease hydrocortisone dose if necessary.
Methylprednisolone *(see also Corticosteroids-class)*	Azole Antifungals [fluconazole, itraconazole, ketoconazole]	Increased effects of methylprednisolone.	Decrease methylprednisolone dose if necessary.
	Macrolide Antibiotics [erythromycin, troleandomycin]	Increased effects of methylprednisolone.	Decrease methylprednisolone dose if necessary.
Prednisolone and Prednisone *(see also Corticosteroids-class)*	Azole Antifungals [fluconazole, itraconazole, ketoconazole]	Increased effects of corticosteroid.	Decrease corticosteroid dose if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Estrogens [chlorotrianisene, conjugated estrogens, diethylstilbesterol, esterified estrogens, estradiol, estrone, estropipate, ethinyl estradiol, quinestrol]	Increased effects of corticosteroid.	Decrease corticosteroid dose if necessary.
DIURETICS			
Loop Diuretics	**Bumetanide, Ethacrynic Acid, Furosemide, Torsemide**		
Loop Diuretics-class	Aminoglycosides, see *Antimicrobial Agents (Antibacterial Antibiotics)*		
	Cisplatin	Increased risk of ototoxicity.	Avoid combination if possible. Otherwise, monitor hearing function.
	Digoxin, see *Antihypertensive and Cardiovascular Agents (Miscellaneous Antihypertensive and Cardiovascular Agents)*		
	Thiazide Diuretics [bendroflumethiazide, benzthiazide, chlorothiazide, chlorthalidone, hydrochlorothiazide, hydroflumethiazide, indapamide, methyclothiazide, metolazone, polythiazide, quinethazone, trichlormethiazide]	Profound diuresis and electrolyte disturbances.	Adjust diuretic dose as needed. Monitor electrolyte abnormalities and hydration status when starting combination therapy.
Furosemide *(see also Loop Diuretics-class)*	Cholestyramine	Decreased GI absorption of furosemide.	Administer cholestyramine at least 2 hours after furosemide.
	Colestipol	Decreased GI absorption of furosemide.	Administer colestipol at least 2 hours after furosemide.
Thiazide Diuretics	**Bendroflumethiazide, Benzthiazide, Chlorothiazide, Chlorthalidone, Hydrochlorothiazide, Hydroflumethiazide, Indapamide, Methyclothiazide, Metolazone, Polythiazide, Quinethazone, Trichlormethiazide**		
Thiazide Diuretics-class	Digoxin, see *Antihypertensive and Cardiovascular Agents (Miscellaneous Antihypertensive and Cardiovascular Agents)*		
	Lithium, see *Sedative/Hypnotics/Agents used in Psychiatry, Antidepressants (Miscellaneous Antidepressants)*		
	Loop Diuretics, see *Diuretics*		
	Sulfonylureas, see *Hypoglycemic Agents*		
GASTROINTESTINAL AGENTS			
Histamine H_2-Antagonists	**Cimetidine, Famotidine, Nizatidine, Ranitidine**		
Histamine H_2-Antagonists-class	Ketoconazole, see *Antimicrobial Agents (Azole Antifungals)*		
Cimetidine *(see also Histamine H_2-Antagonists-class)*	Beta-Blockers, see *Antihypertensive and Cardiovascular Agents (Cardio-Selective and Noncardio-Selective Beta-Blockers)*		
	Carbamazepine, see *Anticonvulsants*		
	Lidocaine, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Metformin, see *Hypoglycemic Agents*		
	Moricizine, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		
	Nifedipine, see *Antihypertensive and Cardiovascular Agents (Calcium-Channel Blockers)*		
	Phenytoin, see *Anticonvulsants—Hydantoins*		
	Praziquantel	Increased concentrations of praziquantel.	Monitor for toxicity. Use alternative histamine H_2-antagonist (eg, ranitidine).
	Procainamide, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		
	Quinidine, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		
	Theophylline, see *Bronchodilators*		
	Tricyclic Antidepressants, see *Sedatives/Hypnotics/Agents used in Psychiatry (Antidepressants)*		
	Warfarin, see *Anticoagulants/Thrombolytic Agents*		
Phosphate Binders/Antacids	**Aluminum Salts (Aluminum Carbonate, Aluminum Hydroxide) Calcium Salts (Calcium Carbonate, Calcium Acetate), Magnesium Salts (Magnesium Carbonate, Magnesium Hydroxide)**		
Phosphate Binders/ Antacids-class	Iron Salts, Oral, see *Anemia Agents (Iron Products)*		
	Ketoconazole, see *Antimicrobial Agents (Azole Antifungals)*		
	Quinidine, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		
	Quinolones, see *Antimicrobial Agents (Antibacterial Antibiotics)*		
	Sodium Polystyrene Sulfonate (Kayexalate), see *Gastrointestinal Agents (Miscellaneous Gastrointestinal Agents)*		
	Tetracyclines, see *Antimicrobial Agents (Antibacterial Antibiotics)*		
Calcium Carbonate *(see also Phosphate Binders/Antacids-class)*	Verapamil, see *Antihypertensive and Cardiovascular Agents (Calcium-Channel Blockers)—Calcium Salts*		
Calcium Acetate *(see also Phosphate Binders/Antacids-class)*	Verapamil, see *Antihypertensive and Cardiovascular Agents (Calcium-Channel Blockers)—Calcium Salts*		
Sevelamer	No drug-drug interaction studies were performed in humans. There is a possibility that sevelamer hydrochloride may bind concomitantly administered drugs and decrease their bioavailability.		
Proton Pump Inhibitors (PPIs)	**Esomeprazole, Lansoprazole, Omeprazole, Pantoprazole, Rabeprazole**		
Proton Pump Inhibitors-class	Itraconazole, see *Antimicrobial Agents (Azole Antifungals)*		
	Ketoconazole, see *Antimicrobial Agents (Azole Antifungals)*		
Miscellaneous Gastrointestinal Agents			
Metoclopramide	Cyclosporine, see *Transplant Immunosuppressants*		
	Digoxin, see *Antihypertensive and Cardiovascular Agents (Miscellaneous Antihypertensive and Cardiovascular Agents)*		
Sodium Polystyrene Sulfonate (Kayexalate)	Phosphate Binders/Antacids [aluminum-magnesium hydroxide, calcium carbonate]	Increased risk of metabolic alkalosis. Decreased potassium binding effects of resin.	Separate administration times.
Sucralfate	Quinolones, see *Antimicrobial Agents (Antibacterial Antibiotics)*		

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
HYPOGLYCEMIC AGENTS			
Insulin	Beta-Blockers, Noncardio-Selective [carteolol, nadolol, penbutolol, pindolol, propranolol, timolol]	Prolonged hypoglycemia with masking of hypoglycemic signs/symptoms (tachycardia)	Use cardio-selective beta-blocker. Monitor for signs/symptoms of hypoglycemia not affected by beta-blockers.
	Ethanol	Increased hypoglycemic effects of insulin.	Ingest ethanol in moderation and with meals.
	MAO Inhibitors [isocarboxazid, phenelzine, tranylcypromine]	Increased hypoglycemic effects of insulin.	Monitor blood glucose concentration. Decrease insulin dose if necessary.
	Salicylates [aspirin, bismuth subsalicylate, choline salicylate, magnesium salicylate, salsalate, sodium salicylate, sodium thiosalicylate]	Increased hypoglycemic effects of insulin.	Monitor blood glucose concentration. Decrease insulin dose if necessary.
Metformin	Cimetidine	Increased concentrations of metformin.	Monitor blood glucose concentration. Decrease metformin dose if necessary.
	Iodinated Contrast Materials, IV	Increased risk of lactic acidosis.	Avoid combination. Discontinue metformin for at least 48 hours prior to and subsequent to the use of IV iodinated contrast materials.
Sulfonylureas	**Acetohexamide, Chlorpropamide, Glimepride, Glipizide, Glyburide, Tolazamide, Tolbutamide**		
Sulfonylureas-class	Chloramphenicol	Increased hypoglycemic effects of sulfonylurea.	Monitor blood glucose concentration. Decrease sulfonylurea dose if necessary.
	Diazoxide	Decreased hypoglycemic effects of sulfonylurea.	Monitor blood glucose concentration. Increase sulfonylurea dose if necessary.
	Ethanol, see *Miscellaneous Agents*		
	MAO Inhibitors [isocarboxazid, phenelzine, tranylcypromine]	Increased hypoglycemic effects of sulfonylurea.	Monitor blood glucose concentration. Decrease sulfonylurea dose if necessary.
	Phenylbutazones [oxyphenbutazone, phenylbutazone]	Increased hypoglycemic effects of sulfonylurea.	Monitor blood glucose concentration. Decrease sulfonylurea dose if necessary. Use alternative NSAID.
	Rifamycins [rifabutin, rifampin, rifapentine]	Decreased concentrations of sulfonylurea.	Monitor blood glucose concentration. Increase sulfonylurea dose if necessary.
	Salicylates [aspirin, choline salicylate, magnesium salicylate, salsalate, sodium salicylate, sodium thiosalicylate]	Increased hypoglycemic effects of sulfonylurea.	Monitor blood glucose concentration. Decrease sulfonylurea dose if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Sulfonamides [sulfacytine, sulfadiazine, sulfamethizole, sulfamethoxazole, sulfasalazine, sulfisoxazole, multiple sulfonamides]	Increased concentrations of sulfonylurea. [Exception: Glyburide]	Monitor blood glucose concentration. Decrease sulfonylurea dose if necessary. Use noninteracting sulfonylurea (eg, glyburide).
	Thiazide Diuretics [bendroflumethiazide, benzthiazide, chlorothiazide, chlorthalidone, hydrochlorothiazide, hydroflumethiazide, indapamide, methyclothiazide, metolazone, polythiazide, quinethazone, trichlormethiazide]	Increased concentrations of fasting blood glucose. Decreased hypoglycemic effects of sulfonylurea.	Monitor blood glucose concentration. Increase sulfonylurea dose if necessary.
Chlorpropamide *(see also Sulfonylureas-class)*	Dicumarol	Increased hypoglycemic effects of chlorpropamide.	Monitor blood glucose concentration. Decrease chlorpropamide dose if necessary.
	Urinary Alkalinizers [potassium citrate, sodium acetate, sodium bicarbonate, sodium citrate, sodium lactate, tromethamine]	Increased elimination of chlorpropamide.	Monitor blood glucose concentration. Increase chlorpropamide dose if necessary.
Glimepride *(see also Sulfonylureas-class)*	Fluconazole	Increased hypoglycemic effects of tolbutamide.	Monitor blood glucose concentration. Decrease tolbutamide dose if necessary.
Tolbutamide *(see also Sulfonylureas-class)*	Dicumarol	Increased hypoglycemic effects of tolbutamide.	Monitor blood glucose concentration. Decrease tolbutamide dose if necessary.
	Fluconazole	Increased hypoglycemic effects of tolbutamide.	Monitor blood glucose concentration. Decrease tolbutamide dose if necessary.
	Sulfinpyrazone	Increased hypoglycemic effects of tolbutamide.	Monitor blood glucose concentration. Decrease tolbutamide dose if necessary.

HYPOLIPIDEMIC AGENTS

Cholestyramine	Digoxin, see *Antihypertensive and Cardiovascular Agents (Miscellaneous Antihypertensive and Cardiovascular Agents)*
	HMG-CoA Reductase Inhibitors, see *Hypolipidemic Agents (Bile Acid Sequestrants)*
	Hydrocortisone, see *Corticosteroids— Bile Acid Sequestrants*
	Furosemide, see *Diuretics (Loop Diuretics)—Bile Acid Sequestrants*
	Levothyroxine, see *Miscellaneous Agents*
	Valproic Acid, see *Anticonvulsants*
	Warfarin, see *Anticoagulants/Thrombolytic Agents*
Clofibrate	Warfarin, see *Anticoagulants/Thrombolytic Agents*
Colestipol	HMG-CoA Reductase Inhibitors, see *Hypolipidemic Agents—Bile Acid Sequestrants*
	Hydrocortisone, see *Corticosteroids—Bile Acid Sequestrants*

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Loop Diuretics, see *Diuretics—Bile Acid Sequestrants*		
Gemfibrozil	HMG-CoA Reductase Inhibitors, see *Hypolipidemic Agents*		
Probucol	Cyclosporine, *see Transplant Immunosuppressants*		
HMG-CoA Reductase Inhibitors (Statins)	**Atorvastatin, Fluvastatin, Lovastatin, Pravastatin, Rosuvastatin, Simvastatin**		
HMG-CoA Reductase Inhibitors-class	Azole Antifungals [fluconazole, itraconazole, ketoconazole, miconazole, voriconazole]	Increased risk of rhabdomyolysis.	Avoid combination if possible. Otherwise, monitor for signs/symptoms of statin toxicity. Decrease statin dose if necessary. Pravastatin is least affected by the interaction.
	Bile Acid Sequestrants [cholestyramine, colestipol]	Decreased GI absorption of HMG-CoA reductase inhibitor.	Separate administration times by at least 4 hours.
	Cyclosporine	Increased risk of rhabdomyolysis.	Avoid combination if possible. Otherwise, monitor for signs/symptoms of statin toxicity. Decrease statin dose if necessary.
	Diltiazem	Increased risk of rhabdomyolysis. [Exceptions: fluvastatin, pravastatin]	Avoid combination if possible. Otherwise, monitor for signs/symptoms of statin toxicity. Use noninteracting statin (eg, fluvastatin, pravastatin).
	Gemfibrozil	Increased risk of severe myopathy and rhabdomyolysis.	Avoid combination.
	Grapefruit Juice	Increased risk of rhabdomyolysis. [Exceptions: fluvastatin, pravastatin]	Avoid combination. Use noninteracting statin (eg, fluvastatin, pravastatin).
	Macrolide Antibiotics [azithromycin, clarithromycin, erythromycin]	Increased risk of severe myopathy and rhabdomyolysis. [Exceptions: fluvastatin, pravastatin]	Avoid combination. Use alternative antibiotic or noninteracting statin (eg, fluvastatin, pravastatin).
	Nefazodone	Increased risk of rhabdomyolysis. [Exceptions: fluvastatin, pravastatin]	Avoid combination. Use noninteracting statin (eg, fluvastatin, pravastatin).
	Rifamycins [rifabutin, rifampin, rifapentine]	Decreased effects of statin. [Exception: pravastatin]	Monitor clinical response. Use noninteracting statin (eg, pravastatin).
	Verapamil	Increased risk of rhabdomyolysis. [Exceptions: fluvastatin, pravastatin]	Avoid combination. Use noninteracting statin (eg, fluvastatin, pravastatin).
Lovastatin *(see also HMG-CoA Reductase Inhibitors-class)*	Cyclosporine	Increased risk of rhabdomyolysis.	Avoid combination. Report unexplained muscle pain, tenderness, or weakness.

PAIN MEDICATIONS

Non-Narcotic

Acetaminophen	Ethanol	Increased risk of acetaminophen-induced hepatotoxicity.	Avoid combination. Advise chronic ethanol consumers to avoid excessive or prolonged use of acetaminophen.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Increased risk of acetaminophen-induced hepatotoxicity.	Avoid chronic and excessive use of acetaminophen with regular hydantoin therapy.
	Sulfinpyrazone	Increased risk of acetaminophen-induced hepatotoxicity.	Avoid chronic and excessive use of acetaminophen with regular sulfinpyrazone therapy.
	Warfarin, see *Anticoagulants/Thrombolytic Agents*		
Aspirin	Carbonic Anhydrase Inhibitors [acetazolamide, dichlorphenamide, methazolamide]	Increased risk of carbonic anhydrase inhibitor toxicity (CNS depression, metabolic acidosis).	Avoid combination.
	Corticosteroids [betamethasone, cortisone, desoxycorticosterone, dexamethasone, fludrocortisone, hydrocortisone, methylprednisolone, paramethasone, prednisolone, prednisone, triamcinolone]	Decreased effects of salicylate.	Monitor aspirin concentrations. Increase salicylate dose if necessary.
	Heparin, see *Anticoagulants/Thrombolytic Agents— Salicylates*		
	Insulin, see *Hypoglycemic Agents—Salicylates*		
	Ketorolac, see *Arthritis and Gout Agents (NSAIDs)—Salicylates*		
	Methotrexate, see *Antineoplastic Agents—Salicylates*		
	Probenecid	Decreased uricosuric action of one or both drugs.	Avoid combination. Use non-antiinflammatory doses of aspirin.
	Sulfonylureas, see *Hypoglycemic Agents—Salicylates*		
	Valproic acid, see *Anticonvulsants—Salicylates*		
	Warfarin, see *Anticoagulants/Thrombolytic Agents—Salicylates*		
Narcotic			
Alfentanil	Ethanol, see *Miscellaneous Agents*		
Codeine	Quinidine	Decreased effects of codeine.	Use alternative analgesic.
Fentanyl	Amiodarone, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*		
Meperidine	MAO Inhibitors [isocarboxazid, phenelzine, selegiline, tranylcypromine]	Agitation, seizures, diaphoresis and fever. May progress to coma, apnea, and death.	Avoid combination.
	Phenothiazines [chlorpromazine]	Excessive sedation and hypotension.	Avoid combination.
	Ritonavir	Decreased efficacy of meperidine and increased risk of neurologic toxicity.	Avoid combination.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
Methadone	Barbiturates [amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital]	Decreased effects of methadone. Possible withdrawal symptoms in patients on chronic methadone therapy.	Increase methadone dose if necessary.
	Fluvoxamine	Increased concentrations of methadone.	Monitor clinical response when starting and stopping fluvoxamine in patients on chronic methadone therapy.
	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased effects of methadone. Possible withdrawal symptoms in patients on chronic methadone therapy.	Increase methadone dose if necessary.
	Protease Inhibitors [nelfinavir, ritonavir]	Decreased effects of methadone. Possible withdrawal symptoms in patients on chronic methadone therapy.	Increased methadone dose if necessary.
	Rifampin	Decreased effects of methadone. Possible withdrawal symptoms in patients on chronic methadone therapy.	Increase methadone dose if necessary.
Morphine	Rifamycins [rifabutin, rifampin, rifapentine]	Decreased analgesic effects of morphine.	Monitor analgesic response. Use alternative analgesic.
Propoxyphene	Carbamazepine, see *Anticonvulsants*		
	Ritonavir	Increased risk of propoxyphene toxicity (seizures, respiratory depression, apnea, cardiac arrhythmias, pulmonary edema).	Avoid combination.

SEDATIVES/HYPNOTICS/AGENTS USED IN PSYCHIATRY

ANTIDEPRESSANTS

Monoamine Oxidase Inhibitors (MAO Inhibitors)	**Isocarboxazid, Phenelzine, Selegiline, Tranylcypromine**
Monoamine Oxidase (MAO) Inhibitors-class	Buproprion, *see Sedatives/Hypnotics/Agents used in Psychiatry, Antidepressants (Miscellaneous Antidepressants)*
	Carbamazepine, see *Anticonvulsants*
	Insulin, see *Hypoglycemic Agents*
	Levodopa, see *Antiparkinson Agents*
	Meperidine, see *Pain Medications (Narcotic)—MAO Inhibitors*
	Serotonin Reuptake Inhibitors, see *Sedatives/Hypnotics/Agents used in Psychiatry (Antidepressants)*
	Sibutramine, see *Miscellaneous Agents*
	Sulfonylureas, see *Hypoglycemic Agents*
	Tricyclic Antidepressants, see *Sedatives/Hypnotics/Agents used in Psychiatry (Antidepressants)*
Serotonin Reuptake Inhibitors	**Citolapram, Escitalopram, Fluoxetine, Fluvoxamine, Nefazodone, Paroxetine, Sertraline, Venlafaxine**
Serotonin Reuptake Inhibitors-class	Clozapine, see *Sedative/Hypnotics/Agents used in Psychiatry (Antipsychotic Agents)*—Serotonin Reuptake Inhibitors

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Cyclosporine	Increased concentrations of cyclosporine.	Monitor cyclosporine concentrations. Decrease cyclosporine dose if necessary.
	Cyproheptadine	Decreased antidepressant effects of serotonin reuptake inhibitor.	Discontinue cyproheptadine if necessary.
	MAO Inhibitors [isocarboxazid, phenelzine, selegiline, tranylcypromine]	Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Avoid combination. Allow at least 2 weeks after stopping MAO inhibitor before starting serotonin reuptake inhibitor, and vice versa. Allow at least 5 weeks after stopping fluoxetine before starting MAO inhibitor.
	Sibutramine, see *Miscellaneous Agents*		
	Sympathomimetics [amphetamine, benzphetamine, dextroamphetamine, dexfenfluramine, diethylpropion, fenfluramine, mazindol, methamphetamine, phendimetrazine, phenmetrazine, phentermine]	Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Avoid combination if possible. Otherwise, monitor for signs/symptoms of CNS toxicity and adjust dose of one or both drugs as needed.
	Tricyclic Antidepressants, see *Sedatives/Hypnotics/Agents used in Psychiatry (Antidepressants)-Serotonin Reuptake Inhibitors*		
Fluoxetine *(see also Serotonin Reuptake Inhibitors-class)*	Carbamazepine, see *Anticonvulsants*		
	Phenytoin, see *Anticonvulsants (Hydantoins)*		
	Thioridazine, see *Sedatives/Hypnotics/Agents used in Psychiatry (Antipsychotic Agents)*		
Fluvoxamine *(see also Serotonin Reuptake Inhibitors-class)*	Methadone, see *Pain Medications (Narcotic)-Protease Inhibitors*		
	Tacrine	Increased concentrations of tacrine.	Avoid combination if possible. Otherwise, monitor liver function tests. Use alternative serotonin reuptake inhibitor (eg, fluoxetine).
	Thioridazine, see *Sedatives/Hypnotics/Agents used in Psychiatry (Antipsychotic Agents)*		
Paroxetine *(see also Serotonin Reuptake Inhibitors-class)*	Desipramine, see *Sedatives/Hypnotics/Agents used in Psychiatry, Antidepressants (Tricyclic Antidepressants)*		
	Imipramine, see *Sedatives/Hypnotics/Agents used in Psychiatry, Antidepressants (Tricyclic Antidepressants)*		
	Phenothiazines, see *Sedatives/Hypnotics/Agents used in Psychiatry (Antipsychotic Agents)*		
Sertraline *(see also Serotonin Reuptake Inhibitors-class)*	Phenytoin, *see Anticonvulsants (Hydantoins)*		

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
Tricyclic Antidepressants (TCAs)	**Amitriptyline, Amoxapine, Clomipramine, Desipramine, Doxepin, Imipramine, Nortriptyline, Protriptyline, Trimipramine**		
Tricyclic Antidepressants-class	Carbamazepine, see *Anticonvulsants*		
	Cimetidine	Increased concentrations of tricyclic antidepressant.	Monitor tricyclic antidpressant concentrations. Adjust tricyclic antidepressant dose as needed when starting or stopping cimetidine. Use alternative histamine H_2-antagonist (eg, ranitidine).
	Clonidine, see *Antihypertensive and Cardiovascular Agents, Adrenergic Modifiers*		
	Serotonin Reuptake Inhibitors [fluoxetine, fluvoxamine, paroxetine, sertraline]	Increased concentrations of tricyclic antidepressant. Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Monitor tricyclic antidepressant concentrations and for signs/symptoms of toxicity. Decrease tricyclic antidepressant dose if necessary.
	MAO Inhibitors [phenelzine, tranylcypromine]	Hyperpyretic crisis, seizures. May progress to death.	Avoid combination. Do not administer tricyclic antidepressant within 2 weeks of MAO inhibitor therapy.
	Rifamycins [rifabutin, rifampin]	Decreased concentrations of tricyclic antidepressant.	Monitor tricyclic antidepressant concentrations. Increase tricyclic antidepressant dose if necessary.
	Sparfloxacin	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination. Use alternative quinolones (eg, ciprofloxacin, levofloxacin).
	Sympathomimetics [dobutamine, dopamine, ephedrine, epinephrine, mephentermine, metaraminol, methoxamine, norepinephrine, phenylephrine]	Increased pressor effects of direct-acting sympathomimetics. Decreased pressor effects of indirect-acting sympathomimetics.	Monitor for hypertension and dysrrhythmias. Adjust sympathomimetic dose as needed.
	Valproic Acid [divalproex, valproate sodium, valproic acid]	Increased concentrations of tricyclic antidepressant. Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Monitor tricyclic antidepressant concentrations and for signs/symptoms of toxicity. Decrease tricyclic antidepressant dose if necessary.
Miscellaneous Antidepressants			
Bupropion	Carbamazepine	Decreased effects of bupropion.	Increase bupropion dose if necessary.
	MAO Inhibitors [phenelzine, tranylcypromine]	Increased risk of acute bupropion toxicity (seizures).	Avoid combination. Allow at least 2 weeks after stopping MAO inhibitor before starting bupropion.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Ritonavir	Increased risk of bupropion toxicity.	Avoid combination.
Lithium	Angiotensing Converting Enzyme Inhibitors [benazepril, captopril, enalapril, fosinopril, lisinopril, moexipril, quinapril, ramipril, trandolapril]	Increased concentrations of lithium.	Monitor lithium concentrations and for signs/symptoms of toxicity.
	Angiotensin II Receptor Blockers [candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, valsartan]	Increased concentrations of lithium.	Monitor lithium concentrations and for signs/symptoms of toxicity.
	Carbamazepine	Increased risk of neurotoxicity (lethargy, muscular weakness, ataxia, tremor, hyperreflexia).	Monitor for signs/symptoms of toxicity. Discontine one or both drugs if necessary.
	Haloperidol, see *Sedatives/Hypnotics/Agents used in Psychiatry (Antipsychotic Agents)*		
	Iodide Salts [calcium iodide, hydrogen iodide, iodide, iodinated glycerol, iodine, potassium iodide, sodium iodide]	Increased risk of hypothyroidism.	Avoid combination if possible. Otherwise, adminsiter thyroid hormone if necessary
	NSAIDs [diclofenac, ibuprofen, indomethacin, ketorolac, meloxicam, naproxen, piroxicam, sulindac]	Increased concentrations of lithium.	Monitor lithium concentrations. Adjust lithium dose as needed when starting or stopping NSAID.
	Sibutramine, see *Miscellaneous Agents*		
	Thiazide Diuretics [bendroflumethiazide, benzthiazide, chlorothiazide, chlorthalidone, hydrochlorothiazide, hydroflumethiazide, indapamide, meloxicam, methyclothiazide, metolazone, polythiazide, quinethazone, sulindac, trichlormethiazide]	Increased concentrations of lithium.	Monitor lithium concentrations. Decrease lithium dose if necessary.
	Urinary Alkalinizers [potassium citrate, sodium acetate, sodium bicarbonate, sodium citrate, sodium lactate, tromethamine]	Decreased concentrations of lithium.	Avoid combination.

ANTIPSYCHOTIC AGENTS

Clozapine	Ritonavir	Increased concentrations of clozapine.	Avoid combination.
	Serotonin Reuptake Inhibitors [fluoxetine, fluvoxamine, sertraline]	Increased concentrations of clozapine.	Monitor clozapine concentrations. Decrease clozapine dose if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
Haloperidol	Anticholinergics [atropine, belladonna, benztropine, biperiden, clidinium, dicyclomine, glycopyrrolate, hyoscyamine, mepenzolate, methscopolamine, orphenadrine, oxybutynin, procyclidine, propantheline, scopolamine, trihexyphenidyl]	Decreased concentrations of haloperidol. Worsening of schizophrenic symptoms. Development of tardive dyskinesia.	Discontinue anticholinergic or increase haloperidol dose if necessary.
	Azole Antifungals [fluconazole, itraconazole, ketoconazole]	Increased concentrations of haloperidol.	Adjust haloperidol dose as needed when starting or stopping azole antifungal.
	Carbamazepine	Decreased effects of haloperidol. Increased effects of carbamazepine.	Adjust dose of one or both drugs as needed.
	Lithium	Alterations in consciousness, encephalopathy, extrapyramidal effects, fever, leukocytosis, and increased serum enzymes.	Avoid combination if possible. Otherwise, discontinue one or both drugs and provide supportive treatment if necessary.
	Rifamycins [rifabutin, rifampin]	Decreased effects of haloperidol.	Adjust haloperidol dose as needed when starting or stopping rifamycin.
Phenothiazines	**Acetophenazine, Chlorpromazine, Fluphenazine, Mesoridazine, Methotrimeprazine, Perphenazine, Prochlorperazine, Promazine, Promethazine, Propiomazine, Thiethylperazine, Thioridazine, Trifluoperazine, Triflupromazine**		
Phenothiazines-class	Anticholinergics [atropine, belladonna, benztropine, biperiden, clidinium, dicyclomine, glycopyrrolate, hyoscyamine, isopropamide, mepenzolate, orphenadrine, oxybutynin, oxyphencyclimine, procyclidine, propantheline, scopolamine, trihexyphenidyl]	Decreased effects of phenothiazine.	Increase phenothiazine dose if necessary.
	Ethanol, see *Miscellaneous Agents*		
	Paroxetine	Increased effects of phenothiazine. Increased risk of life-threatening cardiac arrhythmias with thioridazine.	Avoid combination if possible (thioridazine is contraindicated). Adjust phenothiazine dose as needed.
	Propranolol, see *Antihypertensive and Cardiovascular Agents (Beta-Blockers)*		
	Sparfloxacin	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination. Use alternative quinolones (eg, ciprofloxacin, levofloxacin).
Chlorpromazine *(see also Phenothiazines-class)*	Meperidine, *see Pain Medications (Narcotic)—Phenothiazines*		
Propiomazine *(see also Phenothiazines-class)*	Meperidine, *see Pain Medications (Narcotic)—Phenothiazines*		

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
Thioridazine *(see also Phenothiazines-class)*	Antiarrhythmic Agents [amiodarone, bretylium, disopyramide, procainamide, quinidine, sotalol]	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination.
	Fluoxetine	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination.
	Fluvoxamine	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination.
	Pimozide	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination.

SEDATIVES

Barbiturates	**Amobarbital, Aprobarbital, Butabarbital, Butalbital, Mephobarbital, Pentobarbital, Phenobarbital, Primidone, Secobarbital**
Barbiturates-class	Beta-Blockers, see *Antihypertensive and Cardiovascular Agents (Cardio-Selective and Noncardio-Selective Beta-Blockers)*
	Corticosteroids, see *Corticosteroids*
	Doxycycline, see *Antimicrobial Agents (Antibacterial Antibiotics - Tetracyclines)*
	Estrogens, see *Miscellaneous Agents*
	Ethanol, see *Miscellaneous Agents*
	Felodipine, see *Antihypertensive and Cardiovascular Agents (Calcium Channel-Blockers)*
	Griseofulvin, see *Antimicrobial Agents (Miscellaneous Antifungals)—Barbiturates*
	Methadone, see *Pain Medications (Narcotic)*
	Metronidazole, see *Antimicrobial Agents (Miscellaneous Antibacterial Antibiotics)*
	Nifedipine, see *Antihypertensive and Cardiovascular Agents (Calcium-Channel Blockers)*
	Quinidine, see *Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)*
	Rifamycins [rifabutin, rifampin], see *Antimicrobial Agents (Antimycobacterial Agents)*
	Theophyllines, see *Bronchodilators*
	Voriconazole, see *Antimicrobial Agents (Azole Antifungals)—Barbiturates*
	Warfarin, see *Anticoagulants/Thrombolytics*
Benzodiazepines	**Alprazolam, Chlordiazepoxide, Clonazepam, Clorazepate, Diazepam, Estazolam, Flurazepam, Halazepam, Lorazepam, Midazolam, Oxazepam, Quazepam, Temazepam, Triazolam**

Benzodiazepines, Oxidative Metabolism-class [alprazolam, chlordiazepoxide, clonazepam, clorazepate, diazepam, estazolam, flurazepam, halazepam, midazolam, quazepam, triazolam]	Azole Antifungals [fluconazole, itraconazole, ketoconazole, miconazole, voriconazole]	Increased concentrations of benzodiazepine. Prolonged CNS depression and psychomotor impairment.	Avoid combination if possible (alprazolam and triazolam are contraindicated with itraconazole and ketoconazole). Otherwise, decrease benzodiazepine dose.
	Diltiazem	Increased effects of benzodiazepine (diazepam, midazolam, triazolam). Prolonged sedation and respiratory depression.	Decrease benzodiazepine dose.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Ethanol, see *Miscellaneous Agents*		
	Grapefruit Juice	Increased effects of benzodiazepine. Delayed onset of benzodiazepine effects.	Avoid combination.
	Macrolide Antibiotics [clarithromycin, erythromycin, troleandomycin]	Increased concentrations of benzodiazepine. Prolonged sedation and respiratory depression.	Decrease benzodiazepine dose if necessary. Use alternative benzodiazepine (eg, lorazepam, oxazepam, temazepam). Use alternative macrolide antibiotic (eg, azithromycin).
	Protease Inhibitors [indinavir, ritonavir, saquinavir]	Increased concentrations of benzodiazepine. Prolonged sedation and respiratory depression.	Avoid combination. Use alternative benzodiazepine (eg, lorazepam, oxazepam, temazepam).
	Ritonavir	Prolonged sedation and respiratory depression.	Substitute lorazepam, oxazepam, or temazepam.
Miscellaneous Sedatives			
Buspirone	Azole Antifungals [fluconazole, itraconazole, ketoconazole, miconazole, voriconazole]	Increased effects of buspirone.	Adjust buspirone dose as needed when starting, stopping, or changing dose of azole antifungal.
	Macrolide Antibiotics [clarithromycin, erythromycin, troleandomycin]	Increased effects of buspirone.	Adjust buspirone dose as needed when starting, stopping, or changing dose of macrolide antibiotic. Use alternative antibiotic if possible.
	Rifamycins [rifabutin, rifampin]	Decreased effects of buspirone.	Adjust buspirone dose as needed when starting, stopping, or changing dose of rifamycin.
Zolpidem	Ritonavir	Severe sedation and respiratory depression.	Avoid combination.
TRANSPLANT IMMUNOSUPPRESSANTS			
Cyclosporine	Amiodarone	Increased concentrations of cyclosporine.	Monitor cyclosporine concentrations and for signs/symptoms of toxicity. Decrease cyclosporine dose if necessary.
	Androgens [danazol, methyltestosterone]	Increased concentrations of cyclosporine.	Monitor cyclosporine concentrations and for signs/symptoms of toxicity. Decrease cyclosporine dose if necessary.
	Azole Antifungals [fluconazole, itraconazole, ketoconazole]	Increased concentrations of cyclosporine.	Monitor cyclosporine concentrations and for signs/symptoms of toxicity. Adjust cyclosporine dose as needed when starting or stopping azole antifungal.
	Carbamazepine	Decreased concentrations of cyclosporine.	Monitor cyclosporine concentrations and for signs/symptoms of organ rejection. Increase cyclosporine dose if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Carvedilol	Increased concentrations of cyclosporine.	Monitor cyclosporine concentrations and for signs/symptoms of toxicity. Decrease cyclosporine dose if necessary.
	Caspofungin	Increased concentrations of caspofungin. Elevated liver function test results.	Avoid combination if possible. Otherwise, monitor for signs/symptoms of hepatotoxicty. Discontinue caspofungin if necessary.
	Colchicine	Increased risk of cyclosporine toxicity (GI, hepatic, renal, neuromuscular).	Monitor cyclosporine concentrations and for signs/symptoms of toxicity. Decrease cyclosporine dose if necessary.
	Digoxin, see *Antihypertensive and Cardiovascular Agents (Miscellaneous Antihypertensive and Cardiovascular Agents)*		
	Diltiazem	Increased concentrations of cyclosporine.	Monitor cyclosporine concentrations and for signs/symptoms of toxicity. Decrease cyclosporine dose if necessary.
	Etoposide	Increased concentrations of etoposide.	Monitor complete blood count for increased bone marrow suppression. Decrease etoposide dose if necessary.
	Foscarnet, see *Antimicrobial Agents (Antiviral Agents)*		
	Grapefruit Juice	Increased concentrations of cyclosporine.	Avoid combination unless specifically indicated.
	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased concentrations of cyclosporine.	Monitor cyclosporine concentrations and for signs/symptoms of organ rejection. Increase cyclosporine dose if necessary.
	Imipenem/Cilastatin	Increased CNS adverse effects of both drugs (confusion, agitation, tremor).	Use alternative antibiotic if interaction develops.
	Lovastatin, see *Hypolipidemic Agents (HMG-CoA Reductase Inhibitors)*		
	Macrolide Antibiotics [azithromycin, clarithromycin, erythromycin, troleandomycin]	Increased concentrations of cyclosporine.	Monitor cyclosporine concentrations and for signs/symptoms of toxicity. Adjust cyclosporine dose as needed when starting or stopping macrolide antibiotic.
	Metoclopramide	Increased concentrations of cyclosporine.	Monitor cyclosporine concentrations and for signs/symptoms of toxicity. Adjust cyclosporine dose as needed when starting, stopping, or changing dose of metoclopramide.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Nefazodone	Increased concentrations of cyclosporine.	Monitor cyclosporine concentrations and for signs/symptoms of toxicity. Decrease cyclosporine dose if necessary.
	Nicardipine	Increased concentrations of cyclosporine.	Monitor cyclosporine concentrations and for signs/symptoms of toxicity. Decrease cyclosporine dose if necessary.
	Orlistat	Increased concentrations of cyclosporine.	Avoid combination.
	Probucol	Decreased concentrations of cyclosporine.	Monitor cyclosporine concentrations and for signs/symptoms of organ rejection. Increase cyclosporine dose if necessary.
	Quinolones [ciprofloxacin, norfloxacin]	Increased risk of nephrotoxicity.	Monitor cyclosporine concentrations and for signs/symptoms of toxicity. Use alternative quinolone (eg, levofloxacin).
	Rifamycins [rifabutin, rifampin]	Decreased concentrations of cyclosporine.	Avoid combination if possible. Otherwise, monitor cyclosporine concentrations and for signs/symptoms of organ rejection. Adjust cyclosporine dose as needed when starting, stopping, or changing dose of rifamycin.
	Serotonin Reuptake Inhibitors, see *Sedatives/Hypnotics/Agents used in Psychiatry (Antidepressants)*		
	Sirolimus, see *Transplant Immunosuppressants*		
	Sulfonamides [sulfadiazine, sulfamethoxazole, trimethoprim/ sulfamethoxazole]	Decreased effects of cyclosporine. Increased risk of nephrotoxicity with oral sulfonamides.	Avoid combination if possible. Otherwise, monitor cyclosporine concentrations and for signs/symptoms of organ rejection. Adjust cyclosporine dose as needed when starting, stopping, or changing dose of sulfonamide.
	Terbinafine	Decreased concentrations of cyclosporine.	Monitor cyclosporine concentrations and for signs/symptoms of organ rejection. Adjust cyclosporine dose as needed when starting or stopping terbinafine.
	Verapamil	Increased concentrations of cyclosporine. Possible nephroprotective effect if verapamil is adminstered before cyclosporine.	Monitor cyclosporine concentrations and for signs/symptoms of toxicity. Decrease cyclosporine dose if necessary.
Mycophenolate mofetil	Iron Salts, Oral [ferrous fumarate, ferrous gluconate, ferrous sulfate, iron polysaccharide]	Decreased effects of mycophenolate.	Separate administration times. Monitor clinical response and increase mycophenolate dose if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Tacrolimus	Increased concentrations of mycophenolate.	Monitor mycophenolic acid levels. Adjust mycophenolate doses as needed when starting or stopping tacrolimus.
Sirolimus	Azole Antifungals [fluconazole, itraconazole, ketoconazole, voriconazole]	Increased concentrations of sirolimus.	Monitor sirolimus concentrations and for signs/symptoms of toxicity. Adjust sirolimus dose as needed when starting or stopping azole antifungal.
	Cyclosporine	Increased concentrations of sirolimus.	Administer sirolimus 4 hours after cyclosporine to prevent changes in sirolimus concentrations.
	Diltiazem	Increased concentrations of sirolimus.	Monitor sirolimus concentrations and for signs/symptoms of toxicity. Adjust sirolimus dose as needed when starting or stopping diltiazem.
Tacrolimus	Azole Antifungals [fluconazole, itraconazole, ketoconazole, miconazole, voriconazole]	Increased concentrations of tacrolimus.	Monitor tacrolimus concentrations and for signs/symptoms of toxicity. Adjust tacrolimus dose as needed when starting or stopping azole antifungal.
	Caspofungin	Decreased concentrations of tacrolimus.	Monitor tacrolimus concentrations. Adjust tacrolimus dose as needed when starting or stopping caspofungin.
	Diltiazem	Increased concentrations of tacrolimus.	Monitor tacrolimus concentrations and for signs/symptoms of toxicity. Decrease tacrolimus dose if necessary.
	Hydantoins [fosphenytoin, phenytoin]	Decreased concentrations of tacrolimus. Increased concentrations of phenytoin.	Monitor tacrolimus and phenytoin concentrations. Adjust doses of one or both drugs as needed.
	Macrolide Antibiotics [clarithromycin, erythromycin, troleandomycin]	Increased concentrations of tacrolimus.	Monitor tacrolimus concentrations and for signs/symptoms of toxicity. Adjust tacrolimus dose as needed when starting or stopping azole antifungal. Use alternative antibiotic.
	Mycophenolate mofetil, see *Transplant Immunosuppressants*		
	Nifedipine	Increased concentrations of tacrolimus.	Monitor tacrolimus concentrations and for signs/symptoms of toxicity. Decrease tacrolimus dose if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Rifamycins [rifabutin, rifampin, rifapentine]	Decreased concentrations of tacrolimus.	Monitor tacrolimus concentrations. Adjust tacrolimus dose as needed when starting or stopping rifamycin.
VITAMINS			
Folic acid	Phenytoin, see *Anticonvulsants*		
Vitamin E (Tocopherol)	Warfarin, see *Anticoagulants/Thrombolytic Agents*		
Vitamin K (Phytonadione)	Warfarin, see *Anticoagulants/Thrombolytic Agents*		
MISCELLANEOUS AGENTS			
Ergot Alkaloids [dihydroergotamine, ergotamine, methysergide}	Beta-Blockers [carteolol, nadolol, penbutolol, pindolol, propranolol, timolol]	Increased risk of ergot toxicity (peripheral ischemia, gangrene).	Discontinue beta-blocker or decrease ergot alkaloid dose if necessary.
	Macrolide Antibiotics [clarithromycin, erythromycin, troleandomycin]	Acute ergotism (peripheral ischemia).	Avoid combination if possible. Use alternative antibiotic. Discontinue one or both drugs if ergotism develops. Administer sodium nitroprusside to decrease macrolide-ergot induced vasopasm if necessary.
	Nitrates [amyl nitrite, isosorbide dinitrate, nitroglycerin]	Increased standing systolic blood pressure. Pharmacologic antagonism between dihydroergotamine and nitroglycerin may decrease antianginal effects of nitroglycerin.	Decrease dihydroergotamine dose if necessary.
	NNRT Inhibitors [delavirdine, efavirenz]	Increased risk of ergot toxicity (peripheral ischemia, peripheral vasospasm).	Avoid combination.
	Protease Inhibitors [amprenavir, indinavir, nelfinavir, ritonavir, saquinavir]	Increased risk of ergot toxicity (peripheral ischemia, peripheral vasospasm).	Avoid combination.
	Sibutramine, see *Miscellaneous Agents*		
	Voriconazole	Increased risk of ergot toxicity (peripheral ischemia, peripheral vasospasm).	Avoid combination.
Estrogens [chlorotrianisene, conjugated estrogens, diethylstilbesterol, esterified estrogens, estradiol, estriol, estrogenic substance, estrone, estropipate, ethinyl estradiol, mestranol, quinestrol]	Barbiturates [amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital, thiamylal]	Decreased concentrations of estrogen.	Use alternative nonhormonal or additional method of contraception. Increase estrogen dose if necessary.
	Hydrocortisone, see *Corticosteroids*		
	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased concentrations of estrogen. Possible loss of seizure control.	Use alternative nonhormonal or additional method of contraception. Increase estrogen dose if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Methylprednisolone, see *Corticosteroids*		
	Prednisolone and Prednisone, see *Corticosteroids*		
	Rifamycins [rifabutin, rifampin, rifapentine]	Decreased concentrations of estrogen	Use alternative nonhormonal or additional method of contraception. Increase estrogen dose if necessary.
Ethanol	Acetaminophen, see *Pain Medications (Non-Narcotic)*		
	Alfentanil	Increased tolerance to alfentanil with chronic ethanol ingestion.	Increase alfentanil dose if necessary.
	Barbiturates [amobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital]	Additive CNS effects with acute ethanol ingestion (potentially fatal).	Avoid combination.
	Benzodiazepines [alprazolam, chlordiazepoxide, clorazepate, diazepam, estazolam, flurazepam, halazepam, lorazepam, midazolam, oxazepam, prazepam, quazepam, temazepam, triazolam]	Additive CNS effects with acute ethanol ingestion.	Avoid combination.
	Cephalosporins [cefamandole, cefoperazone, ceforanide, cefonicid, cefotetan moxalactam]	Disulfuram-like reaction.	Avoid combination.
	Chloral Hydrate	Additive CNS depression. Disulfiram-like reaction.	Avoid combination.
	Chlorpropamide, see *Hypoglycemic Agents (Sulfonylureas)*		
	Disulfiram	Flushing, tachycardia, bronchospasm, sweating, nausea, and vomiting. May progress to death.	Avoid combination.
	Furazolindone	Disulfiram-like reaction.	Avoid combination.
	Glutethimide	Additive CNS depression.	Avoid combination.
	Insulin, *see Hypoglycemic Agents*		
	Levothyroxine, see *Miscellaneous Agents*		
	Meprobamate	Increased CNS depression.	Avoid combination.
	Metronidazole	Disulfiram-like reaction.	Avoid combination.
	Phenothiazines [acetophenazine, chlorpromazine, fluphenazine, mesoridazine, perphenazine, prochlorperazine, promazine, promethazine, thioridazine, trifluoperazine, triflupromazine, trimeprazine]	Increased CNS depression and psychomotor impairment.	Avoid combination.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Sulfonylureas [acetohexamide, chlorpropamide, glipizide, glyburide, tolazamide, tolbutamide]	Prolonged hypoglycemia. Disulfiram-like reaction when taken with chlorpropamide.	Avoid combination.
	Verapamil	Increased and prolonged CNS depression and psychomotor impairment.	Limit ethanol ingestion.
Levothyroxine	Cholestyramine	Decreased GI absorption of levothyroxine.	Separate administration times by at least 6 hours. Monitor thyroid function. Increase levothyroxine dose if necessary.
	Estrogens [conjugated estrogens, esterified estrogens, estradiol, estrone, estropipate, esthinyl estradiol, mestranol]	Decreased serum concentrations of free thyroxine. Increased serum concentrations of thyrotropin.	Monitor serum thyrotropin concentrations approximately 12 weeks after starting estrogen. Adjust levothyroxine dose as needed.
	Iron Salts (Oral) [ferrous fumarate, ferrous gluconate, ferrous sulfate, iron polysaccharide]	Decreased GI absorption of levothyroxine.	Separate administration times. Monitor thyroid function. Increase levothyroxine dose if necessary.
	Sucralfate	Decreased GI absorption of levothyroxine.	Separate administration times by at least 8 hours. Monitor thyroid function. Increase levothyroxine dose if necessary.
	Theophylline, see *Bronchodilators (Theophyllines)—Thyroid Hormones*		
	Warfarin, see *Anticoagulants/Thrombolytic Agents—Thyroid Hormones*		
Metyrapone	Cyproheptadine	Decreased pituitary-adrenal response to metyrapone.	Discontinue cyproheptadine before testing pituitary-adrenal axis with metyrapone.
	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased pituitary-adrenal response to metyrapone.	Consider doubling metyrapone dose when testing pituitary-adrenal axis function in patients on chronic hydantoin therapy.
Quinine	Digoxin, see *Antihypertensive and Cardiovascular Agents (Miscellaneous Antihypertensive and Cardiovascular Agents)*		
	Rifamycins [rifabutin, rifampin, rifapentine]	Decreased concentrations of quinine.	Monitor ECG and quinine concentrations. Increase quinine dose if necessary.
	Warfarin, see *Anticoagulants/Thrombolytic Agents*		
Sibutramine	Dextromethorphan	Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Avoid combination if possible. Otherwise, obtain medical treatment if serotonin syndrome develops.
	Ergot Alkaloids	Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Avoid combination if possible. Otherwise, obtain medical treatment if serotonin syndrome develops.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Lithium	Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Avoid combination if possible. Otherwise, obtain medical treatment if serotonin syndrome develops.
	MAO Inhibitors [isocarboxazid, phenelzine, tranylcypromine]	Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Avoid combination. Allow at least 2 weeks after stopping MAO inhibitor before starting sibutramine, and vice versa.
	Meperidine	Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Avoid combination if possible. Otherwise, obtain medical treatment if serotonin syndrome develops.
	Selective 5HT-1 Receptor Antagonists [almotriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan]	Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Avoid combination if possible. Otherwise, obtain medical treatment if serotonin syndrome develops.
	Serotonin Reuptake Inhibitors [fluoxetine, fluvoxamine, nefazodone, paroxetine, sertraline, venlafaxine]	Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Avoid combination if possible. Otherwise, obtain medical treatment if serotonin syndrome develops.
	Tryptophan	Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Avoid combination if possible. Otherwise, obtain medical treatment if serotonin syndrome develops.

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