Course Description

This fourth year course is designed to give students in the Health and Related Professions (H.A.R.P.) Academy a general and coherent explanation of the science of pharmacology in terms of its basic concepts and principles. Students will learn the properties and interactions between chemical agents (drugs) and living organisms for the rational and safe use of drugs in the control, prevention, and therapy of human disease. The emphasis will be on the fundamental concepts as they apply to the actions of most prototype drugs. In order to exemplify important underlying principles, many of the agents in current use will be singled out for fuller discussion.

The course will include the following topics:
- The History of Pharmacology
- Terminology Used in Pharmacology
- Drug Action on Living Organisms
- Principles of Pharmacokinetics
- Dose-Response Relationships
- Time-Response Relationships
- Human Variability: Factors that will modify effects of drugs on individuals
- Effects of Drugs Attributable to Varying Modes of Administration
- Drug Toxicity
- Pharmacologic Aspects of Drug Abuse and Drug Dependence

Pre-requisites

Students must have completed successfully the following courses:
Biology, Chemistry, Anatomy and Physiology, Algebra I and II

Credits: 5 credits
Basic Principles of Drug Action

Introduction to Pharmacology
   a. Basic Mechanisms of Drug Actions
   b. Dose-response relationships
   c. Drug absorption
   d. Biotransformation of Drugs
   e. Pharmacokinetics
   f. Factors Affecting Drug Distribution
   g. Drug Allergy and Pharmacogenetics
   h. Case History
   i. Laboratory Reports and Problem Solving

Drugs Affecting the Autonomic Nervous System
   a. Adrenergic drugs
   b. Adrenergic blocking drugs
   c. Adrenergic nerve terminal
   d. Cholinergic Agonists
   e. Ganglionic blockers
   f. Diuretic drugs
   g. Antihypertensive drugs

Pharmacology of the Cardiovascular System
   a. Clinical Correlation
   b. Cardiac Review
   c. Cardiac Glycosides
   d. Antiarrhythmic Drugs
   e. Anti-Anginal drugs
   f. Anticoagulants
   g. Prescription writing
   h. Autonomic Laboratory
   i. Case History
Pharmacology of Drugs Affecting the CNS

a. Drugs affecting the basal ganglia
b. Treatment of sleep disorders
c. Anxiety drugs
d. Anticonvulsant drugs
e. Stimulant drugs
f. Antidepressant drugs
g. Conferences
h. Histamine and Antihistaminic drugs
i. Case history
j. Emetics and Antiemetics

The Pharmacologic Management of Pain

a. Pharmacologic intervention of pain
b. Centrally acting analgesics
c. Clinical correlation
d. Peripherally acting analgesics
e. Non-steroidal anti-inflammatory agents
f. General anesthetics
g. Neuromuscular blocking agents
h. Local anesthetics
i. Alcohol and drugs of abuse

Principles and Mechanisms of Anti-Infective and Antineoplastic Agents

a. Introduction to Chemotherapy
b. Treatment of urinary tract infections
c. Sulfonamides
d. Penicillin
e. Cephalosporin
f. Penicillin Substitutes
g. Broad Spectrum Anti-biotics  
h. Amino glycosides  
i. Antifungal and Antiviral drugs  
j. Chemotherapy and Tuberculosis  
k. Antimalarial drugs  
l. Clinical correlation  
m. Antiprotozoal and antihelmintic drugs  
n. Cancer chemotherapy  
o. Case history  

**Pharmacology of the Endocrine Drugs**  
a. Hypothalamic-Pituitary interactions  
b. Androgens, anabolic steroids, and estrogens  
c. Antifertility agents and Uterotropics  
d. Adrenal steroids  
e. Insulin and Oral hypoglycemic agents  
f. Thyroid and antithyroid drugs  
g. Parathyroid drugs  

**Toxicology and Special Topics**  
a. Introduction to Toxicology  
b. Self-study  
c. Environmental Toxicology  
d. Clinical Toxicology  
e. Toxicology of heavy metals  
f. Clinical correlations  
g. Drug interactions  
h. Pharmacology and Toxicology of ionizing radiation  
i. Drugs affecting the Gastrointestinal system  
j. Case history  
k. Immunosuppressives
1. Role of nutrition in Pharmacology
m. Developmental and perinatal Pharmacology
DRUGS AFFECTING THE AUTONOMIC NERVOUS SYSTEM

h. Adrenergic drugs
i. Adrenergic blocking drugs
j. Adrenergic nerve terminal
k. Cholinergic Agonists
l. Ganglionic blockers
m. Diuretic drugs
n. Antihypertensive drugs

Adrenergic drugs

1. GENERIC NAME: albuterol

BRAND NAMES: Ventolin; Proventil

DRUG CLASS: Albuterol is a bronchodilator used in treating asthma and other conditions with reversible airway obstruction. Asthma is a breathing problem involving widespread narrowing of the airways (bronchial tubes). Airways are breathing passages that allow air to move in and out of the lungs. These airways can be narrowed due to the accumulation of mucus, spasm of the muscles that surround these airways, or swelling of the lining of the airways. Airway narrowing leads to shortness of breath, wheezing, cough, and congestion. Albuterol dilates bronchial airways by relaxing the surrounding bronchial muscles. Albuterol can also be helpful in patients with emphysema and chronic bronchitis when their symptoms are partially related to reversible airway obstruction.

PRESCRIBED FOR: Albuterol is used in the relief and prevention of airway obstruction (bronchospasm) in patients with asthma and in patients with exercise-induced asthma. Albuterol can also be used in treating those patients with emphysema and chronic bronchitis when their symptoms are related to reversible airway obstruction. The inhaled form of albuterol starts working within 15 minutes and can last up to 6 hours.

DOSING: Albuterol inhalations should not be administered more often than prescribed. Excessive use of inhaled albuterol can have adverse effects on the heart. Albuterol inhalations should be administered with proper technique and the specific instructions accompanying the drug packaging should be exactly followed. Use in children should be supervised by an adult. Patients requiring more inhalations for relief of symptoms should seek medical advice.

DRUG INTERACTIONS: Albuterol is used with caution in patients with coronary heart disease or in patients with cardiac rhythm disturbances (arrhythmias). Use of albuterol together with other stimulant medications is discouraged because of their combined effects on the heart rate, blood pressure, and the potential for causing chest pain in patients with underlying coronary heart disease. Tricyclic antidepressants, such as Elavil, should not be used together with albuterol because of their combined toxicity to the vascular system. In rare patients, inhaled albuterol can paradoxically precipitate life threatening bronchospasm. Allergic reactions may rarely occur and can cause rash, hives, swelling, bronchospasm, and anaphylaxis (shock). Worsening of diabetes and lowering of potassium have also been reported.
SIDE EFFECTS: Albuterol can cause side effects including palpitations, fast heart rate, elevated blood pressure, tremor, nausea, nervousness, dizziness, and heart burn. Throat irritation and nose bleeds can also occur.

2. GENERIC NAME: amphetamine and dextroamphetamine

BRAND NAME: Adderall, Adderall XR

DRUG CLASS AND MECHANISM: Amphetamine and dextroamphetamine are used in combination to treat attention-deficit hyperactivity disorder (ADHD) and narcolepsy. Adderall stimulates the brain and also can increase blood pressure. In a recent small study in children with ADHD, the effects of Adderall lasted longer and were preferred over methylphenidate (Ritalin), the most commonly used drug for ADHD. Adderall XR is an extended release form of Adderall. Adderall was approved by the FDA in 1996.

PRESCRIBED FOR: Adderall is used for the treatment of attention-deficit hyperactivity disorder (ADHD) and narcolepsy.

DOsing: Adderall usually is taken once or twice a day. Adderall XR is taken once daily. The dose is adjusted carefully by the physician to achieve the desired effects.

DRUG INTERACTIONS: Adderall should not be taken with monoamine oxidase (MAO) inhibitor drugs including phenelzine (Nardil) and tranylcypromine (Parnate). Patients receiving antihypertensive medications may experience loss of blood pressure control with Adderall.

SIDE EFFECTS: Side effects of Adderall include excessive stimulation of the nervous system leading to nervousness, restlessness, excitability, dizziness, headache, fear, anxiety, tremor, and even hallucinations and convulsions (seizures). Blood pressure and heart rate may increase, and patients may experience palpitations of the heart.

Adrenergic blocking drugs.

1. GENERIC NAME: doxazosin mesylate

BRAND NAME: Cardura

DRUG CLASS AND MECHANISM: Cardura is an inhibitor of the alpha 1 adrenergic nervous system. It is in a class of drugs referred to as alpha blockers that includes alfuzosin (Uroxatral), terazosin (Hytrin), tamsulosin (Flomax), and prazosin (Minipress). Elevated blood pressure (hypertension) is lowered as the action of these nerves, which promote constriction of blood vessels, is blocked.

Cardura was also found to relax the muscles around the prostate gland which is also under the influence of the alpha adrenergic portion nervous system. This can makes urination easier for men affected by enlarged prostate glands.

PRESCRIBED FOR: Cardura is used for the control of elevated blood pressure (hypertension) and for benign prostatic hyperplasia (noncancerous enlargement of the prostate gland).

DOsing: Cardura should be taken at doses specifically directed by your physician. This medication can be taken with or without food. Cardura should be taken the same time each day
to maintain proper blood levels. Do not take Cardura within two hours of taking an antacid. If stopped you must taper the dose.

**DRUG INTERACTIONS:** Do not use in excess. First doses of Cardura or any Alpha 1 inhibitor should be taken with caution. The first doses may cause excessive lowering of the blood pressure and cause dizziness and fainting. Strict compliance with dosing is mandatory. Usually a slow increase in dosing is desirable.

**SIDE EFFECTS:** An uncommon but dangerous side effect is a drop in the white blood cells which normally help to fight infection. Liver damage is uncommon. Dizziness and fainting can occur if the blood pressure is lowered too fast. Swelling of the ankles and fatigue may occur. Most persons should have periodic blood studies while taking Cardura. This medication will rarely cause nausea, headaches, anxiety, insomnia, drowsiness, nasal congestion and sexual dysfunction. Consult your pharmacist and physician for additional drug interactions.

2. **GENERIC NAME:** atenolol

**BRAND NAME:** Tenormin

**DRUG CLASS AND MECHANISM:** Atenolol is a beta-adrenergic blocking agent. Atenolol blocks the action of the sympathetic nervous system, a portion of the involuntary nervous system. The sympathetic nervous system stimulates the pace of the heart beat. By blocking the action of these nerves, atenolol reduces the heart rate and is useful in treating abnormally rapid heart rhythms. Atenolol also reduces the force of heart muscle contraction and lowers blood pressure. By reducing the heart rate and the force of muscle contraction, atenolol reduces heart muscle oxygen demand. Since angina occurs when oxygen demand of the heart exceeds supply, atenolol is helpful in treating angina.

**PRESCRIBED FOR:** Atenolol is prescribed for patients with high blood pressure (hypertension). It is also used to treat chest pain (angina pectoris) related to coronary artery disease. Atenolol is also useful in slowing and regulating certain types of abnormally rapid heart rates (tachycardias). Other uses for atenolol include the prevention of migraine headaches and the treatment of certain types of tremors (familial or hereditary essential tremors).

**DOSING:** Should be taken before meals or at bedtime.

**DRUG INTERACTIONS:** Atenolol can aggravate breathing difficulties in patients with asthma, chronic bronchitis, or emphysema. In patients with existing slow heart rates (bradycardias) and heart blocks (defects in the electrical conduction of the heart), atenolol can cause dangerously slow heart rates, and even shock. Atenolol reduces the force of heart muscle contraction and can aggravate symptoms of heart failure. Calcium channel blockers, and digoxin (Lanoxin) can cause lowering of blood pressure and heart rate to dangerous levels when administered together with atenolol. In patients with coronary artery disease, abruptly stopping atenolol can suddenly worsen angina, and occasionally precipitate heart attacks. If it is necessary to discontinue atenolol, its dosage can be reduced gradually over several weeks. Atenolol can mask the early warning symptoms of low blood sugar (hypoglycemia), and should be used with caution in patients receiving treatment for diabetes. It is not habit forming.

**SIDE EFFECTS:** Atenolol is generally well tolerated, and side effects are mild and transient. Rare side effects include abdominal cramps, diarrhea, constipation, fatigue, insomnia, nausea, depression, dreaming, memory loss, fever, impotence, lightheadedness, slow heart rate, low blood pressure, numbness, tingling, cold extremities, sore throat, and shortness of breath or wheezing.
Cholinergic Agonists

1. GENERIC NAME: pilocarpine oral

BRAND NAME: Salagen

DRUG CLASS AND MECHANISM: Pilocarpine is a "cholinergic" drug, that is, a drug that mimics the effects of the chemical, acetylcholine which is produced by nerve cells. Acetylcholine serves as a messenger between nerve cells and between nerve cells and the organs they control. For example, acetylcholine is responsible for causing the salivary glands to make saliva and the lacrimal glands to make tears to lubricate the eyes.

In addition to its effects on the salivary and lacrimal glands, acetylcholine controls the production of fluid within the eye, and pilocarpine eye drops have been used to treat glaucoma for many years. In 1994, an oral formulation of pilocarpine was approved by the FDA for the treatment of dry mouth caused by radiation therapy for head and neck cancer, a treatment that damages the salivary glands and reduces their production of saliva. In 1998, the oral preparation was approved for the management of Sjogren's syndrome, an autoimmune disease that damages the salivary and lacrimal glands. Pilocarpine was first isolated from the leaves of Pilocarpus microphyllus (also called jaborandi) in 1875.

PRESCRIBED FOR: Oral pilocarpine is used to treat dry mouth caused by Sjogren's syndrome and radiation therapy to the head and neck.

DOSING: Oral pilocarpine usually is taken three or four times daily. The maximum effect occurs in approximately one hour but may occur later if it is taken with food. The effects last three to five hours.

DRUG INTERACTIONS: Medications possessing anticholinergic effects or side effects should not be used with pilocarpine since they will counter pilocarpine's cholinergic effects. Such medications include atropine, e.g., Lomotil; some antihistamines, e.g., carboxinomine (Cardec-DM, Rondec-D), clemastine (Tavist), diphenhydramine (Benadryl), promethazine (Phenergan), trimeprazine (Temaril); some phenothiazines, e.g., mesoridazine (Serentil), promazine (Sparine), thioridazine (Mellaril), triflupromazine (Vesprin); clozapine (Clozaril), cyclobenzaprine (Flexeril), disopyramide Norpace); some antidepressants, e.g., amitriptyline (Elavil), amoxapine (Asendin), bupropion (Wellbutrin; Zyban), clomipramine (Anafranil), doxepin (Sinequan), maprotiline (Ludiomil), and protriptyline (Vivactil).

SIDE EFFECTS: Excessive sweating (diaphoresis) is a frequent side effect of pilocarpine. Other side effects include chills, dizziness, excessive tearing, flushing, voice change, stuffy nose, tremor, increased need to urinate, visual disturbances, diarrhea, difficulty swallowing, abdominal pain, nausea, vomiting, and slow heart rate.

2. GENERIC NAME: tacrine

BRAND NAME: Cognex

DRUG CLASS AND MECHANISM: Tacrine is an oral medication used to treat patients with Alzheimer's disease. Tacrine is in a class of drugs called cholinesterase inhibitors that also includes rivastigmine (Exelon), donepezil (Aricept), and galantamine (Reminyl). Cholinesterase inhibitors inhibit (block) the action of acetylcholinesterase, the enzyme responsible for the
destruction of acetylcholine. Acetylcholine is one of several neurotransmitters in the brain, chemicals that nerve cells use to communicate with one another. Reduced levels of acetylcholine in the brain are believed to be responsible for some of the symptoms of Alzheimer's disease. By blocking the enzyme that destroys acetylcholine, rivastigmine increases the concentration of acetylcholine in the brain, and this increase is believed to be responsible for the improvement in thinking seen with tacrine. Tacrine was approved by the FDA in 1993.

**PRESCRIBED FOR:** Tacrine is used for the treatment of mild to moderate dementia of the Alzheimer's type.

**DOSING:** Tacrine is usually taken four times a day on an empty stomach (one hour before, or two hours after meals). The doctor may increase the dose gradually if liver tests are normal. (See side effects, below.) However, the dose is usually not more than 40 mg four times daily.

**DRUG INTERACTIONS:** Drugs with anticholinergic properties and which cross into the brain, such as atropine, benztropine (Cogentin), and trihexyphenidyl (Artane) produce opposite effects of tacrine and should be avoided during therapy with tacrine.

Unlike donepezil (Aricept), tacrine does not reduce the elimination of other drugs, increasing their levels in blood and the likelihood of their side effects.

**SIDE EFFECTS:** The most common side effect of tacrine is an increase in a liver test called alanine aminotransferase (ALT) as a result of liver damage. When a patient starts taking tacrine, blood is drawn on a weekly basis to measure ALT. If there is an increase in blood ALT, the dosage of tacrine can be reduced. Other side effects of tacrine include nausea, indigestion, vomiting, diarrhea, abdominal pain, and skin rash.

**Ganglionic blockers**

1. **GENERIC NAME:** hyoscyamine sulfate, atropine sulfate, scopolamine sulfate and phenobarbital

**BRAND NAME:** Donnatal

**DRUG CLASS AND MECHANISM:** Donnatal is a medicine which combines naturally occurring belladonna alkaloids (atropine, scopolamine and hyoscyamine) with phenobarbital. This provides multiple effects, including reduction of bowel spasms caused by overly active nerves and mild sedation.

**PRESCRIBED FOR:** Donnatal is used in the treatment of abdominal pain, bloating and cramps in patients with irritable bowel syndrome. It is also used in patients with acute inflammation of the stomach and intestines (gastroenteritis), in reducing pain and diarrhea. It is frequently used as additional therapy in patients with duodenal ulcer.

**DOSING:** May be taken with or without food. The dosage is adjusted to the individual patient to assure control of symptoms with a minimum of side effects.

**DRUG INTERACTIONS:** Caution is advised in patients with glaucoma, myasthenia gravis and urinary obstruction as symptoms of these conditions may worsen with the use of Donnatal. Patients with an unstable cardiac status, severe ulcerative colitis and acute intermittent porphyria
should avoid Donnatal. Elderly patients may experience adverse neurological effects even from small doses.

**SIDE EFFECTS:** Adverse reactions include dry eyes, dry mouth and urinary hesitancy and retention. Blurred vision, rapid heart rates, palpitations may also occur. Headache, nervousness, drowsiness, and dizziness can also be seen.

2. **GENERIC NAME: MECAMYLAMINE**

**BRAND NAME(S):** Inversine

**USES:** This medication is used to treat high blood pressure (hypertension).

**HOW TO USE:** Take this medication by mouth after meals as prescribed. Try to take it at the same time(s) each day. Follow your dosing instructions closely. Do not increase your dose or stop taking this medication without first consulting your doctor. It is important to continue taking this medication even if you feel well. Most people with high blood pressure do not feel sick.

**SIDE EFFECTS:** Headache, lightheadedness, dizziness, drowsiness, loss of appetite, nausea, or constipation may occur the first several days as your body adjusts to the medication. Dry mouth, weakness or fatigue may also occur. If any of these effects continue or become bothersome, inform your doctor. Notify your doctor if you experience: tremors, unusual or uncontrolled movements (especially of the tongue or face), diarrhea, stomach distress, bloating, difficulty urinating, mental confusion, vision changes. To avoid dizziness and lightheadedness when rising from a seated or lying position, get up slowly. Also limit your intake of alcoholic beverages and avoid overheating which will aggravate these effects. If you notice other effects not listed above, contact your doctor or pharmacist.

**PRECAUTIONS:** Tell your doctor if you have: kidney disease, heart disease, prostate trouble, bladder disorder, glaucoma, allergies. Do not go on a salt-restricted diet without your doctor's supervision. This medication should be used only if clearly needed during pregnancy. Discuss the risks and benefits with your doctor. Since it is not known if this medication is found in breast milk, consult your doctor before breast-feeding.

**DRUG INTERACTIONS:** Tell your doctor of any over-the-counter or prescription medication you may take, including: heart drugs, other blood pressure medication, water pills, antacids, antibiotics, sulfa drugs, neostigmine, pyridostigmine. Do not take any medication for cough, colds, hay fever, allergies or weight control without first checking with your doctor or pharmacist. These medications may contain ingredients which can increase blood pressure. Avoid intake of alcoholic beverages while taking this medication. Do not start or stop any medicine without doctor or pharmacist approval.

---

**Diuretic drugs**

1. **GENERIC NAME: furosemide**

**BRAND NAME:** Lasix

**DRUG CLASS AND MECHANISM:** Furosemide is a potent diuretic (water pill). Furosemide works by blocking the absorption of salt and fluid in the kidney tubules, causing a profound
increase in urine output (diuresis). The diuretic effect of furosemide can cause body water and electrolyte depletion. Therefore, careful medical supervision is necessary during treatment.

**PRESCRIBED FOR:** Furosemide is a powerful diuretic. Furosemide is used to treat excessive fluid accumulation and swelling (edema) of the body caused by heart failure, cirrhosis, chronic kidney failure, and nephrotic syndrome. It is sometimes used in conjunction with other blood pressure pills to treat high blood pressure.

**PRECAUTIONS:** Patients allergic to sulfa may also be allergic to furosemide because of a similarity in the chemical structure of the medications. Furosemide should be avoided in kidney failure. Even though furosemide is important in treating excess fluid accumulation in patients with cirrhosis, sudden loss of fluid and electrolytes in these patients can worsen kidney function and even cause the patient to go into a coma. Furosemide can cause lowering of blood potassium, sodium, and magnesium levels. Low potassium and magnesium levels can lead to heart rhythm abnormalities, especially in patients already taking digoxin (Lanoxin). Please visit the digoxin (Lanoxin) site for further information.

Blood uric acid levels can increase during furosemide treatment, but precipitation of acute gout is rare. Furosemide may increase the toxic effect of aminoglycoside antibiotics on the ear, especially in patients with kidney dysfunction. Furosemide reduces the kidney excretion of lithium and can lead to lithium toxicity. Furosemide may impair kidney function when administered together with aspirin or other nonsteroidal anti-inflammatory drugs (NSAIDs). Periodic blood tests are performed to monitor kidney function and electrolytes during treatment with furosemide.

**SIDE EFFECTS:** Commonly observed side effects are low blood pressure, and water and electrolyte depletion. Less common side effects include jaundice, ringing in ears (tinnitus), light sensitivity, rash, pancreatitis, nausea, abdominal pain, dizziness, anemia, and other blood disorders.

2. **GENERIC NAME:** bumetanide

**BRAND NAME:** Bumex

**DRUG CLASS AND MECHANISM:** Bumetanide is a potent diuretic (water pill) that causes a profound increase in urine output (diuresis) by preventing the kidney from retaining fluid. (Specifically, it blocks the reabsorption of sodium and fluid from the kidney's tubules.) It is in a class of diuretics called "loop" diuretics which also includes furosemide (Lasix) and torsemide (Demadex). One mg of bumetanide is approximately equivalent to 10-20 mg of torsemide and 40 mg of furosemide. The potent diuretic effect of bumetanide can cause the loss of large amounts of body water leading to dehydration as well as the loss of electrolytes (e.g., sodium, potassium, magnesium, calcium. Therefore, careful medical supervision is necessary during treatment. Bumetanide was approved for use by the FDA in 1983.

**PRESCRIBED FOR:** Bumetanide is used in the treatment of mild to moderate hypertension (high blood pressure), and in the management of edema (excessive fluid accumulation) associated with congestive heart failure, renal disease and liver cirrhosis.

**DOOSING:** Dosing of bumetanide and other loop diuretics vary greatly among patients, and doses are carefully adjusted by physicians. Bumetanide may be taken with or without food.

**DRUG INTERACTIONS:** Bumetanide can cause low blood potassium, calcium, and magnesium levels. These changes can increase the risk of toxicity from digoxin (Lanoxin). Combining bumetanide with other diuretics such as metolazone (Zaroxolyn), hydrochlorothiazide, or chlorthalidone (Hygroton) can exaggerate the losses of potassium and magnesium.
The body's ability to eliminate lithium may decrease in patients receiving bumetanide. Therefore, careful monitoring of lithium levels in blood is recommended when bumetanide and lithium are taken together in order to prevent increases in lithium levels and lithium toxicity.

Indomethacin (Indocin) can reduce the diuretic and blood pressure-lowering effects of other loop diuretics (e.g. furosemide) and it probably can do the same with bumetanide. Other non-steroidal anti-inflammatory drugs, e.g., ibuprofen (Motrin), naproxen (Naprosyn) may interact similarly.

**SIDE EFFECTS:** Potent diuretics like bumetanide can cause low blood levels of potassium, magnesium, sodium and calcium. Additionally, fluid losses can occur leading to dehydration. The symptoms of dehydration may include dry mouth, thirst, weakness, drowsiness, reduced kidney function, heart arrhythmias, muscle aches and pains, and/or nausea and vomiting.

Toxicity to the inner ear in the form of tinnitus (ringing in the ear) and hearing loss have been associated with other loop diuretics. High plasma levels of bumetanide are toxic to the inner ear of animals. These effects on the inner ear are far more common with intravenous use of the drugs.

High uric acid concentrations in the blood leading to attacks of gouty arthritis may occur during diuretic therapy.

### Antihypertensive drugs

1. **GENERIC NAME:** metoprolol

**BRAND NAMES:** Lopressor, Toprol XL

**DRUG CLASS AND MECHANISM:** Metoprolol is a beta-adrenergic blocking agent. Metoprolol blocks the action of the sympathetic nervous system, a portion of the involuntary nervous system. The sympathetic nervous system stimulates the pace of the heart beat. By blocking the action of these nerves, metoprolol reduces the heart rate and is useful in treating abnormally rapid heart rhythms. Metoprolol also reduces the force of heart muscle contraction and lowers blood pressure. By reducing the heart rate and the force of muscle contraction, metoprolol reduces heart muscle oxygen demand. Since angina occurs when oxygen demand of the heart exceeds supply, metoprolol is helpful in treating angina.

**PRESCRIBED FOR:** Metoprolol is prescribed for patients with high blood pressure (hypertension). It is also used to treat chest pain (angina pectoris) related to coronary artery disease. Metoprolol is also useful in slowing and regulating certain types of abnormally rapid heart rates (tachycardias). Other uses for metoprolol include the prevention of migraine headaches and the treatment of certain types of tremors (familial or hereditary essential tremors).

**DOSING:** Should be taken before meals or at bedtime.

**DRUG INTERACTIONS:** Metoprolol can aggravate breathing difficulties in patients with asthma, chronic bronchitis, or emphysema. In patients with existing slow heart rates (bradycardias) and heart blocks (defects in the electrical conduction of the heart), metoprolol can cause dangerously slow heart rates, and even shock. Metoprolol reduces the force of heart muscle contraction and can aggravate symptoms of heart failure. Calcium channel blockers and digoxin (Lanoxin) can cause lowering of blood pressure and heart rate to dangerous levels when administered together with metoprolol. In patients with coronary artery disease, abruptly stopping metoprolol can suddenly worsen angina, and occasionally precipitate heart attacks. If it is necessary to discontinue metoprolol, its dosage can be reduced gradually over several weeks.
Metoprolol can mask the early warning symptoms of low blood sugar (hypoglycemia), and should be used with caution in patients receiving treatment for diabetes. Safe use of metoprolol in children has not been established. It is not habit forming.

**SIDE EFFECTS:** Metoprolol is generally well tolerated, side effects are mild and transient. Rare side effects include abdominal cramps, diarrhea, constipation, fatigue, insomnia, nausea, depression, dreaming, memory loss, fever, impotence, lightheadedness, slow heart rate, low blood pressure, cold extremities, sore throat, and shortness of breath or wheezing.

2. **GENERIC NAME:** captopril

**BRAND NAME:** Capoten

**DRUG CLASS AND MECHANISM:** Captopril is an ACE (angiotensin converting enzyme) inhibitor. ACE is an enzyme in the body which is important for the formation of angiotensin II. Angiotensin II causes constriction of arteries in the body, thereby elevating blood pressure. ACE inhibitors such as captopril lower blood pressure by inhibiting the formation of angiotensin II, thus relaxing the arteries. Relaxing the arteries not only lowers blood pressure, but also improves the pumping efficiency of a failing heart and improves cardiac output in patients with heart failure.

**PRESCRIBED FOR:** Captopril can be used alone in treating high blood pressure. Its blood pressure lowering effect can be further enhanced by the addition of a diuretic (water pill) medication. Capozide is an example of a medication that combines the effect of captopril with a diuretic (water pill). By reducing resistance in the arteries, captopril can be useful in the treatment of congestive heart failure. In treating heart failure, captopril usually supplements conventional treatment, including a diuretic and digoxin (Lanoxin). After a heart attack, captopril has been found to be effective in improving functioning of the damaged heart. It is also used to treat kidney disease associated with diabetes.

**DOSING:** Should be taken on an empty stomach one hour before meals.

**DRUG INTERACTIONS:** Captopril should not be taken by people with a known allergy to ACE inhibitors. Swelling of the facial tissues and even the upper airways has been reported with ACE inhibitors on very rare occasions, and can lead to serious breathing difficulties. Captopril can interact with diuretics (water pills) and other blood pressure medicines to cause an excessive drop in blood pressure, which can cause symptoms of weakness, dizziness, and lightheadedness. Impairment of kidney function has been reported with ACE inhibitors, especially in patients with severe heart failure or pre-existing kidney disease. Combining captopril with potassium supplements, potassium containing salt substitutes, and potassium-conserving diuretics such as amiloride (Moduretic), spironolactone (Aldactone), and triamterene (Dyazide, Maxzide), can lead to dangerously high blood levels of potassium. Indomethacin (Indocin) and possibly other anti-inflammatory medications may decrease the blood pressure lowering effect of captopril. In rare instances, low white blood cell counts have been reported with the use of captopril. Low white blood cells increase the patient's risk of infections. Anticancer drugs or chloramphenicol taken with captopril can increase the chance of having a low blood cell count. When taken with lithium, captopril can increase lithium to toxic levels in the blood. Safe use in children is not established. It is not habit forming.

**SIDE EFFECTS:** Captopril is generally well tolerated and side effects are usually mild and transient. A dry, persistent cough has been reported with the use of captopril and other ACE inhibitors. Coughing resolves after discontinuing the medication. Other side effects are rare and include abdominal pain, constipation, diarrhea, dizziness, fatigue, headache, loss of taste, loss of appetite, nausea and vomiting, easy bruising or bleeding, chest pain, chills, difficulty breathing,
severe dizziness or fainting, fever, numbness or tingling in the hands or feet, rash, and a sore or
swollen throat. In rare instances, liver dysfunction and skin yellowing (jaundice) have been
reported with ACE inhibitors.

Pharmacology of the Cardiovascular System

j. Clinical Correlation
k. Cardiac Review
l. Cardiac Glycosides
m. Antiaryrrhythmic Drugs
n. Anti-Anginal drugs
o. Anticoagulants
p. Prescription writing
q. Autonomic Laboratory
r. Case History

Antiarrhythmic Drugs

1. GENERIC NAME: propafenone

BRAND NAME: Rythmol

DRUG CLASS AND MECHANISM: Propafenone is used to treat heart rhythm abnormalities
(antiarrhythmic agent). The primary mechanism of action is blocking channels which transport
sodium across cell borders, which prolongs the beginning of the phase during which heart muscle
cells become electrically stimulated (action potential).

Propafenone slows conduction throughout the heart and is referred to as a type IC antiarrhythmic.
Propafenone also has some beta adrenergic receptor blocking properties, and, to a lesser extent,
calcium channel blocking effect. These are class II and class IV properties, respectively.
Propafenone also blocks electrical conduc on through accessory pathways, such as seen in
WPW syndrome.

PRESERVED FOR: Propafenone is an antiarrhythmic agent and is only approved for use in
patients with life-threatening ventricular arrhythmias, such as ventricular tachycardia.
Propafenone is also effective in suppressing the recurrence of atrial fibrillation once sinus rhythm
has been restored. Propafenone is at least as effective as any other type I agent in converting
atrial fibrillation to sinus rhythm. Propafenone is effective in atrial tachycardia, AV nodal
tachycardia, and bypass tract tachycardias.

DOSING: Propafenone is given with or without food every eight hours. In most patients
propafenone is metabolized, primarily by the liver, and excreted in the urine over 2 to 10 hours. In
up to 10% of patients this metabolism is slow and occurs over 12 to 32 hours. Doses may need to
be lowered in these patients, and those with reduced liver and kidney function.
**DRUG INTERACTIONS**: Because of its beta blocking activity, propafenone must be used with caution in patients with weak heart muscle (congestive heart failure), slow heart rate, any form of heart electrical conduction block, low blood pressure, or asthma. The most serious side effect of propafenone is the causing of serious life-threatening irregular heart rhythms (ventricular arrhythmias or proarrhythmia). It is for this reason that propafenone is started and doses increased while patients are hospitalized in a monitored setting.

Quinidine inhibits the metabolism of propafenone and, therefore, their combined use should be avoided. Propafenone increases the levels of digoxin (Lanoxin), warfarin (Coumadin), and beta blockers which may require dose reductions. The electrical safety margins of artificial pacemakers can be compromised by the effects of propafenone and should be closely monitored. Safety and efficacy in children has not been established.

**SIDE EFFECTS**: Common side effects include dizziness, blurred vision, anorexia, unusual taste, fatigue, nausea and vomiting.

2. **GENERIC NAME**: quinidine

**BRAND NAMES**: Quinaglute, Quinidx

**DRUG CLASS AND MECHANISM**: Quinidine is used to correct heart rhythm disturbances and is an antiarrhythmic medication. Three actions are responsible for quinidine’s ability to stop heart rhythm disturbances (arrhythmias) and prevent their recurrence. Quinidine decreases the speed of electrical conduction in the heart muscle. It prolongs the electrical phase during which heart muscle cells become electrically stimulated (action potential) and prolongs the recovery period during which the heart muscle cells cannot be stimulated (refractory period).

Quinidine also blocks the normal effect of the vagus nerve on the heart, causing an increase in heart rate. Quinidine reduces the force of contraction of heart muscle cells, and therefore may further impair the pumping efficiency of a failing heart muscle. Quinidine blocks alpha-receptors in peripheral arteries which lowers blood pressure, and can cause excessively low blood pressure when combined with other blood vessel relaxing drugs (vasodilators).

**PRESCRIBED FOR**: Quinidine is an antiarrhythmic drug used in the treatment of abnormal heart rhythms, such as:

- Early (premature) atrial and ventricular beats;
- Intermittent rapid rhythms (tachycardias) involving the atria and AV junction as well as extra pathways (bypass tracts) between the atria and ventricles;
- Intermittent atrial fibrillation and flutter;
- Sinus rhythm after conversion from atrial fibrillation or flutter to prevent recurrence; and
- Ventricular tachycardia.

**DOSING**: Quinidine is administered with food. It is metabolized mainly by the liver with a small amount of kidney excretion. Dosages may need to be lowered in patients with liver or kidney dysfunction.

**DRUG INTERACTIONS**: Quinidine should not be taken by people who are known to be allergic to it or quinine. Rarely, quinidine causes a low platelet count by stimulating production of an antiplatelet antibody. Quinidine has also been reported to cause diffuse joint aches as well as liver toxicity (hepatitis). Excess quinidine can induce a syndrome called “cinchonism” consisting of various sound and visual disturbances, rashes, and central nervous system changes including headache, confusion, and loss of consciousness. Quinidine can depress heart muscle function, lower blood pressure, and worsen slow heart beats (bradycardia) as well as aggravate heart
Quinidine can slow the rate of atrial flutter. When quinidine is used for this indication, a second agent such as digoxin is used to slow conduction from the atria to the ventricles. Quinidine is avoided in patients who might be adversely affected by an agent with vagus nerve blocking effects (anticholinergic), such as those with the disease myasthenia gravis.

Quinidine can cause ventricular tachycardia with loss of consciousness which can develop into ventricular fibrillation, resulting in death. Therefore, patients are usually started on quinidine while being monitored in a hospital setting with constant observation of their heart rhythm.

Serum levels of digoxin are raised by quinidine, usually requiring dose reduction of digoxin to prevent toxicity. Quinidine also increases the action of the blood thinner warfarin (Coumadin), requiring a decrease in warfarin dose. Liver metabolism of quinidine is accelerated by phenobarbital, phenytoin (Dilantin), and rifampin (Rifamate), requiring an increase in quinidine dose. Amiodarone (Cordarone), cimetidine (Tagamet), and ketoconazole (Nizoral) increase quinidine levels, requiring a decrease in quinidine dose.

SIDE EFFECTS: The most common side effects are diarrhea and nausea which can occur even at low doses. These symptoms cause discontinuation of the drug in 1/4 to 1/3 of patients. Other side effects include vomiting, heartburn, rash, fever, dizziness, and headache.

Anti-Anginal drugs

1. GENERIC NAME: nitroglycerin

BRAND NAME: Nitro-Bid; Nitro-Dur; Nitrostat; Transderm-Nitro; Minitran; Deponit; Nitrol

DRUG CLASS AND MECHANISM: Nitroglycerin is a vasodilator (a medication that dilates blood vessels) that frequently is used in the management of angina pectoris. Synthesized in 1846, nitroglycerin was first used to treat anginal attacks in 1879. It was granted FDA approval in 1938.

Blood returning from the body in the veins must be pumped by the heart through the lungs and into the arteries against the high pressure in the arteries. In order to accomplish this work, the heart's muscle must produce and use energy ("fuel"). The production of energy requires oxygen. Angina pectoris (angina) or "heart pain" is due to an inadequate flow of blood (and oxygen) to the muscle of the heart. It is believed that all nitrates, including nitroglycerin, correct the imbalance between the flow of blood and oxygen to the heart and the work that the heart must do by dilating the arteries and veins in the body. Dilation of the veins reduces the amount of blood that returns to the heart that must be pumped. Dilation of the arteries lowers the pressure in the arteries against which the heart must pump. As a consequence, the heart works less and requires less blood and oxygen.

Additionally, in patients with angina, nitroglycerin preferentially dilates blood vessels that supply the areas of the heart where there is not enough oxygen, thereby delivering oxygen to the heart tissue that needs it most.

PREScribed FOR: Nitroglycerin is indicated for the acute treatment and prevention of angina.
**DOSING:** For the treatment of acute angina attacks or for acute prevention (i.e. immediately before encountering situations likely to bring on an anginal attack): one tablet is allowed to dissolve under the tongue or in the buccal pouch (between the cheek and gums), or one spray is given of the lingual spray. (Nitroglycerin for sublingual or buccal use as well as spray are rapidly absorbed from the lining of the mouth for immediate effects.) This may be repeated every 5 minutes as needed. If angina is not relieved after a total of 3 doses, the patient should be taken to a hospital or a physician should be contacted. If lingual spray is used, the canister of spray should not be shaken prior to use, and it should be sprayed onto or under the tongue and then the mouth closed.

For prevention of angina, ointment may be applied using special dose-measuring application papers provided with the ointment. The appropriate amount of ointment is squeezed as a thin layer onto the paper, and the paper is used to spread the ointment onto nonhairy area of skin. The ointment should not be allowed to come into contact with the hands so that there is no absorption from the hands. Transdermal patches also are used for prevention. Patches may be applied to any hairless site but should not be applied to areas with cuts or calluses. Firm pressure should be used over the patch to ensure contact with the skin. The patch should not be cut or trimmed. Patches are waterproof and should not be affected by showering or bathing. Capsules of long-acting nitroglycerin also are used for prevention. They usually are prescribed 2 to 3 times per day and are taken 1 to 2 hours after a meal.

**DRUG INTERACTIONS:** Since nitroglycerin can cause hypotension (low blood pressure), other medications which also cause hypotension may produce an unwanted additive effect. Such drugs might include medicines used to treat high blood pressure, some antidepressants; some antipsychotics, quinidine, procainamide, benzodiazepines such as diazepam (Valium) or opiates (e.g. morphine). Since alcohol also may intensify the blood pressure lowering effect of nitroglycerin, patients receiving nitroglycerin should be advised to drink alcoholic beverages with caution.

Ergot alkaloids (e.g. Cafergot) and Imitrex can oppose the vasodilatory actions of nitroglycerin and may precipitate angina. A similar effect can occur with ephedrine and the decongestants pseudoephedrine (Sudafed) and propanolamine.

**SIDE EFFECTS:** A persistent, throbbing headache commonly occurs with nitroglycerin therapy. Aspirin, acetaminophen, or ibuprofen may be used to relieve the pain. Flushing of the head and neck can occur with nitroglycerin therapy as can an increase in heart rate or palpitations. This can be associated with a drop in blood pressure which can be accompanied by dizziness or weakness. To reduce the risk of low blood pressure, patients often are told to sit or lie down during and immediately after taking nitroglycerin.

2. **GENERIC NAME:** diltiazem

**BRAND NAMES:** Cardizem, Dilacor, Tiazac

**DRUG CLASS AND MECHANISM:** Diltiazem belongs to a class of medications called calcium channel blockers. These medications block the transport of calcium into the smooth muscle cells lining the coronary arteries and other arteries of the body. Since calcium is important in muscle contraction, blocking calcium transport relaxes artery muscles and dilates coronary arteries and other arteries of the body. By relaxing coronary arteries, diltiazem is useful in treating and preventing chest pain (angina) resulting from coronary artery spasm. Relaxing the muscles lining
the arteries of the rest of the body lowers blood pressure, which reduces the burden on the heart as it pumps blood to the body. Reducing heart burden lessens the heart muscle's demand for oxygen, and further helps to prevent angina in patients with coronary artery disease. For more detailed information related to coronary artery disease, please read articles: Cholesterol and Heart Attack. Diltiazem can decrease electrical conduction in the heart and slow heart rate.

**PRESCRIBED FOR:** Chest pain (angina) occurs because of insufficient oxygen delivered to the heart muscles. Insufficient oxygen may be a result of coronary artery blockage or spasm, or because of physical exertion which increases heart oxygen demand in a patient with coronary artery narrowing. Diltiazem is used for the treatment and prevention of angina resulting from coronary artery spasm, as well as from exertion. Diltiazem is also used in the treatment of high blood pressure. By slowing electrical conduction in the heart, diltiazem has been used in treating abnormally fast heart rhythms, such as atrial fibrillation.

**DOsING:** Diltiazem may be taken with or without food. Since diltiazem is excreted by the kidney and metabolized by the liver, dosages may need to be lowered in patients with liver or kidney dysfunction.

**DRUG INTERACTIONS:** Diltiazem slows heart electrical conduction, and can cause a dangerously slow heart rate in patients with existing electrical conduction disease of the heart. Concurrent use of diltiazem with a beta blocker (another class of medications that slow heart rate) can occasionally cause profound heart slowing. Diltiazem can aggravate heart failure and cause excessive lowering of blood pressure.

Administration of diltiazem with digoxin can increase digoxin blood levels. Therefore, blood levels of digoxin are usually monitored to avoid toxicity. Similarly, concurrent administration of diltiazem with an anti-seizure medication carbamazepine (Tegretol) can increase blood levels of the seizure medication, and occasionally lead to toxicity. Concurrent administration of cimetidine (Tagamet) interferes with the liver breakdown of diltiazem, and significantly increases diltiazem blood levels. Therefore, cautious dosing is necessary when both medications are administered. Safety in children has not been established.

**SIDE EFFECTS:** Side effects are generally mild and transient. Diltiazem can cause difficulty breathing or wheezing as a result of worsening heart failure. It can cause dizziness, weakness or fainting because of slow heart rate or low blood pressure. Other side effects include swelling of the lower extremities, rash, headache, and constipation. Diltiazem can also cause mildly abnormal liver tests that are generally reversible with discontinuation of the medication.

---

**Anticoagulants**

1. **GENERIC NAME:** warfarin

**BRAND NAME:** Coumadin

**DRUG CLASS AND MECHANISM:** Coumadin is an oral anticoagulant that inhibits the synthesis of clotting factors, thus preventing blood clot formation. Blood clots can occur in the veins of the lower extremities, usually after periods of immobility. These clots can break off and become
lodged in the blood vessels of the lung (pulmonary embolism), causing shortness of breath, chest pain, and even life-threatening shock. Blood clots can also occur in the atria of the heart during atrial fibrillation (see Atrial Fibrillation article), and around artificial heart valves. One of these clots can also break off and obstruct a blood vessel in the brain, causing an embolic stroke with paralysis. Coumadin is important in preventing the formation of blood clots. It is also important to prevent extension of clots already formed, and to minimize the risk of blood clot embolization to other vital organs such as the lungs and brain.

**PRESCRIBED FOR:** Coumadin is used in treating patients with blood clots in the lower extremities to prevent extension of the clot, and to reduce the risk of pulmonary embolism. Patients with pulmonary embolism are treated with Coumadin to prevent further blood clot emboli. Coumadin is also used in patients with atrial fibrillation and artificial heart valves to reduce the risk of strokes. It is also helpful in preventing blood clot formation in certain orthopedic surgeries such as knee or hip replacements. Coumadin is also used in preventing blood clot closure of coronary artery stents.

**DOSSING:** Coumadin may be taken with or without food. Since Coumadin is metabolized by the liver and excreted by the kidneys, dosages need to be lowered in patients with liver and kidney dysfunction. Frequent blood tests are performed to measure blood clotting time (protime) during Coumadin treatment. Protime results help doctors adjust medication dose to avoid excessive blood thinning and risk of bleeding.

**DRUG INTERACTIONS:** Many drugs, both prescription and nonprescription (OTC), can affect the anticoagulant action of Coumadin. Some medications can enhance the action of Coumadin and cause excessive blood thinning and life-threatening bleeding. A few examples of such medications include Aspirin, Tylenol, alcohol, ibuprofen (Motrin), cimetidine (Tagamet), oxandrolone (Oxandrin), certain vitamins, and antibiotics. Patients on Coumadin should regularly consult their doctor before instituting any medications on their own. It is also advisable for patients on Coumadin to carry identifications to alert other health professionals.

**SIDE EFFECTS:** The two most serious side effects are bleeding and necrosis (gangrene) of the skin. Bleeding can occur in any organ or tissue. Bleeding around the brain can cause severe headache and paralysis. Bleeding in the joints can cause joint pain and swelling. Bleeding in the stomach or intestines can cause weakness, fainting spells, black tarry stools, vomiting of blood, or coffee ground material. Bleeding in the kidneys can cause back pain and blood in urine. Other side effects include purple, painful toes, rash, hair loss, bloating, diarrhea, and jaundice (yellowing of eyes and skin). Signs of overdose include bleeding gums, bruising, nosebleeds, heavy menstrual bleeding, and prolonged bleeding from cuts.

2. **GENERIC NAME:** alteplase

**BRAND NAME:** Activase; TPA

**DRUG CLASS AND MECHANISM:** Alteplase is an injectable drug, given directly into a vein, that is used to treat conditions caused by arterial blood clots including heart attacks, strokes, chest pain at rest (unstable angina), blood clots in the lungs (pulmonary thrombosis), and other less common conditions involving blood clots. Alteplase is an enzyme that occurs naturally in man and causes blood clots to dissolve. It is a man-made protein manufactured by recombinant DNA technology. The naturally occurring protein, known as tissue plasminogen activator (TPA), is made by ovarian cells from the Chinese hamster. The amount that is given to patients is far greater than the amount naturally made by the body itself. Alteplase was first approved for heart attacks in 1987. In 1996, it was approved for strokes.
**PRESCRIBED FOR:** Alteplase is used to treat persons with heart attacks (acute myocardial infarctions), strokes, chest pain at rest (unstable angina), blood clots in the lungs (pulmonary thrombosis or embolism), and other less common conditions involving blood clots.

**DOSING:** Alteplase is injected intravenously. Depending on the condition being treated, it is given once quickly or as a brief infusion over 30 to 60 minutes.

**DRUG INTERACTIONS:** Alteplase breaks down clots and thereby interferes with the body's ability to stop bleeding. Therefore, drugs which also interfere with the body's ability to form blood clots (or the clot-promoting effects of platelets) increase the risk of bleeding in patients receiving alteplase. Such medicines include warfarin (Coumadin), aspirin, and nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen (Motrin), naproxen (Naprosyn), and nabumetone (Relafen). Specific platelet inhibitors, for example, clopidogrel (Plavix) do not appear to interact with alteplase and increase the risk of bleeding.

**SIDE EFFECTS:** The most common and serious side effect with alteplase is bleeding. Most commonly, such bleeding is minor, but significant, even fatal bleeding has been reported.

---

**Pharmacology of Drugs Affecting the CNS**

k. Drugs affecting the basal ganglia  
l. Treatment of sleep disorders  
m. Anxiety drugs  
n. Anticonvulsant drugs  
o. Stimulant drugs  
p. Antidepressant drugs  
q. Conferences  
r. Histamine and Antihistaminic drugs  
s. Case history  
t. Emetics and Antiemetics

**Drugs affecting the basal ganglia**

1. GENERIC NAME: levodopa-carbidopa  

**BRAND NAME:** Sinemet
**DRUG CLASS AND MECHANISM:** Levodopa-carbidopa is a combination of two drugs, levodopa and carbidopa. Levodopa-carbidopa is used in the treatment of Parkinson's disease. Parkinson's disease is believed to be related to low levels of dopamine in certain parts of the brain. When levodopa is taken orally, it crosses through the "blood-brain barrier." Once it crosses, it is converted to dopamine. The resulting increase in brain dopamine concentrations is believed to improve nerve conduction and assist the movement disorders in Parkinson disease. Carbidopa does not cross the blood-brain barrier. Carbidopa is added to the levodopa to prevent the breakdown of levodopa before it crosses into the brain. The addition of carbidopa allows lower doses of levodopa to be used. This reduces the risk of side effects from levodopa such as nausea and vomiting. This combination medicine was approved by the FDA in 1988.

**PRESCRIBED FOR:** Levodopa-carbidopa is indicated for the management of Parkinson's disease.

**DOSING:** Levodopa-carbidopa is taken several times per day. It may be administered with food to reduce the likelihood of nausea. However, a high-protein diet may reduce its absorption.

**DRUG INTERACTIONS:** The use of amantadine (Symmetrel), benztropine (Cogentin), procyclidine (Kemadrin), or trihexyphenidyl (Artane) with levodopa-carbidopa can enhance the anti-Parkinson's effects of levodopa. Droperidol, haloperidol (Haldol), loxapine (Loxitane), metoclopramide (Reglan), phenothiazines such as prochlorperazine (Thorazine); thioanthenes as thiothixene (Navane) inhibit dopamine in the brain. These drugs, therefore, can worsen Parkinson's disease and reverse the beneficial effects of levodopa. Methyldopa (Aldomet) and reserpine also can interfere with the beneficial actions of levodopa-carbidopa and can increase the risk of side effects.

Phenytoin (Dilantin) can increases the break-down of levodopa-carbidopa, reducing its effectiveness.

Use of levodopa-carbidopa with monoamine oxidase inhibitors (MAOI's) antidepressants, for example, isocarboxazid (Marplan), phenelzine (Nardil), tranylcypromine (Parnate), and procarbazine (Matulane), can result in severe and dangerous elevations in blood pressure. MAOI's should be stopped 2-4 weeks before starting levodopa-carbidopa therapy.

The side effects associated with levodopa, including dizziness upon rising, confusion, movement disorders, nausea, and hallucinations, all can be increased by selegliline (Eldepryl).

**SIDE EFFECTS:** Most patients receiving levodopa-carbidopa experience side effects, but these are usually reversible. Occasional involuntary movements are the most common of the serious side effects of levodopa-carbidopa therapy. These may include chewing, gnawing, twisting, tongue or mouth movements, head bobbing, or movements of the feet, hands, or shoulder. These may respond to a reduction in the dose. Muscle twitching, dizziness, muscle jerks during sleep, and hand tremor also may occur. Various psychiatric disturbances may occur during levodopa-carbidopa therapy. Such disturbances include memory loss, anxiety, nervousness, agitation, restlessness, confusion, inability to sleep, nightmares, daytime tiredness, mental depression or euphoria.

Gastrointestinal side effects are common in patients receiving levodopa-carbidopa. Nausea, vomiting, loss of appetite, and weight loss may occur. Patients may experience dizziness upon standing up, associated with a drop in blood pressure. Fortunately, the body develops tolerance to this side effect within a few months.

Infrequently, patients may develop a drop in white blood cell count during levodopa-carbidopa therapy. This is a cause to temporarily, if not permanently, stop treatment.
2. GENERIC NAME: SELEGILINE

BRAND NAME(S): Carbex, Eldepryl

USES: This medication is used to treat Parkinson's disease. It is used along with levodopa or levodopa/carbidopa to make it more effective.

HOW TO USE: Take this medication as prescribed. Do not increase your dose or take it more often than directed. It may take a few weeks for the full benefits of the drug to be noticed. Do not stop taking this drug without first consulting your doctor.

DRUG INTERACTIONS: This drug should not be used with the following medications because very serious interactions may occur: apraclonidine, brimonidine, bethanidine, bupropion, buspirone, carbamazepine, dextromethorphan, entacapone, herbal products (e.g., ma huang), indoramin, meperidine, papaverine, sibutramine, SSRI antidepressants (e.g., fluoxetine, citalopram), sympathomimetics (e.g., methylphenidate, ephedrine), tolcapone, tricyclic antidepressants (e.g., amitriptyline, doxepin), "triptans" (e.g., sumatriptan, zolmitriptan). If you are currently using any of these medications, tell your doctor or pharmacist before starting selegiline. Before using this medication, be sure to tell your doctor what medicines (both prescription and nonprescription) you are taking, including: levodopa, insulin and oral antidiabetic drugs, other MAO inhibitors (e.g., furazolidone, linezolid, moclobemide, phenelzine), tryptophan, sedatives and drugs used to aid sleep, drugs used for blood pressure. Consult your doctor about the need to watch your intake of foods containing tyramine. It is possible consuming tyramine-containing foods while using this medication could cause headache and/or increased blood pressure and could lead to a medical emergency. Tyramine food precautions should be observed for at least 2 weeks after you stop using this medication. The following is a partial list of tyramine-containing foods: Meat or Fish - pickled herring/liver/dry sausage/salami/meats prepared with tenderizer; Dairy - yogurt/sour cream/aged cheeses (cream or cottage cheese are okay); Beverages - beer/red wine/sherry - Avoid excessive amount of caffeine-containing colas/coffee/tea; Fruits and Vegetables - avocado/bananas/figs/raisins/broad beans/sauerkraut; Other - yeast extract/soy sauce/large amounts of chocolate. Do not start or stop any medicine without doctor or pharmacist approval.

SIDE EFFECTS: This medication may cause stomach upset, loss of appetite, nausea, heartburn or dry mouth. These effects should subside as your body adjusts to the medication. If they continue or become bothersome, inform your doctor. To relieve dry mouth, suck on (sugarless) hard candy or ice chips, chew (sugarless) gum, drink water or use saliva substitute. Infrequently, this medication may increase the skin's sensitivity to sunlight. If this happens to you, avoid prolonged sun exposure, wear protective clothing and use a sunscreen. Avoid sunlamps. This medication can cause dizziness and lightheadedness especially during the first few days of therapy. Avoid tasks requiring alertness if you experience these effects. Notify your doctor promptly if you develop any of the following side effects: severe headache, chest pain, irregular heartbeat, tremors, clumsiness, confusion, involuntary movements (especially of the hands or face), nightmares, hallucinations, difficulty breathing, difficulty urinating. If you notice other effects not listed above, contact your doctor or pharmacist.

PRECAUTIONS: Before using this drug, tell your doctor your medical history, especially of: peptic ulcer, allergies (especially drug allergies). Selegiline should be used only when clearly needed during pregnancy. Discuss the risks and benefits with your doctor. It is not known if this drug is excreted into breast milk. Consult your doctor before breast-feeding.
Treatment of sleep disorders

1. GENERIC NAME: zolpidem

BRAND NAME: Ambien

DRUG CLASS AND MECHANISM: Zolpidem belongs to a class of medicines that effects the central nervous system, called sedative hypnotics. Zolpidem is closely related to a family of drugs called benzodiazepines. These drugs cause sedation, muscle relaxation, act as anti-convulsants (anti-seizure), and have anti-anxiety properties. Zolpidem has selectivity in that it has little of the muscle relaxant or anti-seizure effect and more of the sedative effect. Therefore, it is used as a medication for sleep.

PRESCRIBED FOR: Zolpidem is used as a sleeping pill to treat insomnia. It has been shown to put patients to sleep faster and keep them asleep longer. Sleeping pills generally are not prescribed for more than 10 days and are usually taken intermittently as needed to avoid problems with addiction, loss of effectiveness, and rebound phenomena.

DOSING: Zolpidem should be taken without food at bedtime to induce a rapid onset of sleep. Zolpidem is metabolized by the liver and dosages need to be decreased in patients with liver dysfunction (hepatitis). Lower doses should be used in the elderly because of their decreased ability to metabolize the medication.

DRUG INTERACTIONS: Alcohol has an additive effect with zolpidem and the two should not be combined. Zolpidem should be used cautiously in patients with respiratory diseases because of its depressing effect on breathing. Zolpidem has few drug interactions with other medicines. However, caution should be used when combining it with other sedative drugs. Zolpidem used at higher dosages can cause withdrawal symptoms (muscle cramps, sweats, shaking, and seizures) when the drug is abruptly discontinued. Zolpidem can cause abnormal behavior with confusion and paradoxical insomnia and should be discontinued if these symptoms appear.

SIDE EFFECTS: The most common side effects of Zolpidem are drowsiness, dizziness, and a "drugged" feeling, which probably reflect the action of the drug. Other side effects include confusion, insomnia, euphoria, ataxia (balance problems), and visual changes.

2. GENERIC NAME: methylphenidate

BRAND NAME: Ritalin, Ritalin SR, Ritalin LA

DRUG CLASS AND MECHANISM: Methylphenidate is a medication that stimulates the central nervous system (brain) in a manner that is similar to the amphetamines; however, its actions are milder than those of the amphetamines. An additional difference is that methylphenidate produces more noticeable effects on mental activities than on motor activities. Methylphenidate and amphetamines both have abuse potential. In treating children with attention-deficit hyperactivity disorder (ADHD), methylphenidate produces a calming effect. This results in a reduction in hyperactivity and an improvement in attention span. Methylphenidate was approved by the FDA in 1955.

PRESCRIBED FOR: Methylphenidate is used in the treatment of narcolepsy (uncontrollable sleepiness) and in the treatment of children with ADHD.
DOsing: The dose of methylphenidate is adjusted based on patients’ responses. It may be given once, twice, or three times daily. Ritalin LA is given once daily.

Drug Interactions: The CNS stimulation effects of methylphenidate can be additive when used with other chemicals and medications that stimulate the CNS, such as caffeine (in coffee, tea, or cola drinks), and pseudoephedrine or phenylpropanolamine (in many cough-and-cold preparations). The combination of methylphenidate and monoamine oxidase inhibitors, for example, isocarboxazid (Marplan), phenelzine (Nardil), tranylcypromine (Parnate), and procarbazine (Matulane), should be avoided since a hypertensive crisis (severely high blood pressure) may occur. Therefore, methylphenidate should not be given to any patient within 14 days of receiving such an inhibitor. The blood pressure lowering effects of medications used to treat hypertension may be reduced by methylphenidate. As a result, blood pressure needs to be monitored when starting or stopping methylphenidate in patients who are receiving blood pressure medicines.

Side Effects: The most common side effects with methylphenidate are nervousness, agitation, anxiety, and insomnia. Insomnia can be limited by taking the drug before noon. For children taking methylphenidate for ADHD, the most common side effects are loss of appetite, abdominal pain, weight loss, and sleep problems. The rate and severity of these side effects are less than that seen with dextroamphetamine (Dexedrine). Other side effects include nausea, vomiting, dizziness, palpitations, headache, involuntary movements, chest pain, increased heart rate, increased blood pressure, and psychosis.

There have been rare reports of Tourette’s syndrome, a syndrome in which there are uncontrollable tics such as grimacing. Because of the potential for the side effects listed above, methylphenidate should be used with caution by patients who have relatives with Tourette’s syndrome or have the syndrome themselves or who have severe anxiety, seizures, psychosis, emotional instability, major depression, glaucoma, or motor tics. Sudden discontinuation of long-term methylphenidate therapy may unmask depression. Gradual withdrawal, under supervision, is recommended.

Anxiety Drugs

1. Generic Name: alprazolam

brand Name: Xanax

Drug Class and Mechanism: Alprazolam is a member of the benzodiazepine family. Benzodiazepines are sedatives that cause dose-related depression of the central nervous system. They are useful in treating anxiety, insomnia, and muscle spasms.

Prescribed For: Alprazolam is used for the treatment of anxiety disorders and panic attacks. Anxiety disorders are characterized by unrealistic worry and apprehension, causing symptoms of restlessness, aches, trembling, shortness of breath, smothering sensation, palpitations, sweating, cold clammy hands, lightheadedness, flushing, exaggerated startle responses, problems concentrating, and insomnia. Panic attacks occur either unexpectedly or in certain situations (i.e. driving), and can require higher dosages of alprazolam.

Dosing: Alprazolam may be taken with or without food. Alprazolam is metabolized by the liver and excreted mainly by the kidney. Dosages of alprazolam may need to be lowered in patients with abnormal kidney function.
**DRUG INTERACTIONS:** Alprazolam should not be taken with ketoconazole or itraconazole. Alcohol should be avoided by patients taking benzodiazepines. Alprazolam can lead to addiction (dependency), especially at high dosages over prolonged periods of time. Because of alprazolam's addicting potential, dosages should never be increased by the patient. In patients addicted to alprazolam, abrupt discontinuation of the medicine can lead to symptoms of withdrawal (insomnia, headaches, nausea, vomiting, light headiness, sweating, anxiety, and fatigue). Seizures can occur in more severe cases of withdrawal. Consequently, patients on alprazolam for extended periods of time should slowly taper the medication under a doctor's supervision rather than abruptly stopping the medication.

**SIDE EFFECTS:** The most frequent side effects of alprazolam taken at lower doses are drowsiness or lightheadedness, which probably reflect the action of the drug. Side effects of higher dosages (those used for panic attacks) include fatigue, memory problems, speech problems, constipation, and changes in appetite with resultant changes in weight.

2. **GENERIC NAME:** temazepam

**BRAND NAME:** Restoril

**DRUG CLASS AND MECHANISM:** Temazepam is a drug that is used for treating anxiety. It is in the benzodiazepine class of drugs, the same family that includes diazepam (Valium), alprazolam (Xanax), clonazepam (Klonopin), flurazepam (Dalmane), lorazepam (Ativan), and others. Temazepam and other benzodiazepines act by enhancing the effects of gamma-aminobutyric acid (GABA) in the brain. GABA is a neurotransmitter (a chemical messenger that nerve cells use to communicate with each other) that inhibits many of the activities of the brain. It is believed that excessive activity in the brain may lead to anxiety or other psychiatric disorders and that temazepam reduces the activity. Temazepam increases total sleep time.

**PRESCRIBED FOR:** Temazepam is used for the short-term (7-10 days) management of insomnia. Insomnia is defined as difficulty falling asleep, frequent awakening during the night after falling asleep, and/or early morning awakening.

**DOSING:** The recommended dose of temazepam is 15-30 mg taken about 30 minutes prior to bedtime. For some patients, 7.5 mg may be sufficient.

**DRUG INTERACTIONS:** Itraconazole (Sporanox) may reduce the rate of elimination of temazepam, increasing levels of temazepam in the blood. This can result in excessive sleepiness. Oral contraceptives have been reported to increase the elimination of temazepam, an effect that may result in reduced effectiveness of temazepam. Alcohol or drugs that cause sleepiness increase the effects of temazepam.

**SIDE EFFECTS:** The most commonly noted side effects associated with temazepam are excessive sleepiness, dizziness, weakness, and unsteadiness. Other side effects include a feeling of depression, loss of orientation, headache, and sleep disturbances. Like all benzodiazepines, temazepam can cause physical dependence. Suddenly stopping temazepam after a few months of daily use may be associated with a feeling of loss of self-worth, agitation, and insomnia. If temazepam is taken continuously for longer than a few months, stopping treatment suddenly may produce seizures, tremors, muscle cramping, vomiting, and/or sweating. Therefore, discontinuation usually is accomplished by slowly reducing the daily dose.

**Anticonvulsant drugs**
1. GENERIC NAME: phenytoin

BRAND NAME: Dilantin

DRUG CLASS AND MECHANISM: Phenytoin is an oral and injectable anti-seizure medication first synthesized in 1908. Phenytoin was originally approved by the FDA in 1939.

PRESCRIBED FOR: Although it has been used in many conditions, phenytoin’s only approved use is as an anti-seizure medication (anticonvulsant), especially to prevent tonic-clonic (grand mal) seizures and complex partial seizures (psychomotor seizures). It may be used alone or with phenobarbital or other anticonvulsants.

DOsing: The dosing of phenytoin is very patient-specific. It may be given once, twice, or three times daily. Doses are often adjusted to find the optimal dose, based on measurement of blood levels. Taking phenytoin with food may reduce some of the side effects. Elderly patients, debilitated persons, and patients with certain kidney or liver diseases may need lower doses. The suspension should not be given at the same time as tube feedings.

DRUG INTERACTIONS: There are many potential drug interactions with phenytoin. Phenytoin can increase the metabolism (elimination) of many drugs, reducing their concentrations in the body. Drugs that may be affected include: digoxin, carbamazepine, clonazepam, corticosteroids (e.g. prednisone), cyclosporine, disopyramide, doxycycline, estrogens, felodipine, levodopa, lidocaine, methadone, mexiletine, oral contraceptives, paroxetine, quinidine, tacrolimus, theophylline, phenobarbital, and warfarin. Phenytoin can interact with these drugs not only when it is added to therapy but also when it is discontinued. In the latter case, the concentration of the other drugs may increase.

Phenytoin’s metabolism may be affected by other drugs. Drugs that can reduce the amount of phenytoin in the body include rifampin and phenobarbital. Drugs that increase phenytoin concentrations include amiodarone, chloramphenicol, cimetidine, disulfiram, fluconazole, fluoxetine, isoniazid (INH), omeprazole, and paroxetine. Thus, measuring levels of phenytoin in the blood may be necessary when patients begin or discontinue other medications.

The oral absorption of phenytoin can be reduced by any of the following: antacids containing magnesium, calcium carbonate, or aluminum; calcium salts; or enteral feeding products (tube feedings). Separating the administration of phenytoin and enteral feeding products, antacids, or calcium salts by at least 2 hours will help avoid this interaction.

SIDE EFFECTS: Many varied adverse effects can occur during phenytoin therapy including dizziness, drowsiness, difficulty focusing (vision), unsteady gate, tiredness, abnormal involuntary movements, nausea, vomiting, constipation, abdominal pain, and loss of appetite. Children and young adults can develop overgrowth of the gums during long-term therapy which requires regular treatment by a dentist. Good oral hygiene and gum massage may reduce the risk. Rashes can occur in between 1 in 20 and 1 in 10 persons; some may be severe. Additionally, darkening coloration of the skin may develop (more commonly in women). Phenytoin can produce unusual growth of hair in some patients. This reaction most commonly affects the arms and legs but can also affect the trunk and face; it may be irreversible.

Various lymph node reactions have been reported with phenytoin therapy. Lymph nodes may swell up, sometimes painfully. Phenytoin cause serum glucose to rise. Thus, blood sugar should be monitored closely when phenytoin is administered to patients with diabetes. Phenytoin can potentially injure the liver although this is an uncommon occurrence. Phenytoin can cause the platelet or white blood cell counts to drop, increasing the risk of bleeding or infection, respectively. Phenytoin also can cause anemia. Because it interferes with vitamin D metabolism, phenytoin
can cause weakening of the bones (osteomalacia). Phenytoin can cause sexual dysfunction including decreased libido, impotence, and priapism (painful, prolonged erections).

2. GENERIC NAME: topiramate

BRAND NAME: Topamax

DRUG CLASS AND MECHANISM: Topiramate is an oral drug that is used to prevent the seizures of epilepsy. (It is an anti-epileptic or anti-seizure drug). It is used primarily among patients who are not controlled by other anti-epileptic drugs. About 1 in 4 Americans diagnosed with epilepsy has seizures that resist treatment with other anti-epileptic drugs. Topiramate also prevents migraine headaches.

Seizures are due to the abnormal activity (“firing”) of nerves in the brain, and the abnormal activity spreads to smaller or larger portions of the brain. Although topiramate’s exact mechanism of action is unknown, scientific studies suggest that it may alter neurotransmitters within the brain. Neurotransmitters are chemicals that nerves manufacture and use to communicate with other nearby nerves. By altering the production or action of the neurotransmitters, topiramate may suppress the abnormal activity of the nerves in the brain that cause the seizures or may prevent the abnormal activity from spreading to other nerves. Other studies suggest that topiramate may suppress the nerves directly (i.e., not by altering neurotransmitters) and make them less likely to fire. The FDA approved topiramate as a tablet in 1997. The Sprinkle Capsules were approved in October, 1998.

PRESCRIBED FOR: Seizures may be classified as either partial if they involve only a small portion of the brain or generalized if they involve more of the brain. Topiramate is used in combination with other anti-seizure drugs among adults and children aged 2-16 years with partial seizures or generalized tonic-clonic seizures (in which there is prolonged contraction of the muscles of the body that causes rigidity as well as jerking motions). Topiramate sprinkle capsules are approved for treatment without other drugs in patients 10 years of age and older. Topiramate also is used in patients two years of age and older with seizures associated with the Lennox-Gastaut Syndrome, a severe form of epilepsy which accounts for up to 10 percent of all cases of childhood epilepsy. Children with Lennox-Gastaut Syndrome experience delays in their development and up to dozens of different, mixed types of seizures a day. The most common types of seizures in this syndrome are tonic (stiffening of the body, with the eyes rolling upwards, dilation of the pupils and shallow, irregular breathing), atonic (brief loss of muscle tone and consciousness, causing abrupt falls), myoclonic (sudden muscle jerks), and absence (staring spells).

Topiramate is also approved for the prevention of migraine headaches in adults.

DRUG INTERACTIONS: The following medications, when taken with topiramate, increase the risk of kidney stones: acetazolamide (Diamox), dorzolamide (Trusopt), methazolamide (Neptazane), dichlorphenamidine (Daranide).

Carbamazepine (Tegretol) and phenytoin (Dilantin) markedly decrease the amount of topiramate in the body by increasing its elimination from the body. As a result, topiramate may lose effectiveness unless doses are increased.

Topiramate may decrease the amount of estrogen in the body in women taking oral contraceptives, possibly increasing the chances of unwanted pregnancy.
Patients with seizure disorders taking anticonvulsant medications, including topiramate, may develop nerve toxicity from a chemical, 4'-O-methylpyridoxine, found as a contaminant in some ginkgo preparations.

**SIDE EFFECTS:** In adults, the most common side effects of topiramate are tiredness, dizziness, coordination problems, speech problems, changes in vision or double vision, difficulty with memory, and sensory distortion.

In children, the most common side effects are drowsiness, tiredness, loss of appetite, nervousness, difficulty with concentration/attention, weight decrease, aggressive reaction and difficulty with memory.

Since topiramate was approved, there have been 23 cases reported (as of 8-17-01) of a sudden onset of vision and eye problems. Symptoms have typically occurred within the first month of therapy, with patients reporting an acute onset of decreased vision and/or eye pain. Eye examination revealed myopia (nearsightedness), redness, decreased depth of the anterior chamber of the eye and elevated ocular pressure, with or without dilation of the pupils. Fluid accumulation within the eye may displace the lens and iris anteriorly causing secondary angle closure glaucoma. If patients develop this syndrome, the treatment is to discontinue topiramate as rapidly as possible, according to the judgment of the treating physician.

### Stimulant drugs

1. **GENERIC NAME:** amphetamine and dextroamphetamine

**BRAND NAME:** Adderall, Adderall XR

**DRUG CLASS AND MECHANISM:** Amphetamine and dextroamphetamine are used in combination to treat attention-deficit hyperactivity disorder (ADHD) and narcolepsy. Adderall stimulates the brain and also can increase blood pressure. In a recent small study in children with ADHD, the effects of Adderall lasted longer and were preferred over methylphenidate (Ritalin), the most commonly used drug for ADHD. Adderall XR is an extended release form of Adderall. Adderall was approved by the FDA in 1996.

**PRESCRIBED FOR:** Adderall is used for the treatment of attention-deficit hyperactivity disorder (ADHD) and narcolepsy.

**DOSING:** Adderall usually is taken once or twice a day. Adderall XR is taken once daily. The dose is adjusted carefully by the physician to achieve the desired effects.

**DRUG INTERACTIONS:** Adderall should not be taken with monoamine oxidase (MAO) inhibitor drugs including phenelzine (Nardil) and tranylcypromine (Parnate). Patients receiving antihypertensive medications may experience loss of blood pressure control with Adderall.

**SIDE EFFECTS:** Side effects of Adderall include excessive stimulation of the nervous system leading to nervousness, restlessness, excitability, dizziness, headache, fear, anxiety, tremor, and
even hallucinations and convulsions (seizures). Blood pressure and heart rate may increase, and patients may experience palpitations of the heart.

2. GENERIC NAME: methylphenidate

BRAND NAME: Ritalin, Ritalin SR, Ritalin LA

DRUG CLASS AND MECHANISM: Methylphenidate is a medication that stimulates the central nervous system (brain) in a manner that is similar to the amphetamines; however, its actions are milder than those of the amphetamines. An additional difference is that methylphenidate produces more noticeable effects on mental activities than on motor activities. Methylphenidate and amphetamines both have abuse potential. In treating children with attention-deficit hyperactivity disorder (ADHD), methylphenidate produces a calming effect. This results in a reduction in hyperactivity and an improvement in attention span. Methylphenidate was approved by the FDA in 1955.

PRESCRIBED FOR: Methylphenidate is used in the treatment of narcolepsy (uncontrollable sleepiness) and in the treatment of children with ADHD.

DOSSING: The dose of methylphenidate is adjusted based on patients' responses. It may be given once, twice, or three times daily. Ritalin LA is given once daily.

DRUG INTERACTIONS: The CNS stimulation effects of methylphenidate can be additive when used with other chemicals and medications that stimulate the CNS, such as caffeine (in coffee, tea, or cola drinks), and pseudoephedrine or phenylpropanolamine (in many cough-and-cold preparations). The combination of methylphenidate and monoamine oxidase inhibitors, for example, isocarboxazid (Marplan), phenelzine (Nardil), tranylcypromine (Parnate), and procarbazine (Matulane), should be avoided since a hypertensive crisis (severely high blood pressure) may occur. Therefore, methylphenidate should not be given to any patient within 14 days of receiving such an inhibitor. The blood pressure lowering effects of medications used to treat hypertension may be reduced by methylphenidate. As a result, blood pressure needs to be monitored when starting or stopping methylphenidate in patients who are receiving blood pressure medicines.

SIDE EFFECTS: The most common side effects with methylphenidate are nervousness, agitation, anxiety, and insomnia. Insomnia can be limited by taking the drug before noon. For children taking methylphenidate for ADHD, the most common side effects are loss of appetite, abdominal pain, weight loss, and sleep problems. The rate and severity of these side effects are less than that seen with dextroamphetamine (Dexedrine). Other side effects include nausea, vomiting, dizziness, palpitations, headache, involuntary movements, chest pain, increased heart rate, increased blood pressure, and psychosis.

There have been rare reports of Tourette's syndrome, a syndrome in which there are uncontrollable tics such as grimacing. Because of the potential for the side effects listed above, methylphenidate should be used with caution by patients who have relatives with Tourette's syndrome or have the syndrome themselves or who have severe anxiety, seizures, psychosis, emotional instability, major depression, glaucoma, or motor tics. Sudden discontinuation of long-term methylphenidate therapy may unmask depression. Gradual withdrawal, under supervision, is recommended.
Antidepressant drugs

1. GENERIC NAME: citalopram

BRAND NAME: Celexa

DRUG CLASS AND MECHANISM: Citalopram is an antidepressant medication that affects neurotransmitters, the chemical transmitters within the brain. Neurotransmitters manufactured and released by nerves attach to adjacent nerves and alter their activities. Thus, neurotransmitters can be thought of as the communication system of the brain. Many experts believe that an imbalance among neurotransmitters is the cause of depression. Citalopram works by preventing the uptake of one neurotransmitter, serotonin, by nerve cells after it has been released. Such uptake is an important mechanism for removing released neurotransmitters and terminating their actions on adjacent nerves. The reduced uptake caused by citalopram results in more free serotonin in the brain to stimulate nerve cells. Citalopram is in the class of drugs called selective serotonin reuptake inhibitors (SSRIs), a class that also contains fluoxetine (Prozac), paroxetine (Paxil) and sertraline (Zoloft). Citalopram was approved by the FDA in July 1998.

PRESCRIBED FOR: Citalopram is used for the management of depression. It also has been tested in persons with obsessive-compulsive disorders and panic disorders.

DOSEING: Citalopram is given as a single daily dose, usually in the morning. As with all antidepressants, it may take several weeks of treatment before maximum effects are seen. Doses are often adjusted slowly upwards to find the most effective dose. Elderly patients, debilitated persons, and patients with certain kidney or liver diseases may need lower doses.

DRUG INTERACTIONS: All SSRIs, including citalopram, should not be taken with any of the mono-amine oxidase (MAO) inhibitor-class of antidepressants, for example, isocarboxazid (Marplan), phenelzine (Nardil), tranylcypromine (Parnate), and procarbazine (Matulane). Such combinations may lead to confusion, high blood pressure, tremor, and hyperactivity. This same type of interaction also may occur with selegiline (Eldepryl), fenfluramine (Pondimin), and dexfenfluramine (Redux). Tryptophan can cause headaches, nausea, sweating, and dizziness when taken with any SSRI.

SIDE EFFECTS: The most commonly-noted side effects associated with citalopram are nausea, vomiting, excessive sweating, headache, tremor, and inability to sleep. Overall, between 1 in 6 and 1 in 5 persons experience a side effect. Some patients may experience withdrawal reactions upon stopping some SSRIs such as paroxetine, and such symptoms also may occur with citalopram. Symptoms of withdrawal include dizziness, tingling sensations, tiredness, vivid dreams, irritability or poor mood.

It has been suggested that SSRIs may cause depression to worsen and even lead to suicide in a small number of patients. These potential side effects are difficult to evaluate in depressed patients because depression can progress with or without treatment, and suicide is itself a consequence of depression. Moreover, the evidence supporting these potential side effects is weak. Therefore, no conclusions can yet be drawn about the relationship between SSRIs and worsening depression and suicide. Until better information is available, patients receiving SSRIs should be monitored for worsening depression and suicidal tendencies.

2. GENERIC NAME: venlafaxine
BRAND NAME: Effexor, Effexor XR

DRUG CLASS AND MECHANISM: Venlafaxine is in a new class of anti-depressant medications that affects chemical messengers within the brain. These chemical messengers are called neurotransmitters, and some examples are serotonin, dopamine, and norepinephrine. Neurotransmitters are manufactured by nerve cells and are released by the cells. The neurotransmitters travel to nearby nerve cells and cause the cells to become more or less active. Many experts believe that an imbalance in these neurotransmitters is the cause of depression and also may play a role in anxiety. Venlafaxine is believed to work by inhibiting the release or affecting the action of these neurotransmitters. Venlafaxine is available in an extended release formulation (Effexor XR).

PRESCRIBED FOR: Venlafaxine is prescribed for the treatment of depression, depression with associated symptoms of anxiety, generalized anxiety disorder, and social anxiety disorder. Effexor XR is approved for the treatment of adults with panic disorder.

DOSES: Venlafaxine should be taken with food at doses specifically directed by a physician. Individual doses vary greatly among individuals. The anti-depressant effects are not maximal for 1-2 weeks. If discontinued, the dose of venlafaxine should gradually be reduced under the direction of a physician. For patients with difficulty swallowing tablets or capsules, capsules of Effexor XR can be opened and the contents sprinkled on a spoonful of applesauce.

DRUG INTERACTIONS: Life-threatening interactions can occur in combination with MAO inhibitors such as Nardil and Parnate. MAO inhibitors and venlafaxine should not be taken together, and a waiting period of 14 days between taking these two classes of medications is strongly advised.

Most medications affecting the brain such as venlafaxine have the potential to slow reflexes or impair judgment. Therefore, caution is advised especially early in the course of treatment.

Safety has not been established in children below the age of 18 years.

SIDE EFFECTS: Venlafaxine, like most anti-depressants, can cause nausea, headaches, anxiety, insomnia, drowsiness, and loss of appetite. Increased blood pressure can occur, and blood pressure should be monitored. Seizures have been reported. If anti-depressants are discontinued abruptly, symptoms may occur such as dizziness, headache, nausea, changes in mood, or changes in the sense of smell, taste, etc. (Such symptoms even may occur when even a few doses of anti-depressant are missed.) Therefore, it is recommended that the dose of anti-depressant be reduced gradually when therapy is discontinued.

Histamine and Antihistaminic drugs

1. GENERIC NAME: diphenhydramine

BRAND NAME: Benadryl

DRUG CLASS AND MECHANISM: Diphenhydramine is an antihistamine with anticholinergic (drying) and sedative properties that is used to treat allergic reactions. Histamine is released by the body during several types of allergic reactions and--to a lesser extent--during some viral infections, such as the common cold. When histamine binds to its receptors on cells, it causes
changes within the cells that lead to sneezing, itching, and increased mucus production. Antihistamines compete with histamine for cell receptors; however, when they bind to the receptors they do not stimulate the cells. In addition, they prevent histamine from binding and stimulating the cells. Diphenhydramine was originally approved by the FDA in 1946.

**PRESCRIBED FOR:** Diphenhydramine is used for the relief of nasal and non-nasal symptoms of various allergic conditions such as seasonal allergic rhinitis. It is also used to treat patients with chronic urticaria. Although antihistamines are the preferred class of drugs in allergic rhinitis, they only reduce symptoms by 40-60%. Diphenhydramine also is used for allergic reactions involving the eyes (allergic conjunctivitis), to prevent or treat active motion sickness, and for mild cases of Parkinsonism, including drug-induced Parkinsonism. The last two uses (motion sickness and Parkinsonism) are based on the anticholinergic effects of diphenhydramine, and not its antihistamine effects. Diphenhydramine also is used as an aid for insomnia.

**DOSING:** Diphenhydramine has its maximal effect about one hour after it is taken. Its effects last for 4 to 6 hours. Therefore, it is often prescribed to be taken every 4 to 6 hours as needed for relief of allergy-related symptoms. When used to combat insomnia, it is prescribed to be taken at bedtime. Patients over the age of 60 years are especially sensitive to the sedating and anticholinergic effects of diphenhydramine, and the dose should be reduced.

**DRUG INTERACTIONS:** Diphenhydramine adds to (exaggerates) the sedating effects of alcohol and other drugs than can cause sedation such as the benzodiazepine class of anti-anxiety drugs (e.g., Valium, Ativan, Klonopin, Xanax), the narcotic class of pain medications and its derivatives (e.g., Percocet, Vicodin, Dilaudid, Codeine, Darvon), the tricyclic class of antidepressants (e.g., Elavil, Tofranil, Norpramin), and certain antihypertensive medications (e.g., Catapres, Inderal). Diphenhydramine can also intensify the drying effects of other medications with anticholinergic properties (e.g., Bentyl, Urecholine, Probanthine).

**SIDE EFFECTS:** Diphenhydramine can commonly cause sedation, tiredness, sleepiness, dizziness, disturbed coordination, drying and thickening of oral and other respiratory secretions, and stomach distress. Diphenhydramine may also cause low blood pressure, palpitations, increased heart rate, confusion, nervousness, irritability, blurred vision, double vision, tremor, loss or appetite, or nausea. Diphenhydramine should be used with caution (if at all) in persons with narrow-angle glaucoma, prostatic hypertrophy (enlarged prostate gland), hyperthyroidism, cardiovascular disease, hypertension, and asthma.

2. **GENERIC NAME:** fexofenadine

**BRAND NAME:** Allegra

**DRUG CLASS AND MECHANISM:** Fexofenadine is an oral, "second generation" antihistamine that is used to treat the signs and symptoms of allergy that are due to histamine. It is similar to the other second generation antihistamines loratadine (Claritin), cetirizine (Zyrtec) and azelastine (Astelin). Histamine is a chemical that is responsible for many of the signs and symptoms of allergic reactions, for example, swelling of the lining of the nose, sneezing, and itchy eyes. Histamine is released from histamine-storing cells (mast cells) and then attaches to other cells that have receptors for histamine. The attachment of the histamine to the receptors causes the cell to be "activated," releasing other chemicals that produce the effects that we associate with allergy, e.g., sneezing. Fexofenadine blocks one type of receptor for histamine (the H1 receptor) and thus prevents activation of H1 receptor-containing cells by histamine. Unlike the first generation antihistamines, fexofenadine and other second-generation antihistamines do not
readily enter the brain from the blood, and, therefore, they cause less drowsiness. Fexofenadine was approved by the FDA in July, 1995.

**PRESCRIBED FOR:** Fexofenadine is used for the treatment of seasonal allergies and chronic urticaria (hives) in adults and children 6 years of age or older.

**DOSES:** For seasonal allergies the recommended dose for adults and children 12 years or older is 60 mg twice daily or 180 mg once daily. Children 6-11 years of age should be given 30 mg twice daily. For chronic urticaria, adults and children 12 years or older should use 60 mg twice daily, and children 6-11 years of age should use 30 mg twice daily. Fexofenadine can be taken with or without food.

**DRUG INTERACTIONS:** In controlled clinical studies there were no interactions with other drugs that significantly affected the safety or effectiveness of fexofenadine.

**SIDE EFFECTS:** The most common side effects of fexofenadine are nausea, vomiting, weakness and sleepiness.

---

**Emetics and Antiemetics**

*Apomorphine*

**GENERIC NAME:** alprazolam

**BRAND NAME:** Xanax

**DRUG CLASS AND MECHANISM:** Alprazolam is a member of the benzodiazepine family. Benzodiazepines are sedatives that cause dose-related depression of the central nervous system. They are useful in treating anxiety, insomnia, and muscle spasms.

**STORAGE:** Alprazolam should be stored at room temperature in a tightly closed container.

**PRESCRIBED FOR:** Alprazolam is used for the treatment of anxiety disorders and panic attacks. Anxiety disorders are characterized by unrealistic worry and apprehension, causing symptoms of restlessness, aches, trembling, shortness of breath, smothering sensation, palpitations, sweating, cold clammy hands, lightheadedness, flushing, exaggerated startle responses, problems concentrating, and insomnia. Panic attacks occur either unexpectedly or in certain situations (i.e. driving), and can require higher dosages of alprazolam.

**DOSES:** Alprazolam may be taken with or without food. Alprazolam is metabolized by the liver and excreted mainly by the kidney. Dosages of alprazolam may need to be lowered in patients with abnormal kidney function.

**DRUG INTERACTIONS:** Alprazolam should not be taken with ketoconazole or itraconazole. Alcohol should be avoided by patients taking benzodiazepines. Alprazolam can lead to addiction (dependency), especially at high dosages over prolonged periods of time. Because of alprazolam's addictive potential, dosages should never be increased by the patient. In patients addicted to alprazolam, abrupt discontinuation of the medicine can lead to symptoms of withdrawal (insomnia, headaches, nausea, vomiting, light headedness, sweating, anxiety, and fatigue). Seizures can occur in more severe cases of withdrawal. Consequently, patients on
alprazolam for extended periods of time should slowly taper the medication under a doctor's supervision rather than abruptly stopping the medication.

SIDE EFFECTS: The most frequent side effects of alprazolam taken at lower doses are drowsiness or lightheadedness, which probably reflect the action of the drug. Side effects of higher dosages (those used for panic attacks) include fatigue, memory problems, speech problems, constipation, and changes in appetite with resultant changes in weight.

The Pharmacologic Management of Pain

j. Pharmacologic intervention of pain
k. Centrally acting analgesics
l. Clinical correlation
m. Peripherally acting analgesics
n. Non-steroidal anti-inflammatory agents
o. General anesthetics
p. Neuromuscular blocking agents
q. Local anesthetics
r. Alcohol and drugs of abuse

Centrally acting analgesics

1. GENERIC NAME: codeine

BRAND NAMES: Empirin #2, 3, 4; Tylenol #2, 3, 4; Tylenol with Codeine Elixir

DRUG CLASS AND MECHANISM: Codeine is a narcotic pain reliever (analgesic). Its precise mechanism of pain relief is not clearly understood. Codeine is frequently combined with Tylenol or aspirin for more effective pain relief. Please visit acetaminophen (Tylenol) and Aspirin sites for further information.

PRESCRIBED FOR: Codeine is used for the relief of mild to moderately severe pain.

DOSING: May be taken with food.
DRUG INTERACTIONS: EMPIRIN contains aspirin and is, therefore, not used in patients with a history of aspirin allergy. Children or teenagers with symptoms of chicken pox or influenza should avoid aspirin because of the association of aspirin with Reye's syndrome, a serious liver and neurologic condition. For more information regarding precautions in the use of aspirin and related medications, please visit Aspirin site. Tylenol with Codeine tablets contain a sulfite that can cause allergic asthma and even life-threatening anaphylaxis reactions in susceptible patients (more frequently seen in asthmatic patients).

Codeine can impair thinking and the physical abilities required for driving or operating machinery. Alcohol and other sedatives, such as Xanax, can produce further brain impairment and even confusion when combined with codeine. Therefore, alcohol and other sedative intake should be limited when taking codeine. Codeine is generally avoided in children. Codeine may be habit forming. Mental and physical dependence can occur, but are unlikely when used for short-term pain relief.

SIDE EFFECTS: The most frequent side effects include lightheadedness, dizziness, nausea, vomiting, shortness of breath, and sedation. Other side effects include allergic reactions, constipation, abdominal pain, and itching.

2. GENERIC NAME: propoxyphene and acetaminophen

BRAND NAMES: Darvocet; Darvocet A500; Wygesic

DRUG CLASS AND MECHANISM: Propoxyphene is a medication for treating pain. It is an opioid analgesic (related to opium) chemically similar to methadone. The use of opium is at least 2300 years old. In 1806, the first alkaloid of opium was isolated by Serturner. He called it morphine, after the Greek god of dreams, Morpheus. Codeine, another opioid analgesic was identified in 1832. Propoxyphene is half to two-thirds as potent as codeine, meaning that 90 to 120mg of propoxyphene provides as much pain relief as 60mg of codeine. This is comparable to the pain relief achieved by 600mg of aspirin. Opioid analgesics, including propoxyphene, reduce pain by blocking the receptors in the brain that are involved in the perception (sensing) of pain.

Acetaminophen is a non-narcotic analgesic (pain reliever) and antipyretic (fever reducer). Acetaminophen relieves pain by elevating the threshold for pain. It reduces fever through its action on the heat-regulating center of the brain. The combination of propoxyphene and acetaminophen achieves greater pain relief than either drug taken alone. For more information please see acetaminophen.

PRESCRIBED FOR: Propoxyphene and acetaminophen is used for the treatment of mild to moderate pain.

DOISING: Propoxyphene and acetaminophen usually are given every 4 hours as needed for the relief of pain.

DRUG INTERACTIONS: Opioids such as propoxyphene can reduce the activity of intestinal muscles. When combined with medications that possess anticholinergic activity, this effect on intestinal muscles may be accentuated leading to constipation. Such drugs include dicyclomine (Bentyl), some antihistamines [carboxamine (Rondec), cлемastine (Tavist), diphenhydramine (Benadryl), promethazine (Phenergan)], some phenothiazines [e.g. thioridazine (Mellaril), triflupromazine (Stelazine)], some tricyclic antidepressants [e.g. amitriptyline (Elavil), amoxapine (Asendin), clomipramine (Anafranil), protriptyline (Vivactil)], clozapine (Clozaril), cyclobenzaprine (Flexeril), and disopyramide (Norpace).
Propoxyphene adds to the sedating effects of alcohol and other drugs that can cause sedation such as the benzodiazepine class of anti-anxiety drugs (e.g., Valium, Ativan, Klonopin, Xanax), the tricyclic class of antidepressants (e.g., Elavil, Tofranil, Norpramin), dicyclomine (Bentyl), certain antihistamines (Benadryl, Vistaril, Atarax, Tavist), and certain antihypertensive medications (e.g., Catapres, Inderal).

**SIDE EFFECTS:** The most frequent adverse reactions of propoxyphene include lightheadedness, dizziness, sedation, nausea, and vomiting. Other side effects include drowsiness, constipation, and spasm of the ureter, which can lead to difficulty in urinating.

Propoxyphene can depress breathing and, therefore, is used with caution in elderly, debilitated patients and in patients with serious lung disease. Propoxyphene can impair thinking and the physical abilities required for driving or operating machinery. Propoxyphene may be habit forming. Mental and physical dependence can occur but are unlikely when it is used short-term.

**Peripherally acting analgesics**

**1. GENERIC NAME:** acetaminophen

**BRAND NAME:** Tylenol and many other

**DRUG CLASS AND MECHANISM:** Acetaminophen belongs to a class of drugs called analgesics (pain relievers) and antipyretics (fever reducers). The exact mechanism of action of acetaminophen is not known. Acetaminophen relieves pain by elevating the pain threshold, that is, by requiring a greater amount of pain to develop before it is felt by a person. It reduces fever through its action on the heat-regulating center of the brain. Specifically, it tells the center to lower the body's temperature when the temperature is elevated. Acetaminophen was approved by the FDA in 1951.

**PRESCRIBED FOR:** Acetaminophen is used for the relief of fever as well as aches and pains associated with many conditions. Acetaminophen relieves pain in mild arthritis but has no effect on the underlying inflammation, redness and swelling of the joint. If the pain is not due to inflammation, acetaminophen is as effective as aspirin. It is as effective as the non-steroidal anti-inflammatory drug ibuprofen (Motrin) in relieving the pain of osteoarthritis of the knee.

**DOsing:** The oral dose for adults is 325 to 650 mg every 4-6 hours. The maximum daily dose is 4 grams. The oral dose for a child is based on the child's age, and the range is 40-650 mg every 4 hours.

When administered as a suppository, the adult dose is 650 mg every 4-6 hours. For children, the dose is 80-325 mg every 4-6 hours depending on age.

**DRUG INTERACTIONS:** Acetaminophen is metabolized (eliminated by conversion to other chemicals) by the liver. Therefore drugs that increase the action of liver enzymes that metabolize acetaminophen (e.g. carbamazepine, isoniazid, rifampin) may decrease the action of acetaminophen. The potential for acetaminophen to harm the liver is increased when it is combined with alcohol or drugs that also harm the liver.
SIDE EFFECTS: When used appropriately, side effects are rare. The most serious side effect is liver damage due to large doses, chronic use or concomitant use with alcohol or other drugs that also damage the liver.

2. GENERIC NAME: naproxen

BRAND NAME: Anaprox, Naprelan, Naprosyn, Aleve

DRUG CLASS AND MECHANISM: Naproxen belongs to a class of drugs called non-steroidal anti-inflammatory drugs (NSAIDs). Other members of this class include ibuprofen (Motrin), indomethacin (Indocin), nabumetone (Relafen) and several others. These drugs are used for the management of mild to moderate pain, fever, and inflammation. They work by reducing the levels of prostaglandins, chemicals that are responsible for pain, fever and inflammation. Naproxen blocks the enzyme that makes prostaglandins (cyclooxygenase ), resulting in lower concentrations of prostaglandins. As a consequence, inflammation, pain and fever are reduced. Naproxen was approved by the FDA in December, 1991.

PRESCRIBED FOR: Naproxen is used for the treatment of mild to moderate pain, inflammation and fever.

DOISING: The usual adult dose is 250-500 mg twice daily using regular naproxen tablets. The usual dose for Naprelan controlled release tablets is 750 to 1000 mg given once daily. For EC-Naprosyn, the usual dose is 375-500 mg twice daily. Naproxen should be given with food to reduce upset stomach.

DRUG INTERACTIONS: Naproxen is associated with several suspected or probable interactions that affect the action of other drugs. The following examples are the most common suspected interactions.

Naproxen may increase the blood levels of lithium (Eskalith) by reducing the excretion of lithium by the kidneys. Increased levels of lithium may lead to lithium toxicity.

Naproxen may reduce the blood pressure lowering effects of blood pressure medications. This may occur because prostaglandins play a role in the regulation of blood pressure.

When naproxen is used in combination with aminoglycosides (e.g., gentamicin) the blood levels of the aminoglycoside may increase, presumably because the elimination of aminoglycosides from the body is reduced. This may lead to more aminoglycoside-related side effects.

Individuals taking oral blood thinners or anticoagulants (e.g., warfarin) should avoid naproxen because naproxen also thins the blood, and excessive blood thinning may lead to bleeding.

SIDE EFFECTS: The most common side effects from naproxen are rash, ringing in the ears, headaches, dizziness, drowsiness, abdominal pain, nausea, diarrhea, constipation, heartburn, fluid retention and shortness of breath. Naproxen also may cause stomach and intestinal bleeding and ulcers. Sometimes, stomach ulceration and intestinal bleeding can occur without any abdominal pain. Black tarry stools, weakness, and dizziness upon standing may be the only signs of the bleeding. People who are allergic to other NSAIDs should not use naproxen.
Non-steroidal anti-inflammatory agents

1. GENERIC NAME: tolmetin

BRAND NAME: Tolectin

DRUG CLASS AND MECHANISM: Tolmetin is a nonsteroidal anti-inflammatory drug (NSAID) effective in treating fever, pain, and inflammation in the body. As a group, NSAIDs are non-narcotic relievers of mild to moderate pain of many causes, including injury, menstrual cramps, arthritis, and other musculoskeletal conditions. Since the response to different NSAIDs varies from patient to patient, it is not unusual for a doctor to try different NSAIDs for any given condition.

PRESCRIBED FOR: Tolmetin is used for the treatment of inflammation and pain that results from rheumatoid arthritis, juvenile arthritis, and osteoarthritis.

DOISING: Should be taken with food.

DRUG INTERACTIONS: Tolmetin should be avoided by patients with a history of asthma exacerbation, hives, or other allergic reactions to aspirin or other NSAIDs. Rare but severe allergic reactions have been reported in such individuals. It also should be avoided by patients with peptic ulcer disease or poor kidney function, since this medication can aggravate both conditions. Tolmetin is generally used with caution in patients taking blood thinning medications (anticoagulants), such as warfarin (Coumadin), because of an increased risk of bleeding. Patients taking lithium can develop toxic blood lithium levels. Patients taking cyclosporine (Sandimmune) can develop kidney toxicity.

Use in children under 2 years of age has not been adequately studied. Tolmetin is not habit forming. Tolmetin should be discontinued prior to elective surgery because of a mild interference with clotting that is characteristic of this group of medicines. Tolmetin is best discontinued at least two days in advance of the procedure.

Persons who have more than 3 alcoholic beverages per day are at increased risk of developing stomach ulcers when taking tolmetin or other NSAIDs.

SIDE EFFECTS: Most patients benefit from tolmetin and other NSAIDs with few side effects. However, serious side effects can occur, and generally tend to be dose related. Therefore, it is advisable to use the lowest effective dose to minimize side effects. The most common side effects of tolmetin involve the gastrointestinal system. It can cause ulcerations, abdominal pain, cramping, nausea, gastritis, and even serious gastrointestinal bleeding and liver toxicity. Sometimes, stomach ulceration and bleeding can occur without any abdominal pain. Black tarry stools, weakness, and dizziness upon standing may be the only signs of internal bleeding. Rash, kidney impairment, ringing in the ears, and lightheadedness can also occur.

2. GENERIC NAME: aspirin

BRAND NAMES: Aspirin, Arthritis Foundation Safety Coated Aspirin, Bayer Aspirin, Bayer Children's Aspirin, Ecotrin, and many others.

DRUG CLASS AND MECHANISM: Aspirin is a nonsteroidal anti-inflammatory drug (NSAID) effective in treating fever, pain, and inflammation in the body. As a group, NSAIDs are non-narcotic relievers of mild to moderate pain of many causes, including injury, menstrual cramps,
arthritis, and other musculoskeletal conditions. Since the response to different NSAIDs varies from patient to patient, it is not unusual for a doctor to try different NSAIDs for any given condition.

PREScribed FOR: Aspirin is used for the treatment of inflammation and pain that results from many forms of arthritis, including rheumatoid arthritis, juvenile arthritis, systemic lupus erythematosus, ankylosing spondylitis, Reiter's syndrome, and osteoarthritis, as well as soft tissue injuries, such as tendinitis and bursitis. Aspirin is also used for rapid relief of mild to moderate pain and fever. Because aspirin inhibits the action of blood clotting element (platelets), it is used to reduce the risk of recurrent stroke and near-stroke (transient ischemic attack). It is similarly used to prevent heart attack.

DOsing: Should be taken with food.

Drug interactions: Aspirin should be avoided by patients with peptic ulcer disease or poor kidney function, since this medication can aggravate both conditions. Aspirin is avoided in patients taking blood thinning medications (anticoagulants) such as warfarin (Coumadin), because of an increased risk of bleeding. Some asthma patients can have worsening of breathing while taking aspirin. Aspirin can alter the blood uric acid level and is avoided in patients with hyperuricemia and gout. Children and teenagers should avoid aspirin for flu or chickenpox symptoms because of the associated risk of Reye's Syndrome, a serious disease of the liver and nervous system that can lead to coma. Aspirin is not habit forming. Aspirin can increase the effect of medicines used to treat diabetes mellitus, resulting in abnormally low blood sugars if not monitored. NSAIDs should be discontinued prior to elective surgery because of a mild tendency to interfere with blood clotting. Aspirin is best discontinued at least ten to fourteen days in advance of the procedure.

side effects: Most patients benefit from aspirin and other NSAIDs with few side effects. However, serious side effects can occur and generally tend to be dose related. Therefore, it is advisable to use the lowest effective dose to minimize side effects. The most common side effects of aspirin involve the gastrointestinal system and ringing in the ears. It can cause ulcerations, abdominal burning, pain, cramping, nausea, gastritis, and even serious gastrointestinal bleeding and liver toxicity. Sometimes, stomach ulceration and bleeding can occur without any abdominal pain. Black tarry stools, weakness, and dizziness upon standing may be the only signs of internal bleeding. Should ringing in the ears occur, the daily dose should be reduced. Rash, kidney impairment, vertigo, and lightheadedness can also occur.

General anesthetics

1. GENERIC NAME: fentanyl transdermal system

BRAND NAME: Duragesic

Drug class and mechanism: Fentanyl is a potent synthetic (man-made) narcotic. A 100 μg dose of fentanyl is approximately equal to 10 mg of morphine. Fentanyl stimulates receptors on nerves in the brain to increase the threshold to pain (the amount of discomfort that a person must feel in order to be considered painful) and reduce the perception of pain (the perceived importance of the pain). Fentanyl is available in transdermal (for application to the skin), transmucosal (for application to mucus membranes) and parenteral (injectable) forms. When
applied to the skin of the upper torso, fentanyl is well absorbed. The amount of fentanyl in the blood increases gradually after topical application, reaching a peak after 12-24 hours. Once this concentration is achieved, blood concentrations remain constant over the 72 hours that the patch is worn. After removal of the patch, blood concentrations of fentanyl decrease slowly due to ongoing absorption of fentanyl remaining on the skin. Fentanyl was originally approved by the FDA for injection in 1968.

**PRESCRIBED FOR:** Fentanyl transdermal system is used for patients with severe chronic pain, for example, the pain of cancer.

**DOsing:** Patches should be applied to a flat, nonirritated area on the upper torso. The area of application should be clean and washed with water only prior to application. The patch should be applied immediately after removing it from the package and pressed firmly against the skin for 10 to 20 seconds especially around the edges. Patches should never be cut or otherwise damaged. Doses vary widely among patients. The manufacturer considers a fentanyl transdermal dose of 100 $\mu$g/hour approximately equivalent to 360 mg/day of oral morphine.

**DRUG INTERACTIONS:** The use of fentanyl with other central nervous system (CNS) depressants can intensify the effects of fentanyl to depress breathing, depress the brain, sedate, and lower blood pressure. Other drugs that should be used cautiously with fentanyl include: antipsychotics (e.g. Thorazine; Stelazine; Haldol), anxiolytics (e.g. Valium; Ativan; Ambien), certain antihistamines (e.g. Benadryl; Vistaril; Tavist, barbiturates (e.g. phenobarbital, tricyclic antidepressants (e.g. Elavil; Sinequan), ethanol, and skeletal muscle relaxants (e.g. Soma; Flexeril; Lioresal). The use fentanyl with amiodarone (Cordarone) may result in slow heart rates. Cimetidine (Tagamet) when used with fentanyl can cause confusion, disorientation, or seizures due to impairment in breathing and brain function.

**SIDE EFFECTS:** Mild physical dependence occurs commonly during therapy with opiate agonists such as fentanyl. Abruptly stopping the drug in patients can precipitate a withdrawal reaction. Symptoms of withdrawal include nausea, diarrhea, coughing, tearing, nasal discharge, profuse sweating, twitching muscles, and yawning.

Fentanyl can cause respiratory depression (decreased rate or depth of breathing). Nausea or vomiting, constipation, and itching can occur during treatment with fentanyl. Transdermal fentanyl can cause a variety of skin reactions. Commonly, redness occurs at the site of application and can last for 6 hours following removal of the patch.

Other side effects include a decrease in sexual drive, hypothyroidism (low thyroid hormone concentrations), dry mouth, abdominal pain, loss of appetite, drowsiness, confusion, headache, dizziness, nervousness, hallucinations, anxiety, depression and euphoria. The FDA is investigating reports of deaths and other serious side effects from the use of the fentanyl transdermal system as well as overdoses.

2. **GENERIC NAME:** diazepam

**BRAND NAME:** Valium

**DRUG CLASS:** Diazepam is a member of the benzodiazepine family. Benzodiazepines are sedatives that cause dose-related depression of the central nervous system. They are useful in treating anxiety, insomnia, seizures, and muscle spasms.
PRESCRIBED FOR: Diazepam is used for the short-term relief of symptoms related to anxiety disorders. Diazepam is also used for the treatment of agitation, tremors, delirium, seizures, and hallucinations as a result of alcohol withdrawal. Diazepam is also used for relief of muscle spasms in certain neurological diseases. Diazepam is used to abort active seizures and can be combined with other drugs in treating severe recurrent seizures.

DOsing: Diazepam may be taken with or without food. Diazepam is metabolized by the liver and excreted mainly by the kidney. Dosages of diazepam may need to be lowered in patients with abnormal kidney function.

DRUG INTERACTIONS: Alcohol should be avoided by patients taking benzodiazepines. Diazepam can lead to addiction (dependency), especially at higher dosages over prolonged periods of time. Because of diazepam's addicting potential, dosages should never be increased by the patient. In patients addicted to diazepam, abrupt discontinuation of the medicine can lead to symptoms of withdrawal (insomnia, headaches, nausea, vomiting, lightheadedness, sweating, anxiety, and fatigue). Seizures can occur in more severe cases of withdrawal. Consequently, patients on diazepam for extended periods of time should slowly taper the medication under a doctor's supervision rather than abruptly stopping the medication. Tagamet can prolong the effects of diazepam and dosages may need to be decreased when these drugs are used together.

SIDE EFFECTS: The most frequent side effects of diazepam are drowsiness, fatigue, and ataxia (loss of balance). Rarely, diazepam causes a paradoxical reaction with excitability, muscle spasm, lack of sleep, and rage. Confusion, depression, speech problems, and double vision are also rare side effects of diazepam.

Neuromuscular blocking agents

Atracurium
Doxacurium
Vecuronium
Tubocurarine

Local anesthetics

1. GENERIC NAME: LIDOCAINE SOLUTION - MUCOUS MEMBRANE

USES: This medication is used to relieve pain and discomfort of certain mouth, nose, and throat problems. It is a topical anesthetic (amide-type) that numbs the mucous membranes (skin) of the mouth, nose, and throat.

SIDE EFFECTS: Minor stinging, burning and tenderness of the mouth, nose, and throat may occur when this drug is applied to these areas. Dizziness, drowsiness, lightheadedness, vomiting, or sensations of heat, cold, or numbness may also occur. Mental/mood changes, ringing in the ears, vision changes, slow or fast heartbeat, rapid breathing, fever, seizures. A serious allergic reaction to this drug is unlikely. Symptoms of a serious allergic reaction include: rash, itching, swelling, severe dizziness, trouble breathing.
DRUG INTERACTIONS: This drug should not be used with the following medications because very serious interactions may occur: arbutamine, dofetilide, halofantrine, pimozide, amprenavir, beta-blockers (e.g., propranolol, metoprolol), cimetidine, succinylcholine.

2. GENERIC NAME: TETRACAINE OPHTHALMIC DROPS

BRAND NAME(S): AK-T-Caine PF, Pontocaine

USES: This medication is used in the eye as an anesthetic to numb the pain that may occur during eye procedures.

SIDE EFFECTS: This medication is generally very well tolerated. Stinging, tearing, swelling and sensitivity to light occur rarely. Blurred vision or pupil dilation are also unlikely, but possible. Prolonged use of this medication may cause eye problems (corneal erosions), including slow eye (corneal) healing. Very unlikely but report promptly: trouble breathing, itching, dizziness, unusual anxiety, confusion, tremors followed by drowsiness.

Principles and Mechanisms of Anti-Infective and Antineoplastic Agents

p. Introduction to Chemotherapy
q. Treatment of urinary tract infections
r. Sulfonamides
s. Penicillin
t. Cephalosporin
u. Penicillin Substitutes
v. Broad Spectrum Anti-biotics
Sulfonamides

1. GENERIC NAME: sulfasalazine

BRAND NAME: Azulfidine

DRUG CLASS AND MECHANISM: Sulfasalazine is a prodrug, that is, it is not active in its ingested form. It is broken down by bacteria in the colon into two products: 5-aminosalicylic acid (5ASA), and sulfapyridine. There is some controversy as to which of these two products are responsible for the activity of azulfidine. Whereas it is known that 5ASA has therapeutic benefit, it is not clear whether sulfapyridine adds any further benefit. In the colon, the products created by the breakdown of sulfasalazine work as anti-inflammatory agents for treating inflammation of the colon. The beneficial effect of sulfasalazine is believed to be due to a local effect on the bowel, although there may also be a beneficial systemic immune-suppressant effect as well. Following oral administration, 33% of the sulfasalazine is absorbed, all of the sulfapyridine is absorbed, and about 33% of the 5ASA is absorbed. Sulfasalazine was approved by the FDA in 1950.

PRESCRIBED FOR: Sulfasalazine is used for the treatment of mild to moderate ulcerative colitis; as adjunctive therapy (i.e. with other medications) in the treatment of severe ulcerative colitis; for the treatment of Crohn's disease; for the treatment of rheumatoid arthritis or ankylosing spondylitis.

DOSING: Doses range from 500mg to 2000mg, and dosing intervals range from every 6 hours to every 12 hours, depending on the clinical condition of the patient. Higher doses have also been used. Sulfasalazine should be taken with a full glass of water after meals or with food to minimize stomach upset. Patients with kidney diseases may need to use lower doses of sulfasalazine.

DRUG INTERACTIONS: Sulfasalazine may cause reduced absorption of folic acid and of digoxin.

SIDE EFFECTS: Gastrointestinal disturbances frequently occur in patients taking sulfasalazine. Nausea, vomiting, gastric distress, and anorexia (loss of appetite) occur in about 1 of every 3 patients receiving the drug. Dizziness can occur during sulfasalazine therapy but does not require
medical attention unless it is persistent. Sulfasalazine frequently causes the skin or the urine to change color. Development of an orange-yellow coloration is of no cause for concern.

Several potentially dangerous side effects have been rarely reported with sulfasalazine. A drop in white blood cell count or a type of anemia in which red blood cells are disrupted (hemolyzed) occur more frequently in patients with arthritis who are treated with sulfasalazine (about 6 per 1,000) than in patients with ulcerative colitis or Crohn's disease who are treated with sulfasalazine (about 6 per 10,000). These effects are characterized by fever, pale skin, sore throat, fatigue, and unusual bleeding and bruising, and require discontinuation of the drug.

Continuing headache, allergic reactions, and photosensitivity may develop during sulfasalazine therapy and require medical attention. Some of the allergic reactions may progress from a rash to difficulty in swallowing, blistering, peeling, or loosening of the skin, aching joints and muscles, and unusual tiredness or weakness. It may be accompanied by fever. The more severe allergic reactions are rare.

2. GENERIC NAME: sulfamethoxazole

BRAND NAME: Gantanol

DRUG CLASS AND MECHANISM: Sulfamethoxazole is an anti- bacterial sulfonamide. It prevents the formation of dihydrofolic acid, a compound that bacteria must be able to make in order to survive. Although it was once a very useful antibiotic, it is almost obsolete as a single agent today due to the development of bacterial resistance to its effects. Sulfamethoxazole is now used primarily in combination with trimethoprim, a combination product known as Bactrim or Septra. Sulfamethoxazole was approved by the FDA in 1961.

PRESCRIBED FOR: Sulfamethoxazole is used for the treatment of malaria (in combination with quinine sulfate and pyrimethamine), conjunctivitis (inflammation of the conjunctiva of the eye) due to chlamydia, toxoplasmosis (in combination with pyrimethamine), and urinary tract infections (UTI).

DOISNG: Sulfamethoxazole usually is taken two or three times daily, with or without meals. It should be taken with 6 to 8 ounces of liquid to prevent crystals from forming in the urine. Persons with advanced kidney diseases may require lower doses.

DRUG INTERACTIONS: Sulfamethoxazole can enhance the blood-thinning effects of warfarin (Coumadin), possibly leading to bleeding. Sulfonamides such as sulfamethoxazole can increase the metabolism (break-down and elimination) of cyclosporine (causing loss of effectiveness of cyclosporine), and can add to the kidney damage caused by cyclosporine. All sulfonamides can crystallize in urine when the urine is acidic. Since methenamine causes an acidic urine, it should not be used with sulfonamides.

SIDE EFFECTS: Sulfamethoxazole may cause dizziness, headache, lethargy, diarrhea, anorexia, nausea, vomiting, and rash. Sulfamethoxazole should be stopped at the first appearance of a skin rash since the rash may become severe. Serious rashes include Stevens-Johnson syndrome (aching joints and muscles; redness, blistering, and peeling of the skin); toxic epidermal necrolysis (difficulty in swallowing; peeling, redness, loosening, and blistering of the skin). Sulfamethoxazole therapy also can cause extensive sunburn, following exposure to sunlight. Patients receiving sulfamethoxazole should avoid excessive exposure to sunlight and should wear sunscreen.

Other rare side effects include liver damage, low white blood cell count, low platelet count, and anemia.
Sulfamethoxazole may form crystals in the urine which may damage the kidney and cause bleeding into the urine. It is important to drink additional liquids during sulfonamide therapy to prevent these side effects.

**Penicillin**

**GENERIC NAME:** penicillin V (phenoxymethyl penicillin)

**BRAND NAMES:** Pen-Vee-K; Veetids

**DRUG CLASS AND MECHANISM:** In 1928, Alexander Fleming noted that mold belonging to the genus *Penicillium*, inhibited the growth of bacteria. Fleming called this unknown antibacterial substance penicillin. Ten years later, a group at Oxford University began to investigate the material in laboratory mice. Penicillin was hailed as a miracle drug and saved countless lives in World War II. Today, many derivatives of penicillin have been developed which inhibit more types of bacteria than this original, life-saving drug. Penicillin itself is active against Streptococci (including *Streptococcus pneumoniae*), *Listeria*, *Neisseria gonorrhoeae*, *Clostridium*, *Peptococcus*, and *Peptostreptococcus*. Most staphylococci now are resistant to penicillin.

**PRESCRIBED FOR:** Oral penicillin V is effective against susceptible bacteria causing throat infections, laryngitis, bronchitis, and pneumonia. Only mild to moderate infections are treated with oral penicillin. Patients with more severe infections can be given penicillin by injection (intramuscular "shots" or intravenously). Penicillin also is given to prevent infection on the valves of the heart in patients with certain diseases of the heart valves who are having dental work or undergoing gastrointestinal endoscopic procedures. (Dental work and some endoscopic procedures can introduce bacteria into the blood, and these bacteria may infect the valves.)

**DOSING:** Penicillin V is ideally given 30 to 60 minutes before meals, but can be given with meals to persons who develop nausea or stomach pain with it. On the other hand, penicillin G (a type of penicillin which is rarely used today) must be given on an empty stomach. Penicillin is most often given four times a day for 7 to 14 days. When given to prevent infections in persons undergoing dental or gastrointestinal procedures, penicillin is given as one dose one hour prior to the procedure, and one more dose is given 6 hours later.

**DRUG INTERACTIONS:** Probenecid (Benemid) causes an increase in the level of penicillin in the blood by reducing the elimination of penicillin by the kidneys. In fact, sometimes probenecid is combined with penicillin so that a smaller amount of penicillin results in higher blood levels.

**SIDE EFFECTS:** Penicillin generally is well tolerated. Between 1% and 10% of all people are allergic to penicillin. Allergic reactions range from a mild rash to moderate-to-severe hives to severe anaphylactic shock. (In anaphylactic shock, the windpipe swells so that breathing is difficult and the blood pressure falls greatly. Anaphylactic shock is a life-threatening emergency that requires immediate treatment.) Anaphylactic shock occurs in approximately 1 in 3,000 persons who are exposed to penicillin; death occurs in approximately 1 in 50,000 persons who are exposed to penicillin. Persons who are allergic to other penicillin products (such as ampicillin or amoxicillin) are generally considered to be allergic to penicillin as well. Persons who are allergic to the cephalosporin class of antibiotics (e.g., Ceclor, Keflex, Cefzil) may or may not be allergic to penicillins.
Cephalosporin

1. GENERIC NAME: cephalexin

BRAND NAME: Keflex, Keftabs, Biocef

DRUG CLASS AND MECHANISM: Cephalexin belongs to a class of antibiotics called cephalosporins. They are similar to penicillin in action and side effects. They stop or slow the growth of bacterial cells by preventing bacteria from forming the cell wall that surrounds each cell. The cell wall protects bacteria from the external environment and keeps the contents of the cell together. Without a cell wall bacteria are not able to survive. Bacteria that are susceptible to cephalexin include Staphylococcus aureus, Streptococcus pneumoniae, Haemophilus influenzae, E. coli and several others.

PRESCRIBED FOR: Cephalexin is used to treat infections caused by bacteria that are susceptible to the effects of cephalexin. Common infections that are treated with cephalexin include infections of the middle ear, tonsils, throat, larynx (laryngitis), bronchi (bronchitis) and pneumonia. It also is used for treating urinary tract, skin and bone infections.

DOsing: The dose of cephalexin for adults is 1 to 4 grams in divided doses. Children are treated with 25-100 mg/kg/day in divided doses.

DRUG INTERACTIONS: Serious interactions of cephalexin with other drugs are uncommon.

SIDE EFFECTS: The most common side effects of cephalexin are diarrhea, nausea, abdominal pain, vomiting, headaches, dizziness, skin rash, fever, abnormal liver tests and vaginitis. Individuals who are allergic to penicillin may also be allergic to cephalexin.

2. GENERIC NAME: cefprozil

BRAND NAME: Cefzil

DRUG CLASS AND MECHANISM: Cefprozil is a semi-synthetic oral antibiotic of the cephalosporin family. The cephalosporin family includes cephalexin (Keflex), cefaclor (Cector), cefuroxime (Zinacef), cefpodoxime (Vantin), cefixime (Suprax), and many injectable antibiotics. Cefprozil is active against a very wide spectrum of bacteria, including: Staphylococcus. aureus, Streptococcus. pneumoniae, Streptococcus pyogenes (the cause of strep throat), Hemophilus influenzae, Moraxella catarrhalis, E. coli, Klebsiella, Proteus mirabilis, Salmonella, Shigella, Clostridium perfringens and difficile, and Neisseria gonorrhoeae. Therapeutic uses of cefprozil include otitis media, soft-tissue infections, and respiratory tract infections.

PRESCRIBED FOR: Cefprozil is effective against susceptible bacteria causing infections of the middle ear, tonsillitis, throat infections, laryngitis, bronchitis, pneumonia, and skin and soft tissue infections.

DOsing: Cefprozil is taken once or twice daily, depending on the nature and severity of the infection. The tablets can be taken with or without food. The suspension has not been studied
with food, and should therefore be taken one hour before meals. Patients with advanced renal diseases may need lower doses.

**DRUG INTERACTIONS:** There are no known clinically important drug interactions with cefprozil.

**SIDE EFFECTS:** Cefprozil is generally well tolerated. The most common side effects are diarrhea or loose stools, nausea, abdominal pain, and vomiting, each of which may occur in fewer than one in thirty persons who receive azithromycin. Rarer side effects include abnormal liver tests and allergic reactions. Persons with phenylketonuria should be advised that the suspension contains phenylalanine 28mL per teaspoonful. Physicians should be reminded of this fact. Cefprozil may cause false test results with some urine sugar tests.

---

**Penicillin Substitutes**

1. **GENERIC NAME:** erythromycin

**BRAND NAMES:** E-Mycin, Eryc, Ery-Tab, PCE, Pedialyte, Ilosone

**DRUG CLASS AND MECHANISM:** Most infections are caused by bacteria that invade and grow in the human body. Medications that control or eradicate these bacteria are called antibiotics. Erythromycin is an antibiotic that prevents bacteria from producing proteins, which interferes with bacterial growth and multiplication, while not affecting human cells.

**PRESCRIBED FOR:** Erythromycin can be used to treat Streptococcal infections of the throat (strep throat) and the skin. It can also be used in treating lung infections (pneumonias) caused by streptococcal pneumoniae, mycoplasma pneumoniae, and legionella pneumophila (Legionnaires disease). Erythromycin is used in patients who are allergic to penicillin for the prevention of recurrent rheumatic fever, and heart valve infections (endocarditis) in patients with heart valve abnormalities before undergoing dental treatments. For further information, please read the Mitral Valve Prolapse, and Aortic Stenosis articles. Erythromycin is also used for the treatment of staphylococcal infections of the skin, and as an alternative drug for syphilis, gonorrhea, and Chlamydia.

**DOSING:** Erythromycin may be taken with or without food. Erythromycin is metabolized mainly by the liver and caution should be used in patients with abnormal liver function.

**DRUG INTERACTIONS:** Erythromycin administered together with theophylline can lead to elevated blood levels of theophylline. Theophylline is used to open airways in the treatment of asthma. For further reading, please read the Asthma article. Toxic levels of theophylline can lead to seizures and disturbances in heart rhythm. Therefore, the dose of theophylline should be reduced in patients also taking erythromycin. Likewise, erythromycin can raise the blood levels of digoxin and warfarin (Coumadin). Elevated digoxin levels can cause disturbances in heart rhythm. Enhanced action of Coumadin (an anticoagulant) can increase risk of bleeding. Serious heart rhythm disturbances (even cardiac arrest) have been observed when erythromycin and terfenadine (Seldane) are used together. Erythromycin can interact with lovastatin (Mevacor) to cause muscle inflammation. Erythromycin can also elevate blood levels of certain anti-seizure medications such as phenytoin (Dilantin), and carbamazepine (Tegretol). The doses of these medications may need to be reduced when given together with erythromycin.
**SIDE EFFECTS:** The most frequent side effects of erythromycin are nausea, vomiting, loss of appetite, diarrhea, and abdominal pain. These gastrointestinal side effects are usually dose related (side effects are more pronounced with higher doses of the medication). Allergic reactions such as hives, rash, or anaphylaxis (a severe allergic reaction which can lead to shock) have been rarely reported. Abnormal liver tests or liver dysfunction can also occur with erythromycin.

1. **GENERIC NAME:** amoxicillin and clavulanic acid

**BRAND NAME:** Augmentin, Augmentin XR

**DRUG CLASS:** Amoxicillin is an antibiotic of the penicillin type. It is effective against different bacteria such as H. influenzae, N. gonorrhea, E. coli, Pneumococci, Streptococci, and certain strains of Staphylococci. Chemically, it is closely related to penicillin and ampicillin. Addition of clavulanic acid to amoxicillin in Augmentin enhances the effectiveness of this antibiotic against many other bacteria that are ordinarily resistant to amoxicillin.

**PRESCRIBED FOR:** Augmentin is effective against susceptible bacteria causing infections of the middle ear, tonsillitis, throat infections, laryngitis, bronchitis, sinusitis, and pneumonia. It is also used in treating urinary tract infections, skin infections, and gonorrhea.

**DOSING:** Augmentin should be taken on a full stomach. No more than one tablet should be taken at a time since the extra clavulanic acid can cause stomach upset.

**DRUG INTERACTIONS:** Augmentin should be avoided by patients with an allergy to penicillin and other related antibiotics. Serious and occasionally fatal allergic reactions (anaphylaxis) have been reported in sensitive individuals. Treatment with Augmentin and other antibiotics can alter the normal bacteria flora of the colon and permit overgrowth of C. difficile, a bacteria responsible for pseudomembranous colitis. Patients who develop pseudomembranous colitis as a result of antibiotic treatment can experience diarrhea, abdominal pain, fever, and sometimes even shock. Co-administration of probenecid, a drug used for treating gout, prevents the normal elimination of amoxicillin by the kidneys and can cause high, toxic blood levels of amoxicillin. Augmentin can decrease the effectiveness of birth control pills, resulting in unexpected pregnancies. Augmentin and allopurinol together can cause skin rash.

**SIDE EFFECTS:** Minor side effects include abdominal discomfort, bloating, diarrhea, gas, headache, heartburn, nausea, and vomiting. Major side effects include bloody or prolonged diarrhea, easy bruising or bleeding, reversible hepatitis, rash, swelling, vaginal itching, and yellowing of the eyes or skin. Rash is common when Augmentin and other ampicillin-related antibiotics are given to patients with mononucleosis.

---

**Broad Spectrum Anti-biotics**

1. **GENERIC NAME:** doxycycline

**BRAND NAME:** Vibramycin
**DRUG CLASS AND MECHANISM:** Doxycycline is a synthetic broad-spectrum antibiotic derived from tetracycline. It is effective against a wide variety of bacteria, such as Hemophilus influenzae, Streptococcus pneumoniae, Mycoplasma pneumoniae, Chlamydia psittaci, Chlamydia trachomatis, Neisseria gonorrhoea, and many others.

**PRESCRIBED FOR:** Doxycycline is used for many different types of infections, including respiratory tract infections due to Hemophilus influenzae, Streptococcus pneumoniae, or Mycoplasma pneumoniae. It also is used for the treatment of nongonococcal urethritis (due to Ureaplasma), Rocky mountain spotted fever, typhus, chancroid, cholera, brucellosis, anthrax, syphilis, and acne.

**DOsing:** The absorption of doxycycline is not markedly affected by food, and therefore, it can be taken with meals. For most infections, doxycycline is taken once or twice daily for 7 to 14 days. Sometimes, the first dose is given as a "double dose," that is, twice as large as the remainder of the doses.

**DRUG INTERACTIONS:** It is recommended that doxycycline not be taken at the same time as aluminum-, magnesium-, or calcium- based antacids, such as Mylanta, Maalox, Tums, or Rolaids because, like food, these medications bind doxycycline in the intestine. Similarly, doxycycline should not be taken with minerals (such as calcium or iron), with bismuth subsalicylate (Pepto Bismol).

Doxycycline may enhance the activity of warfarin (Coumadin) and cause excessive "thinning" of the blood, necessitating a reduction in the dose of warfarin. Phenytoin (Dilantin), carbamazepine (Tegretol), and barbiturates (such as phenobarbital) may enhance the metabolism (destruction) of doxycycline thus making it less effective.

**PREGNANCY:** Tetracycline antibiotics, such as doxycycline, can have toxic effects on development of bone in the fetus. Therefore, tetracyclines are not recommended during pregnancy unless there is no other appropriate antibiotic.

**NURSING MOTHERS:** Doxycycline is secreted into breast milk. Since tetracyclines can cause decreased bone, the use of tetracyclines in nursing mothers is of concern. The physician must decide whether to recommend that a nursing mother discontinue nursing during treatment with tetracyclines or to choose a different antibiotic.

**SIDE EFFECTS:** Doxycycline is generally well-tolerated. The most common side effects are diarrhea or loose stools, nausea, abdominal pain, and vomiting. Tetracyclines, such as doxycycline, may cause tooth discoloration if used in persons below 8 years of age. Exaggerated sunburn can occur with tetracyclines; therefore, sunlight should be minimized during treatment.

2. **GENERIC NAME:** tetracycline

**BRAND NAME:** Achromycin; Sumycin

**DRUG CLASS AND MECHANISM:** Tetracycline is a broad-spectrum antibiotic. It is effective against a wide variety of bacteria including Hemophilus influenzae, Streptococcus pneumoniae, Mycoplasma pneumoniae, Chlamydia psittaci, Chlamydia trachomatis, Neisseria gonorrhoeae, and many others. The first drug of the tetracycline family, chlortetracycline, was introduced in 1948.

**PRESCRIBED FOR:** Tetracycline is used for many different infections including respiratory tract infections due to Hemophilus influenzae, Streptococcus pneumoniae, or Mycoplasma pneumoniae.
pneumoniae. It also is used for nongonococcal urethritis (due to Ureaplasma), Rocky mountain spotted fever, typhus, chancroid, cholera, brucellosis, anthrax, syphilis, and acne. It is used in combination with other medications to treat Helicobacter pylori, the bacteria associated with ulcers of the stomach and duodenum.

**DOSING:** Tetracycline should be taken at least one hour before or two hours after meals to prevent binding to food and the resulting reduced absorption of the tetracycline. For most infections, tetracycline is taken two to four times daily for 7 to 14 days.

**DRUG INTERACTIONS:** It is recommended that tetracycline not be taken at the same time as aluminum-, magnesium-, or calcium- based antacids, such as Mylanta, Maalox, Tums, or Rolaids since, like food, these compounds bind tetracycline in the intestine. Similarly, tetracycline should not be taken with minerals (such as calcium or iron), with bismuth subsalicylate (Pepto-Bismol) or with dairy products.

Tetracycline may enhance the activity of warfarin (Coumadin) and result in excessive “thinning” of the blood, necessitating a reduction in the dose of warfarin. Phenytoin (Dilantin), carbamazepine (Tegretol), and barbiturates (such as phenobarbital) can enhance the metabolism of tetracycline.

**SIDE EFFECTS:** Tetracycline is generally well-tolerated. The most common side effects are diarrhea or loose stools, nausea, abdominal pain, and vomiting. Tetracyclines may cause discoloration of teeth if used in patients below 8 years of age. Exaggerated sunburn can occur with tetracyclines; therefore, sunlight should be minimized during treatment.

### Amino glycosides
- Gentamicin
- Tobramycin

### Antifungal drugs

1. **GENERIC NAME:** fluconazole
2. **BRAND NAME:** Diflucan
3. **DRUG CLASS AND MECHANISM:** Antifungal (treatment of certain fungus infections).
4. **PRESCRIBED FOR:** Oral, esophageal, urinary, vaginal and possibly other organ infections caused by the fungus Candida. Fluconazole has also been used in the fungal infection Cryptococcus.
5. **DOSSING:** Fluconazole is taken orally or by intravenous injection. Modified dosing is needed if the patient has impaired renal function or if taking certain other medications at the same time. Please consult your pharmacist or physician if taking other medications with fluconazole. This drug can be used in children and has been effective down to the age of 6 months of age. Fluconazole can cause liver damage in rare cases and the liver should be monitored if taken for several days.
6. **DRUG INTERACTIONS:** Caution if taking certain other medications with fluconazole such as phenytoin, cyclosporin, theophylline and coumadin.
SIDE EFFECTS: The incidence of side effects from this medication is relatively high (up to 25%). Many (13%) may get headaches. Some patients develop nausea, abdominal pain, diarrhea or dizziness. Severe skin rash may occur but is uncommon.

2. GENERIC NAME: terbinafine

BRAND NAME: Lamisil

DRUG CLASS AND MECHANISM: Terbinafine is an antifungal agent that is taken by mouth or applied to the skin. Terbinafine acts by interfering with the ability of fungi to make chemicals called sterols that are an important part of the membrane that surrounds fungal cells and holds them together. This weakens the cell membrane. Oral terbinafine is more effective for treating fungal nail infections than griseofulvin (Fulvicin; Gris-Peg) and itraconazole (Sporanox), two other antifungal agents used for treating fungal nail infections. Topical terbinafine was approved by the FDA in 1993. Terbinafine oral tablets were approved in 1996.

PRESCRIBED FOR: Tablets: Fungal infections of the toe, or fingernail, caused by the fungus, tinea unguium.

Cream: Fungal infections of the skin including tinea pedis ("athlete's foot"), tinea corporis, and tinea cruris ("jock itch").

DOSING: Tablets: The usual dose is 250 mg once daily for 6 weeks for treatment of the fingernails, and 12 weeks for treatment of toenails. Alternatively, terbinafine may be given as two tablets (500 mg) once daily for 7 days during the first week of each month for 3 months for toenail infections. For children under 20kg (44 pounds), a dose of 62.5 mg/day and for children between 20 and 40kg (44 and 88 pounds) a dose of 125 mg/day have been recommended. Terbinafine may be taken with or without food.

Cream: The cream is rubbed gently into the affected area (s). The cream usually is applied twice daily for 1 to 4 weeks.

DRUG InterACTIONS: Rifampin reduces terbinafine blood concentrations, potentially reducing the efficacy of terbinafine, and cimetidine (Tagamet) may increase terbinafine blood levels. The latter effect would not be expected to lead to problems.

SIDE EFFECTS: Terbinafine is a very safe medication. The need to discontinue therapy because of side effects is quite rare. The most frequently reported side effects are diarrhea, and abdominal pain. Increases in liver enzymes, hives, itching and altered taste sensation also have been observed.

Antiviral drugs

1. GENERIC NAME: amantadine

BRAND NAME: Symmetrel
**DRUG CLASS AND MECHANISM:** Amantadine is a synthetic (man-made) anti-viral drug that can inhibit the replication of viruses in cells. To prevent a viral infection, the drug should be present before exposure to the virus. Clearly, this is not practical for most viral infections. It was initially used to prevent influenza A during flu season, and, if given within 24 to 48 hours of the onset of flu symptoms, to decrease the severity of the flu. Later amantadine was found to cause improvement in the symptoms of Parkinson's disease. Amantadine's mechanism of action in Parkinson's disease is not fully understood. Its effects may be related to its ability to augment (amplify) the effects of dopamine, a neurotransmitter in the brain, that is reduced in Parkinson's disease. Amantadine is less effective than levodopa in Parkinson's disease but can offer additional benefit when taken with levodopa. Amantadine was approved by the FDA in 1966.

**PRESCRIBED FOR:** Amantadine is used for the prevention or treatment of infections with influenza A virus, especially for individuals at high-risk such as immunosuppressed patients and nursing home residents. It should not be used as a substitute for vaccination. Amantadine also is used for control of the symptoms of Parkinson's disease.

**DOSING:** Amantadine is taken once or twice daily with or without food. If it causes an upset stomach, it can be taken with food.

For treatment of influenza, amantadine should be started within 24 to 48 hours after the onset of signs or symptoms and should be continued for 24 to 48 hours after the disappearance of signs or symptoms. To prevent influenza, amantadine should be started as soon as possible after exposure to the influenza virus and continued for at least 10 days.

Persons with reduced kidney function and elderly persons may need lower doses (or less frequent doses).

**DRUG INTERACTIONS:** Amantadine adds to the sedating effects alcohol and other sedating drugs such as the benzodiazepine class of anti-anxiety drugs (e.g., Valium, Ativan, Klonopin, Xanax, Ambien), the tricyclic class of antidepressants (e.g., Elavil, Tofranil, Norpramin), dicyclomine (Bentyl), certain antihistamines (Benadryl, Vistaril, Atarax, Tavist), opiate agonists (e.g., Dilaudid; Vicodin; Percocet; Codeine) and certain antihypertensive medications (e.g., Catapres, Inderal). Such combinations can cause dizziness, confusion, lightheadedness, fainting, or dizziness upon standing.

Since amantadine amplifies the actions of dopamine in the brain, drugs which block the effects of dopamine should be avoided in persons taking amantadine when amantadine is used for the treatment of Parkinson's disease. Such drugs include haloperidol (Haldol), metoclopramide (Reglan), and phenothiazines, e.g., thioridazine (Mellaril) or triflupromazine (Stelazine).

The use of the diuretics hydrochlorothiazide or triamterene (Dyazide; Maxzide) with amantadine can reduce the kidney's ability to eliminate amantadine. This can lead to high levels of amantadine in the blood and amantadine-associated toxicity.

**SIDE EFFECTS:** The most frequent side effects associated with amantadine include dizziness, loss of coordination, inability to sleep, and nervousness, nausea, and vomiting. All of these side effects have been reported to occur in about 1 in 20 persons. Effects can appear after a few hours or several days of therapy. Less common side effects include headache, irritability, nightmares, depression, confusion, drowsiness, and hallucinations, weakness, amnesia, slurred speech, diarrhea, constipation, and loss of appetite, and discolorations in the eye.

2. **GENERIC NAME:** rimantadine

**BRAND NAME:** Flumadine
**DRUG CLASS AND MECHANISM:** Rimantadine is a synthetic (man-made) anti-viral drug that can prevent viruses in cells from multiplying. To prevent a viral infection, the drug should be started before exposure to the virus. Clearly, this is not practical for most viral infections. Rimantadine initially was used to prevent influenza A during flu season, and, if given within 24 to 48 hours after the onset of flu symptoms, to decrease the severity of the flu. Rimantadine is chemically related to amantadine (Symmetrel), but rimantadine has fewer side effects on the nervous system than amantadine. Rimantadine was approved for use in 1993.

**PRESCRIBED FOR:** Rimantadine is used for the prevention or treatment of infections with influenza A virus, especially for individuals at high-risk such as immunosuppressed patients and nursing home residents. It should not be used as a substitute for vaccination.

**DOsing:** Rimantadine is taken once or twice daily with or without food. If it causes an upset stomach, it can be taken with food. If used for treatment of an established infection, rimantadine should be started as soon as possible, preferably within 48 hours after the onset of the symptoms of infection with influenza A. It should be continued for 5 to 7 days or for 24 to 48 hours after the disappearance of symptoms.

**DRUG INTERACTIONS:** There are no known, clinically important drug interactions with rimantadine.

**SIDE EFFECTS:** The risk of side effects with rimantadine is less than 3% or 1 in 30 patients who are treated. The most common side effects are nausea (1 in 35), vomiting (1 in 60), sleep disturbances (1 in 50), dizziness (1 in 50), loss of appetite (1 in 60), and dry mouth (1 in 60).

3. **GENERIC NAME:** lamivudine

**BRAND NAME:** Epivir

**DRUG CLASS AND MECHANISM:** Lamivudine is an oral medication that is used for the treatment of infections with the human immunodeficiency (HIV) and hepatitis B viruses. It is in a class of drugs called reverse transcriptase inhibitors which also includes zalcitabine (Hivid), zidovudine (Retrovir), didanosine (Videx), and stavudine (Zerit). During infection with HIV, the HIV virus multiplies within the body's cells. The viruses then are released from the cells and spread throughout the body where they infect other cells. In this manner, HIV infection spreads to new, uninfected cells that the body is continually producing, and HIV infection is perpetuated. When producing new viruses, the HIV virus must manufacture new DNA for each virus. Reverse transcriptase is the virus’ enzyme that forms this new DNA. Lamivudine first is converted within the body to its active form, lamivudine triphosphate. This active form is similar to a chemical, deoxycytidine triphosphate, that is used by reverse transcriptase to make new DNA. The reverse transcriptase uses lamivudine triphosphate instead of deoxycytidine triphosphate, and the lamivudine triphosphate interferes with the reverse transcriptase. Lamivudine does not kill existing HIV virus, and it is not a cure for HIV. Lamivudine was approved by the FDA in 1995.

**PRESCRIBED FOR:** Lamivudine is used for the treatment of HIV infection, prevention of HIV in those accidentally exposed to HIV, and the treatment of the hepatitis B infection.

**DOsing:** For the treatment of HIV infection the recommended dose for adults is 150 mg twice daily for those weighing 50 kg or more and 2 mg/kg twice daily if less than 50 kg.

Children (12 to 16 years old) weighing 50 kg or more should receive 150 mg twice daily.
Children (3 months to 12 years old) should be treated with 4 mg/kg twice daily up to a maximum dose of 300 mg daily.

For postexposure prevention of HIV infection, 150 mg twice daily of lamivudine is administered in conjunction with 600 mg daily of zidovudine (Retrovir) for 28 days.

Hepatitis B is treated with 100 mg twice daily.

Lamivudine may be administered without regard to meals.

**DRUG INTERACTIONS:** Trimethoprim/sulfamethoxazole (Bactrim) increases the concentration of lamivudine in the body.

**SIDE EFFECTS:** The most severe side effects are pancreatitis, liver failure and metabolic disturbance (lactic acidosis). Lamivudine also causes a decrease in blood cells, muscle pain and weakness, and nerve damage in the extremities (peripheral neuropathy). Symptoms of peripheral neuropathy are tingling, numbness and pain in the feet or hands. Other side effects are fever, abdominal pain, weight loss, nausea, vomiting, diarrhea, hair loss and difficulty sleeping.

**Antimalarial drugs**
- chloroquine and chloroguanide
- artemisinin, mefloquine

**Antiprotozoal and antihelmintic drugs**
- Chloroquine, emetin

1. **GENERIC NAME:** metronidazole

**BRAND NAME:** Flagyl

**DRUG CLASS AND MECHANISM:** Metronidazole is an antibiotic effective against anaerobic bacteria and certain parasites. Anaerobic bacteria are single-cell living organisms that thrive in low oxygen environments and can cause disease in the abdomen (bacterial peritonitis) liver (liver abscess), and pelvis (abscess of the ovaries and the fallopian tubes). Giardia lamblia and ameba are parasites that can cause abdominal pain and chronic diarrhea in infected individuals. Metronidazole selectively blocks some of the cell functions in these microorganisms, resulting in their demise.

**PRESCRIBED FOR:** Metronidazole is used to treat giardia infections of the small intestines, amebic liver abscess and dysentery (amebic colon infection causing bloody diarrhea), trichomonas vaginal infections, and carriers of trichomonas (both sexual partners) who do not have symptoms of infection. Metronidazole is also used alone or in combination with other antibiotics in treating abscesses in the liver, pelvis, abdomen and brain caused by susceptible anaerobic bacteria. Metronidazole is also used in treating colon infection caused by a bacteria called C. difficile. Many commonly used antibiotics can alter the normal type of bacteria that inhabit the colon. C. difficile is an anaerobic bacteria that can infect the colon when the normal bacteria types of the colon are altered by common antibiotics. This leads to inflammation of the colon (pseudomembranous colitis) with severe diarrhea and abdominal pain.
DOSING: Metronidazole may be taken with or without food. In the hospital, metronidazole can be administered intravenously to treat serious infections. Metronidazole is metabolized mainly by the liver and dosages may need to be reduced in patients with abnormal liver function.

DRUG INTERACTIONS: Alcohol should be avoided because metronidazole and alcohol together can cause severe nausea, vomiting, cramps, flushing, and headache. Metronidazole can increase the blood thinning effects of warfarin (Coumadin) and increase the risk of bleeding. Cimetidine (Tagamet) increases the blood level of metronidazole.

SIDE EFFECTS: Metronidazole is a valuable antibiotic, and is generally well tolerated with appropriate use. Serious side effects of metronidazole are rare; and include seizures and damage of nerves resulting in numbness and tingling of extremities (peripheral neuropathy). Metronidazole should be stopped if these symptoms appear. Minor side effects include nausea, headaches, loss of appetite, a metallic taste, and rarely a rash.

Ivermectin, mebendazole

Cancer chemotherapy

1. GENERIC NAME: tamoxifen

BRAND NAME: Nolvadex

DRUG CLASS AND MECHANISM: Tamoxifen is an antiestrogen (blocks the effect of estrogen on tissue). The precise mechanism of its action is unknown, but one possible mechanism is that it binds and blocks estrogen receptors on the surface of cells, preventing estrogens from binding and activating the cell. It is used in patients for treating and preventing breast cancer. Controversy currently exists as to which breast cancer patients will benefit from this treatment.

PRESCRIBED FOR: Tamoxifen is used for the treatment of invasive breast cancer, the most common type of breast cancer, following surgery and/or radiation and for preventing invasive breast cancer in women at high risk for developing it. Tamoxifen also is used for the treatment of women following surgery and radiation for a less common type of breast cancer called ductal carcinoma in situ (DCIS or intraductal carcinoma). Women who have had ductal carcinoma in situ are at high risk for developing invasive breast cancer at a later date, and tamoxifen prevents development of the invasive cancer in almost half of the women during the first five years of treatment. Occasionally, tamoxifen is used to stimulate ovulation.

DOSING: Tamoxifen should be taken at doses specifically directed by the physician. Currently, long term dosing is recommended (in excess of 2 years). Tamoxifen can be taken with food.

DRUG INTERACTIONS: Tamoxifen can cause abnormalities of liver tests and other blood tests, and patients taking it should keep appointments for blood work to monitor for these side effects. Patients should report any suspected side effects immediately, especially bleeding and yellowing of the skin.

SIDE EFFECTS: The most common side effects associated with tamoxifen are: hot flashes, weight gain, abnormal menstrual periods, and nausea.

2. GENERIC NAME: capecitabine
BRAND NAME: Xeloda

DRUG CLASS AND MECHANISM: Capecitabine is an oral medication for treating advanced breast cancers that are resistant to combination therapy with the drugs of choice, paclitaxel (Taxol) and a drug from the anthracycline family of drugs, for example, doxorubicin (Adriamycin). Capecitabine is converted by the body to 5-fluorouracil (5-FU), a drug which has been given intravenously for many years to treat various types of cancer. It is not surprising, therefore, that capecitabine also is effective in the treatment of colorectal cancer, a type of cancer which is treated frequently with 5-FU. 5-FU inhibits the production of both DNA and protein by the cancerous cells that are necessary for the cells to divide and the cancer to grow in size. Capecitabine was approved by the FDA in 1998 for the treatment of breast cancer and in 2005 for the treatment of colorectal cancer.

PRESCRIBED FOR: Capecitabine is used for treating women with breast cancer that is resistant to other more commonly-used drugs. It also is used following surgery for colorectal cancer if the cancer has spread to lymph nodes (Dukes' C stage).

DOsing: Capecitabine generally is taken twice daily, with the two doses approximately 12 hours apart. Tablets should be taken 30 minutes after eating. Capecitabine usually is prescribed in repeated cycles of 3-weeks, with the drug taken for two consecutive weeks followed by a week without drug. Some patients may need lower or delayed dosing. As always, the physician's dosing instructions should be followed.

DRUG INTERACTIONS: There are no known drug interactions with capecitabine.

SIDE EFFECTS: The most common side effects with capecitabine are diarrhea, nausea, vomiting, painful swelling of the mouth, fatigue, painful rash and swelling of the hands or feet, low white blood cell count (which can lead to infections), low blood platelet counts (which can lead to bleeding), and anemia. About one of every three patients who receives capecitabine has serious side effects, but these side effects usually are reversible when the drug is stopped or when the dose is lowered.

Pharmacology of the Endocrine Drugs

h. Hypothalamic-Pituitary interactions
i. Androgens, anabolic steroids, and estrogens
j. Antifertility agents and Uterotropics
k. Adrenal steroids
l. Insulin and Oral hypoglycemic agents
m. Thyroid and antithyroid drugs
n. Parathyroid drugs
Androgens, anabolic steroids, and estrogens

1. GENERIC NAME: estradiol

BRAND NAME: Estrace; Climara; Estraderm; Menostar

DRUG CLASS AND MECHANISM: Estrogens occur in nature in several forms. In women with active menstrual cycles, the ovaries produce between 70 and 500 micrograms of estradiol daily. This is converted to estrone and to a lesser extent estriol. After menopause, estrone is the most active circulating estrogen. (After menopause estrone is made in the adrenal glands.) Estrogens cause growth and development of female sex organs and maintain sex characteristics, including underarm and pubic hair and the shape of body contours and skeleton. Estrogens also increase secretions from the cervix and growth of the inner lining of the uterus (endometrium). Estrogens reduce LDL-cholesterol ("bad" cholesterol) and increase HDL-cholesterol ("good" cholesterol) concentrations in the blood. Estrogens, when taken alone or in combination with a progestin, have been shown to reduce the risk for hip fracture due to osteoporosis by 25%.

PRESCRIBED FOR: Estradiol is prescribed for symptomatic treatment of the usual symptoms associated with menopause (hot flashes, vaginal dryness, etc.), prevention of bone fractures associated with osteoporosis, reduction of the risk of heart attacks and strokes, and dysfunctional (excessive and painful) uterine bleeding. The vaginal cream is prescribed for vaginal or vulvar atrophy associated with menopause.

DOSEING: Estradiol tablets are generally prescribed once daily. In some patients, a so-called cyclic regimen is used, wherein estradiol is given daily for 23 consecutive days, followed by 5 days of no medication, after which the cycle resumes.

The adhesive part of the patch should be applied to a dry, hairless, clean part of the trunk, but not on the breasts. It should not be placed onto irritated or damaged skin. Sites of application should be rotated, with at least one week between repeated applications to any one site. The patch should be applied immediately after removing the protective layer, and pressure should be applied to the patch when it is attached for about 10 seconds.

DRUG INTERACTIONS: Estrogens can inhibit the metabolism of cyclosporine, resulting in increased cyclosporine blood levels. Such increased blood levels can result in kidney and/or liver damage. If this combination cannot be avoided, cyclosporine concentrations can be monitored, and the dose of cyclosporine can be adjusted to assure that its blood levels are not elevated.

Estrogens appear to increase the risk of liver disease in patients receiving dantrolene through an unknown mechanism. Women over 35 years of age and those with a history of liver disease are especially at risk.

Estrogens increase the liver's ability to manufacture clotting factors. Because of this, patients receiving warfarin (Coumadin) need to be monitored for loss of anticoagulant (blood thinning) effect if an estrogen is added when warfarin is already being taken.

Rifampin, barbiturates, carbamazepine (Tegretol), griseofulvin, phenytoin (Dilantin) and primidone, can all increase the elimination of estrogen by enhancing the liver's ability to metabolize it. Concurrent use may result in reduction of the beneficial effects of estrogens.

SIDE EFFECTS: Among the most common endocrine side effects are break-through bleeding or spotting, loss of periods or excessively prolonged periods, breast pain, breast enlargement, and changes in sexuality (increase or decrease in libido). Abdominal pain may indicate the
development of gallstones or occasionally hepatitis. Migraine headaches have been associated with estrogen therapy. Estrogens can cause sodium and fluid retention. Melasma, tan or brown patches, may develop on the forehead, cheeks, or temples. These may persist even after the estrogen is stopped. Conjugated estrogens may cause an increase in the curvature of the cornea. Patients with contact lenses may develop intolerance to their lenses.

Blood clots are an occasional but serious adverse effect and are dose-related. (The higher the dose, the more likely the clots.) Cigarette smokers are at a higher risk for clots, and, therefore, patients requiring estrogen therapy are strongly encouraged to quit smoking.

Estrogens can promote a buildup of the uterine lining (endometrial hyperplasia) and increase the risk of endometrial carcinoma. At diagnosis, endometrial cancers in estrogen recipients are generally of an earlier stage and a lower grade. Survival is also better in women exposed to estrogens than in those not exposed to estrogens. The addition of a progestin to estrogen therapy prevents endometrial carcinoma.

Conflicting data exists on the association between estrogens and breast cancer. There may be a small increase in risk. The effect of concomitant progestin therapy on the risk of estrogen-induced breast carcinoma is unclear.

2. GENERIC NAME: Oral Contraceptives or OCs (also known as Birth Control Pills or BCPs)

BRAND NAMES: see below

DRUG CLASS AND MECHANISM: Oral contraceptives (OCs) are medications that prevent pregnancy. They are one type of birth control. OCs may contain combinations of estrogen and progestin or progestin alone. Combinations of estrogen and progestin prevent pregnancy by inhibiting the release of the hormones LH and FSH from the pituitary gland in the brain. LH and FSH play key roles in the development of the egg and preparation of the lining of the uterus for implantation of the embryo. Progestin also makes the uterine mucus that surrounds the egg more difficult for sperm to penetrate and, therefore, for fertilization to take place. In some women, progestin inhibits ovulation (release of the egg).

The combination OCs are called "monophasic," "biphasic," or "triphasic." Monophasic OCs deliver the same amount of estrogen and progestin every day. Biphasic OCs deliver the same amount of estrogen every day for the first 21 days of the cycle. During the first half of the cycle, the progestin/estrogen ratio is lower to allow the endometrium to thicken as it normally does. During the second half of the cycle, the progestin/estrogen ratio is higher to allow normal shedding of the lining of the uterus to occur. The triphasic OCs have constant or changing estrogen concentrations and varying progestin concentrations throughout the cycle. There is no evidence that bi- or tri-phasic OCs are superior to monophasic OCs, or vice-versa.

PRESCRIBED FOR: OCs are prescribed for the prevention of pregnancy. When taken as directed, OCs fail in less than 1 in every 200 users over the first year of use. OCs also are prescribed to treat mid-cycle pain which some women experience with ovulation. OCs, while regulating the menstrual cycle, reduce menstrual cramps and heavy bleeding, and, because of the reduced bleeding, they may prevent the anemia that can develop in some women. Doctors sometimes prescribe higher doses of OCs for use as "morning after" pills to be taken up to 72 hours after unprotected intercourse to prevent fertilization and pregnancy.

DOSING: Many of the OCs come in easy to use dispensers in which the day of the week or a consecutive number (1, 2, 3, etc.) is written on the dispenser with a corresponding tablet for each day or number. For example, some Ortho-Novum dispensers are labeled "Sunday" next to the
first tablet. Thus, the first tablet is to be taken on the first Sunday after menstruation begins (the first Sunday following the first day of a woman's period). If her period begins on Sunday, the first tablet should be taken on that day. For OCs that use consecutive numbers, the first tablet (#1) is taken on the first day of the menstrual period (the first day of bleeding). Tablet #2 is taken on the second day, and so on. Still other packages instruct women to begin on day 5 of the cycle. For such products, women count from day 1 of their menstrual cycle (day 1 is the first day of bleeding). On the fifth day, the first tablet is taken. Tablets then are taken daily.

OCs are packaged as 21-day or 28-day units. For 21-day packages, tablets are taken daily for 21 days. This is followed by a 7-day period during which no OCs are taken. Then the cycle repeats. For the 28-day units, tablets containing medication are taken for 21 consecutive days, followed by a seven-day period during which placebo tablets (containing no medication) are taken.

Women just starting to take OCs should use additional contraception for the first 7 days of use because pregnancy may occur during this period of time.

If women forget to take tablets, pregnancy may result. If a single tablet is forgotten, it should be taken as soon as it is realized that it is forgotten. If more than one tablet is forgotten, the instructions that come with the packaging should be consulted, or a physician or pharmacist should be called.

**DRUG INTERACTIONS:** Estrogens can inhibit the metabolism (elimination) of cyclosporine, resulting in increased cyclosporine blood levels. Such increased blood levels can result in kidney and/or liver damage. If this combination cannot be avoided, cyclosporine concentrations can be monitored, and the dose of cyclosporine can be adjusted to assure that its blood levels do not become elevated.

Estrogens appear to increase the risk of liver disease in patients receiving dantrolene through an unknown mechanism. Women over 35 years of age and those with a history of liver disease are especially at risk.

Estrogens increase the liver's ability to manufacture clotting factors. Because of this, patients receiving warfarin (Coumadin) need to be monitored for loss of anticoagulant (blood thinning) effect if an estrogen is begun.

A number of medications, including some antibiotics, can decrease the blood levels of OC hormones that would otherwise have been achieved during OC use, but an actual decrease in the effectiveness of the OC has not been convincingly proven. Nonetheless, because of this theoretical possibility, some physicians recommend back-up contraceptive methods during antibiotic use. Carbamazepine (Tegretol), phenobarbital, phenytoin (Dilantin), primidone (Mysoline), rifampin (Rifadin), rifabutin (Mycobutin), and ritonavir (Norvir) each increase the elimination of estrogens. OCs with higher concentrations of estrogen or alternative forms of contraception may be necessary in women using those medications.

**SIDE EFFECTS:** The most common side effects of the oral contraceptives include nausea, headache, breast tenderness, weight gain, irregular bleeding, and mood changes. These side effects often subside after a few months' use. Scanty periods, or breakthrough bleeding may occur, but are often temporary, and neither side effect is worrisome. Women with a history of migraines may notice an increase in migraine frequency. On the other hand, women whose migraines are triggered by fluctuations in their own hormone levels may notice improvement in migraines with oral contraceptive use, because of the more smooth and uniform hormone levels during oral contraceptive use. Uncommonly, OCs may contribute to increased blood pressure, blood clots, heart attack, and stroke. Women who smoke, especially those over 35, and women
with certain medical conditions, such as a history of blood clots or breast or endometrial cancer, may be advised against taking OCs, as these conditions can increase the adverse risks of OCs.

Antifertility agents and Uterotropics

Adrenal steroids

1. GENERIC NAME: risedronate

BRAND NAME: Actonel

DRUG CLASS AND MECHANISM: Risedronate is in a class of drugs called bisphosphonates which also includes the drugs alendronate (Fosamax) and etidronate (Didronel). It is used for the treatment of Paget's disease of bone (a disease in which the formation of bone is abnormal) and in persons with osteoporosis (in which the density and strength of bones are reduced). Bone is continually being formed and dissolved. By slowing down the rate at which bone is dissolved, risedronate increases the amount of bone. Risedronate has a chemically unique component as compared with the other bisphosphonates which is believed to reduce the likelihood of gastrointestinal side effects. Risedronate is more potent in blocking the dissolution of bone than etidronate and alendronate. The FDA approved risedronate for treatment of Paget's disease in 1998 and for the prevention and treatment of osteoporosis in 1999.

PRESCRIBED FOR: Risedronate is used for the treatment of Paget's disease of bone (osteitis deformans) and to treat or prevent osteoporosis. It is also used to prevent and treat osteoporosis that is caused by cortisone-related medications (glucocorticoid-induced osteoporosis).

DOSING: For osteoporosis, 5 mg of risedronate is taken once daily or 35 mg is taken weekly with 6 to 8 ounces of plain water. For Paget's disease, initial treatment is 30 mg daily for two months. Because food interferes with the absorption of risedronate, it should be taken first thing in the morning before anything is eaten or drunk. Also, no food or drink should be taken for at least 30 minutes afterwards. To avoid pills sticking and irritating the throat or esophagus, persons should not lie down for at least 30 minutes after taking risedronate. It should also not be taken at the same time as iron supplements, vitamins with minerals, or antacids containing calcium, magnesium, or aluminum.

DRUG INTERACTIONS: Food, calcium and other minerals reduces the absorption of risedronate, resulting in loss of effectiveness. Thus, it should be taken with plain water only.

SIDE EFFECTS: Risedronate generally is well-tolerated. The most common side effects are headache (1 in 5 persons), joint pain (1 in 3), diarrhea (1 in 5), abdominal pain (1 in 9), rash (1 in 9), and nausea (1 in 10). A related drug, alendronate, can irritate the esophagus and cause heartburn in patients when it sticks in the esophagus.

2. GENERIC NAME: prednisone

BRAND NAME: Deltasone, Orasone, Prednicen-M, Liquid Pred
DRUG CLASS AND MECHANISM: Prednisone is an oral, synthetic (man-made) corticosteroid used for suppressing the immune system and inflammation. It has effects similar to other corticosteroids such as triamcinolone (Kenacort), methylprednisolone (Medrol), prednisolone (Prelone) and dexamethasone (Decadron). These synthetic corticosteroids mimic the action of cortisol (hydrocortisone), the naturally-occurring corticosteroid produced in the body by the adrenal glands. Corticosteroids have many effects on the body, but they most often are used for their potent anti-inflammatory effects, particularly in those conditions in which the immune system plays an important role. Such conditions include arthritis, colitis, asthma, bronchitis, certain skin rashes, and allergic or inflammatory conditions of the nose and eyes. Prednisone is inactive in the body and, in order to be effective, first must be converted to prednisolone by enzymes in the liver. Therefore, prednisone may not work as effectively in people with liver disease whose ability to convert prednisone to prednisolone is impaired

PRESCRIBED FOR: Prednisone is used in the management of inflammatory conditions or diseases in which the immune system plays an important role. Since prednisone is used in so many conditions, only the most common or established uses are mentioned here. Prednisone most often is used for treating several types of arthritis, ulcerative colitis, Crohn’s disease, systemic lupus, allergic reactions, asthma and severe psoriasis. It also is used for treating leukemias, lymphomas, idiopathic thrombocytopenic purpura and autoimmune hemolytic anemia. Corticosteroids, including prednisone, are commonly used to suppress the immune system and prevent the body from rejecting transplanted organs. Prednisone is used as replacement therapy in patients whose adrenal glands are unable to produce sufficient amounts of cortisol.

DOsing: The initial dose of prednisone varies depending on the condition being treated and the age of the patient. The starting dose may be from 5 to 60 mg per day and often is adjusted based on the response of the condition being treated. Corticosteroids typically do not produce immediate effects and must be used for several days before maximal effects are seen. It may take much longer before conditions respond to treatment. Prolonged therapy with prednisone causes the adrenal glands to atrophy and stop producing cortisol. When prednisone is discontinued after a period of prolonged therapy, the dose of prednisone must be tapered (lowered gradually) to allow the adrenal glands time to recover. (See side effects.) It is recommended that prednisone be taken with food.

DRUG INTERACTIONS: Prednisone may interact with estrogens and phenytoin (Dilantin). Estrogens may reduce the action of enzymes in the liver that break down (eliminate) the active form of prednisone, prednisolone. As a result, the levels of prednisolone in the body may increase and lead to more frequent side effects. Phenytoin increases the activity of enzymes in the liver that break down (eliminate) prednisone and thereby may reduce the effectiveness of prednisone. Thus, if phenytoin is being taken, an increased dose of prednisone may be required.

SIDE EFFECTS: Side effects of prednisone and other corticosteroids range from mild annoyances to serious, irreversible damage, and they occur more frequently with higher doses and more prolonged treatment. Side effects include retention of sodium (salt) and fluid, weight gain, high blood pressure, loss of potassium, headache and muscle weakness. Prednisone also causes puffiness of the face (moon face), growth of facial hair, thinning and easy bruising of the skin, impaired wound healing, glaucoma, cataracts, ulcers in the stomach and duodenum, worsening of diabetes, irregular menses, rounding of the upper back ("buffalo hump"), obesity, retardation of growth in children, convulsions, and psychiatric disturbances. The psychiatric disturbances include depression, euphoria, insomnia, mood swings, personality changes, and even psychotic behavior.

Prednisone suppresses the immune system and, therefore, increases the frequency or severity of infections and decreases the effectiveness of vaccines and antibiotics. Prednisone may cause osteoporosis that results in fractures of bones. Patients taking long-term prednisone often receive supplements of calcium and vitamin D to counteract the effects on bones. Calcium and vitamin D
probably are not enough, however, and treatment with bisphosphonates such as alendronate (Fosamax) and risedronate (Actonel) may be necessary. Calcitonin (Miacalcin) also is effective. The development of osteoporosis and the need for treatment can be monitored using bone density scans.

Insulin and Oral hypoglycemic agents

1. GENERIC NAME: insulin

BRAND NAME: various

DRUG CLASS AND MECHANISM: Insulin is a naturally-occurring hormone secreted by the pancreas. Insulin is required by the cells of the body in order for them to remove and use glucose from the blood. From glucose the cells produce the energy that they need to carry out their functions. Researchers first gave an active extract of the pancreas containing insulin to a young diabetic patient in 1922, and the FDA first approved insulin in 1939. Currently, insulin used for treatment is derived from beef and pork pancreas as well as recombinant (human) technology. The first recombinant human insulin was approved by the FDA in 1982.

Patients with diabetes mellitus have an inability to take up and use glucose from the blood, and, as a result, the glucose level in the blood rises. In type 1 diabetes, the pancreas cannot produce enough insulin. Therefore, insulin therapy is needed. In type 2 diabetes, patients produce insulin, but cells throughout the body do not respond normally to the insulin. Nevertheless, insulin also may be used in type 2 diabetes to overcome the resistance of the cells to insulin. By increasing the uptake of glucose by cells and reducing the concentration of glucose in the blood, insulin prevents or reduces the long-term complications of diabetes, including damage to the blood vessels, eyes, kidneys, and nerves. Insulin is administered by injection under the skin (subcutaneously). The subcutaneous tissue of the abdomen is preferred because absorption of the insulin is more consistent from this location than subcutaneous tissues in other locations.

Regular (rapid onset of action, short duration of action) and NPH (slower onset of action, longer duration of action) human insulin are the most commonly-used preparations. Regular insulin has an onset of action (begins to reduce blood sugar) within 30 minutes of injection, reaches a peak effect at 1-3 hours, and has effects that last 6-8 hours.

NPH insulin is an insulin with an intermediate duration of action. It has an onset of action starting about 2 hours following injection. It has a peak effect 4-12 hours after injection, and a duration of action of 18-26 hours.

Lente insulin also is an insulin with an intermediate duration of action. It has an onset of action 2-4 hours after injection, a peak activity 6-12 hours after injection, and a duration of action of 18 to 26 hours. Ultralente insulin is a long-acting insulin with an onset of action 4-8 hours after injection, a peak effect 10-30 hours after injection, and a duration of action of more than 36 hours.

An ultra rapid-acting insulin, insulin lispro is a chemically-modified, natural insulin. It was approved by the FDA in June, 1996. As compared to regular insulin, insulin lispro has a more rapid onset of action, an earlier peak effect, and a shorter duration of action. It reaches peak
activity 0.5-2.5 hours after injection. Therefore, insulin lispro should be injected 15 minutes before a meal as compared to regular insulin which is injected 30-60 minutes before a meal.

Insulin aspart and insulin glargine are both human insulin that have had their chemical composition slightly altered. The chemical changes provide insulin aspart with a faster onset of action (20 minutes) and a shorter duration of action (3-5 hours) than regular human insulin. It reaches peak activity 1-3 hours after injection. Insulin glargine has a slower onset of action (70 minutes) and a longer duration of action (24 hours) than regular human insulin. Its activity does not peak.

PRESCRIBED FOR: Insulin is prescribed for the treatment of type 1 and type 2 diabetes mellitus.

DOSING: The abdomen is the preferred site for insulin injection, but the sites of injection must be rotated in order to prevent erosion of the fat beneath the skin, a condition called lipodystrophy.

DRUG INTERACTIONS: Several drugs augment the action of insulin and may lower blood glucose to a dangerous level (hypoglycemia). To prevent hypoglycemia when these drugs are used, the dose of insulin may need to be reduced. Such drugs include alcohol, MAO inhibitors like phenelzine (Nardil), beta-blockers like propranolol (Inderal), salicylates like aspirin (Bayer) or salsalate (Disalcid), and anabolic steroids like methyltestosterone (Android).

There are other drugs that augment the blood glucose-lowering effect of insulin, but they are less likely to interact with insulin or have less of an effect. Such drugs include tetracycline antibiotics like doxycycline (Vibramycin), guanethidine (Ismelin), oral hypoglycemic drugs like glyburide (Diabeta), sulfa antibiotics like sulfadiazine, and ACE inhibitors like captopril (Capoten).

There also are drugs that decrease the effect of insulin. Interactions are less likely and/or less serious. These drugs include diltiazem (Cardizem), niacin, corticosteroids like prednisone, estrogens, oral contraceptives, thyroid hormones like levothyroxine (Synthroid), isoniazid, epinephrine, thiazide diuretics like hydrochlorothiazide, and furosemide (Lasix).

SIDE EFFECTS: Hypoglycemia is the most common side effect that may occur during insulin therapy. Symptoms of hypoglycemia include confusion, nausea, hunger, tiredness, perspiration, headache, heart palpitations, numbness around the mouth, tingling in the fingers, tremors, muscle weakness, blurred vision, cold temperature, excessive yawning, irritability, and loss of consciousness.

Patients may experience blurred vision if they have had elevated blood sugar levels for a prolonged period of time and then have the elevated levels rapidly brought to normal. This is due to a shift of fluid within the lens of the eye. Over time, vision returns to normal. Other possible side effects that may occur include skin reactions (redness, swelling, itching or rash at the site of injection), worsening of diabetic retinopathy, changes in the distribution of body fat (lipodystrophy), allergic reactions, sodium retention, and general body swelling.

2. GENERIC NAME: exenatide

BRAND NAME: Byetta

DRUG CLASS AND MECHANISM: Exenatide is an injectable drug that reduces the level of sugar (glucose) in the blood. It is used for treating type 2 diabetes. Exenatide belongs in a class of drugs called incretin mimetics because these drugs mimic the effects of incretins. Incretins, such as human-glucagon-like peptide-1 (GLP-1), are hormones that are produced and released
GLP-1 increases the secretion of insulin from the pancreas, slows absorption of glucose from the gut, and reduces the action of glucagon. (Glucagon is a hormone that increases glucose production by the liver.) All three of these actions reduce levels of glucose in the blood. In addition, GLP-1 reduces appetite. Exenatide is a synthetic (man-made) hormone that resembles and acts like GLP-1. In studies, exenatide-treated patients achieved lower blood glucose levels and experienced weight loss. Exenatide was approved by the FDA in May, 2005.

**PRESCRIBED FOR:** Exenatide is used in combination with other drugs for reducing blood glucose in patients with type 2 diabetes who have not achieved adequate blood glucose reduction while taking metformin (Glucophage) or a combination of metformin (Glucophage) and a sulfonylurea (glyburide, glipizide etc). Exenatide should not be used in patients with type 1 diabetes or as a substitute for insulin in patients who require insulin.

**DOSING:** The initial dose of exenatide is 5 mcg injected under the skin (subcutaneously) twice daily, 60 minutes before breakfast or dinner. Exenatide should not be administered after a meal. Each dose should be injected in the thigh, abdomen or upper arm. The dose can be increased to 10 mcg twice daily after 1 month of therapy.

**DRUG INTERACTIONS:** Exenatide slows down transit of food and drugs through the intestine and, therefore, can reduce the absorption of drugs that are taken orally. To avoid this interaction, administer oral medications one hour before exenatide is administered. Orally administered drugs that need to be administered with food should be given with a light meal or snack when exenatide is not administered.

**SIDE EFFECTS:** The most common side effect of exenatide is nausea. Nausea from exenatide is more common with the higher doses and decreases over time. Other common side effects include hypoglycemia (excessively low blood glucose), vomiting, diarrhea, headache, nervousness and stomach discomfort. Patients may also experience decreased appetite, acid reflux and increased sweating.

### Thyroid and antithyroid drugs

1. **GENERIC NAME:** levothyroxine sodium

**BRAND NAME:** Synthroid, Levoxyl, Levothroid, Unithroid

**DRUG CLASS AND MECHANISM:** Levothyroxine is a synthetic (man-made) version of the principle thyroid hormone, thyroxine (T4), that is made and released by the thyroid gland. Thyroid hormone increases the metabolic rate of cells of all tissues in the body. In the fetus and newborn, thyroid hormone is important for the growth and development of all tissues including bones and the brain. In adults, thyroid hormone helps to maintain brain function, food metabolism, and body temperature, among other effects.

**GENERIC AVAILABLE:** Yes. Generic and branded tablets of levothyroxine may differ in the amount of levothyroxine they contain, the absorption of the levothyroxine into the body, and the distribution of levothyroxine throughout the body. This means that ingestion of one mg of generic levothyroxine may not have the same effect on the body as one mg of another generic or branded levothyroxine. Practically speaking, this means that when changing between levothyroxine
manufactured by different pharmaceutical companies, a change in dose may be necessary to maintain the desired effect or to prevent toxicity.

**PRESCRIBED FOR:** Levothyroxine is approved to treat hypothyroidism and to suppress thyroid hormone release in the management of cancerous thyroid nodules and growth of goiters. In addition, Synthroid, Levoxyl and Levothroid also are prescribed with anti-thyroid drugs, for example methimazole (Tapazole), to manage thyrotoxicosis (high thyroid hormone levels due to over-activity of the thyroid gland). Thyrotoxicosis may result in the growth of goiters and/or hypothyroidism.

**DOSING:** Levothyroxine is usually started at 0.05 mg/day. Starting doses and dose changes may differ with individual patients based upon the presence of cardiovascular disease, the development of tolerance (reduced effectiveness with continued use), side effects to the medication, and blood levels of thyroid hormone. It may take one to three weeks after initiating therapy with levothyroxine or changing the dose before effects are seen.

**DRUG INTERACTIONS:** Initiation or discontinuation of therapy with levothyroxine in diabetic patients may create a need for an increase or decrease in the required dose of insulin and/or antidiabetic drug, e.g., glyburide (Micronase).

Levothyroxine may increase the effect of blood thinners such as warfarin (Coumadin). Therefore, monitoring of blood clotting is necessary, and a decrease in the dose of warfarin may be necessary.

Intravenous administration of epinephrine to patients with coronary artery disease may lead to complications ranging from difficulty in breathing to a heart attack. These complications may occur more frequently among patients also taking levothyroxine. Therefore, careful observation is needed when intravenous epinephrine is given to patients receiving levothyroxine who also have coronary artery disease.

Converting a state of hypothyroidism (underactivity) to a normal state (euthyroid state) with levothyroxine may decrease the actions of certain beta-blocking drugs, e.g., metoprolol (Lopressor) or propranolol (Inderal). It may be necessary, therefore, to change the dose of beta-blocker. For the same reason, the dose of digoxin (Lanoxin), a drug used to manage heart failure or an irregular heart rhythm (e.g., atrial-fibrillation), also may need to be changed.

Converting hypothyroidism to the euthyroid state with levothyroxine may increase the blood level of theophylline (Slo-Bid), and it may be necessary to change the dose of theophylline.

Taking levothyroxine at the same time as cholestyramine (Questran) or colestipol (Colestid), two cholesterol-lowering drugs, may decrease the effect of levothyroxine and lead to hypothyroidism. This occurs because the levothyroxine binds to the cholesterol-lowering drugs and is not absorbed. Taking the levothyroxine one hour before or four hours after cholestyramine or colestipol is necessary to prevent the binding.

**SIDE EFFECTS:** Levothyroxine therapy is usually well-tolerated. If symptoms occur, often they are due to toxic levels of thyroid hormone and the symptoms are those of hyperthyroidism. Symptoms may include all or some of the following: chest pain, increased heart rate or pulse rate, excessive sweating, heat intolerance, nervousness, headache, insomnia, diarrhea, vomiting, weight loss, or fever. Women may experience irregular menstrual cycles.
2. GENERIC NAME: methimazole

BRAND NAME: Tapazole

DRUG CLASS AND MECHANISM: Methimazole is used to manage hyperthyroidism (overactivity of the thyroid gland). It is considered an antithyroid agent, like propylthiouracil (PTU).

Grave’s disease is the most common cause of hyperthyroidism. It is an autoimmune disease in which an individual's own antibodies attach to thyroid stimulating hormone receptors within thyroid cells and thereby trigger overproduction of thyroid hormones. The two thyroid hormones manufactured by the thyroid gland, thyroxine (T4) and triiodothyronine (T3), are formed by combining iodine with a protein called thyroglobulin with the assistance of an enzyme called peroxidase. Methimazole inhibits iodine and peroxidase from their normal interactions with thyroglobulin to form T4 and T3. This action decreases thyroid hormone production. (methimazole also interferes with the conversion of T4 to T3, and, since T3 is more potent than T4, this also reduces the activity of thyroid hormones.)

PRESCRIBED FOR: Methimazole is used to manage hyperthyroidism associated with Grave’s disease. It is also used to decrease symptoms of hyperthyroidism in preparation for surgically removing the thyroid gland or before inactivating the thyroid gland with radioactive iodine.

DOSSING: The initial adult dose of methimazole is 15 mg/day for mild hyperthyroidism, 30-40 mg/day for moderately severe hyperthyroidism and 60 mg/day for severe hyperthyroidism. The drug is usually taken every eight hours but may be taken once daily under physician supervision. A common, long-term, adult dose after initial treatment is 5-30 mg/day. Children's initial and continuing doses vary.

DRUG INTERACTIONS: There are no known drug interactions with methimazole.

SIDE EFFECTS: Methimazole is generally well-tolerated with side effects occurring in 3 out of every 100 patients. The most common side effects are related to the skin and include rash, itching, hives, abnormal hair loss, and skin pigmentation. Other common side effects are swelling, nausea, vomiting, heartburn, loss of taste, joint or muscle aches, numbness and headache.

Less common but serious side effects have occurred with methimazole therapy. A decrease of white blood cells in the blood (agranulocytosis) may occur. Symptoms and signs of agranulocytosis include infectious lesions of the throat, the gastrointestinal tract and skin with an overall feeling of illness and fever. A decrease in blood platelets (thrombocytopenia) also may occur. Since platelets are important for the clotting of blood, thrombocytopenia may lead to problems with excessive bleeding.

There also have been rare occurrences with methimazole of hepatitis and death of liver cells (hepatic necrosis). Failure of the liver due to hepatic necrosis may lead to severe brain swelling, gastrointestinal bleeding, and death.

Parathyroid drugs
Toxicology and Special Topics

n. Introduction to Toxicology
o. Self-study
p. Environmental Toxicology
q. Clinical Toxicology
r. Toxicology of heavy metals
s. Clinical correlations
t. Drug interactions
u. Pharmacology and Toxicology of ionizing radiation
v. Drugs affecting the Gastrointestinal system
w. Case history
x. Immunosuppressives
y. Role of nutrition in Pharmacology
z. Developmental and perinatal Pharmacology