

# Drugs for Pain, Fever, and Inflammation

## CHAPTER OBJECTIVES

- Match brand and generic names of commonly used drugs for pain, fever, and inflammation
- Identify the classification of commonly used drugs for pain, fever, and inflammation
- Recognize commonly used drugs for pain, fever, and inflammation as prescription or over-the-counter drugs
- Describe the different uses of aspirin
- Compare and contrast the mechanisms of action for salicylates, acetaminophen, and NSAIDs
- List common adverse reactions of commonly used drugs for pain, fever, and inflammation
- Match common drug interactions of commonly used drugs for pain, fever, and inflammation with the appropriate drug and category
- Match brand and generic names of opioid agonists, mixed agonist-antagonists, and antagonists with the appropriate category
- Identify commonly used inhalation anesthetics
- Identify commonly used injection anesthetics

## KEY TERMS

**acetaminophen**—an OTC drug that has analgesic and antipyretic properties

**analgesic**—a drug used to control or relieve pain without causing the patient to lose consciousness

**anesthetic drugs**—drugs that block the perception or cause a loss of feeling, allowing the patient to undergo medical procedures without distress and pain

**angioedema**—swelling of the mucosal tissues beneath the skin resulting in welts

**antipyretic**—a drug that lowers an elevated body temperature

**ataxia**—a loss of control of voluntary movements, especially producing an unsteady gait

**black box warning**—a warning required by the FDA for certain drugs that lists any serious or life-threatening adverse reactions

**competitive inhibition**—process in which an antagonist drug stops an agonist drug from acting by filling up the receptor cells

**endorphins**—naturally occurring opiates that are part of the body's pain relief system

**epidural block**—a type of anesthesia administered during childbirth in which a drug is injected into the outer lining of the spinal cord (epidural space)

**inhalation anesthetics**—anesthetic drugs that are brought into the body through the lungs

**intravenous anesthetics**—anesthetic drugs that are administered directly into a vein

**leukopenia**—an abnormal decrease in a specific type of white blood cell, or leukocytes

**local anesthetics**—drugs that block pain and other sensations in a specific body part

**mixed opioid agonist-antagonists**—drugs that act like agonists and antagonists by relieving pain and reducing the risk of adverse reactions

**myasthenia gravis**—a disease that causes fatigue of skeletal muscles because of the lack of acetylcholine released at the nerve endings of parasympathetic nerve fibers

**narcotic agonists**—see *opioid agonists*

**neurotoxicity**—condition involving damage to the nerves or nervous tissue

**nonsteroidal anti-inflammatory drugs (NSAIDs)**—a class of drugs that act to reduce pain, fever, and inflammation by stopping the body from producing prostaglandins

**opioids**—derivatives of the opium plant or synthetic drugs that imitate natural narcotics

**opioid agonists**—controlled substances used to relieve or decrease pain without causing loss of consciousness in the patient

**opioid antagonists**—drugs that work against opioid agonists to block their effects and reverse adverse reactions; also known as *narcotic antagonists*

**osteoarthritis**—a chronic disease that involves wear and deterioration of joints in the body, causing inflammation

**phenazopyridine hydrochloride**—dye used in commercial coloring that helps relieve symptoms associated with urinary tract infections

**phlebitis**—inflammation of a vein

**prostaglandin**—a chemical found in most body fluids and tissues that makes nerve cells sensitive to pain

**pruritus**—itching

**Reye syndrome**—a potentially life-threatening disorder that affects children by damaging the brain and liver

**rheumatic fever**—a disease associated with a delayed response to a previous streptococcal infection in the body and characterized by fever and pain in the joints

**rheumatoid arthritis**—a chronic inflammatory disease of the peripheral joints

**salicylates**—a commonly used class of drugs for controlling pain, fever, and inflammation

**thrombocytopenia**—an abnormal decrease in the number of platelets circulating in the blood

**tinnitus**—a sensation of ringing or buzzing in the ears

**topical anesthetics**—drugs that are applied to the skin and mucous membranes to block pain and other sensations in a specific area of the body

**urticaria**—a skin condition commonly known as hives that involves red, itchy, or swollen areas of the skin

**volatility**—a property of liquids that causes them to evaporate and become gas when exposed to air

A wide range of drugs are used to control pain. They range from mild over-the-counter (OTC) drugs, such as aspirin and acetaminophen, to strong general anesthetics. Drugs that relieve pain often reduce fever and inflammation (swelling), too. In this chapter, you'll learn about drugs for pain, fever, and inflammation that are used to treat conditions such as:

- mild to moderate pain caused by injury or surgery
- fever, headaches, and painful menstruation
- **rheumatoid arthritis** (a chronic inflammatory disease of the peripheral joints)
- **osteoarthritis** (a chronic disease that involves wear and deterioration of joints in the body, causing inflammation)
- chronic pain associated with cancer, AIDS, multiple sclerosis, or sickle cell disease

Acute pain lasts for short periods of time, often less than three months. Chronic pain may last for years.

## NONOPIOID ANALGESICS, ANTIPYRETICS, AND NONSTEROIDAL ANTI-INFLAMMATORY DRUGS

Drugs that control pain without causing the patient to lose consciousness are referred to as **analgesics**.

- Nonopioid analgesic drugs are drugs that are not derived from the opium plant. They do not cause physical dependence in patients.
- Opioid analgesic drugs are synthetic (human made) or are made from the opium plant. These drugs may cause physical dependence.

**Nonsteroidal anti-inflammatory drugs** are better known as **NSAIDs**. The body's natural response to injury, irritation, or infection is inflammation. Signs of inflammation include redness, swelling, pain, and heat. Anti-inflammatory drugs reduce the swelling and pain of inflammation.

Nonopioid analgesics and NSAIDs affect the body in similar ways. When nonopioid analgesics and NSAIDs enter the body, they stop the body from producing **prostaglandin**. Prostaglandin is a chemical that makes nerve cells sensitive to pain. It is found in almost all body fluids and tissues. Preventing the body from making prostaglandin may have two main effects:

- *Analgesic effect.* When prostaglandin is released, the body becomes sensitive to pain. By stopping the body from producing prostaglandin, nonopioid analgesics and NSAIDs reduce the pain response.
- *Anti-inflammatory effect.* Stopping prostaglandin is also believed to reduce the pain and swelling of the body's inflammatory response. However, only some nonopioid analgesics have an anti-inflammatory effect.

Nonopioid analgesic drugs and NSAIDs are also **antipyretics**, meaning they can reduce body temperature to control fever. These drugs reduce fever by stimulating a gland called the hypothalamus. With the hypothalamus (a region of the brain that regulates temperature and other body processes) in action, peripheral blood vessels (in the feet, legs, arms, lower abdomen, neck, or head) enlarge, and sweating increases. This results in the body's loss of heat through the skin and cooling by evaporation.

There are four main groups of nonopioid analgesic and antipyretic drugs:

- salicylates
- nonsalicylate analgesics
- NSAIDs
- the urinary tract analgesic phenazopyridine hydrochloride

Because nonopioid analgesic drugs and NSAIDs are often taken with other medications, patients need to be aware of possible drug interactions.

## Salicylates

**Salicylates** are among the most commonly used medications for controlling pain, fever, and inflammation. They are available over the counter or by prescription and usually cost less than other analgesics. Salicylates are mainly used for the following:

- relieving mild to moderate pain
- reducing fever
- reducing inflammation from **rheumatic fever** (a disease characterized by fever and pain in the joints), rheumatoid arthritis, and osteoarthritis

Salicylates relieve headache and muscle aches at the same time. They can provide considerable relief in 24 hours for the inflammation of arthritis. However, they are not effective for relieving pain of the organs or smooth muscles. They are also not effective for controlling severe pain from trauma.

The various forms of salicylates have different ways of acting on the body and producing effects. They relieve pain by stopping the body from producing prostaglandin. Stopping prostaglandin production may reduce inflammation. Because prostaglandin E increases body temperature, this also reduces fever. Although salicylates will bring down a higher-than-normal body temperature, they won't decrease the temperature below normal.

Salicylates are taken orally or rectally. Some salicylates are given rectally using suppositories. This form is absorbed slowly and in an unpredictable way. Most salicylates are given by mouth.

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Food or antacids in the stomach will slow down the body's absorption of salicylates.

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Salicylates have specific interactions with several types of drugs. Patients need to be aware of the following interactions:

- Oral anticoagulants, heparin, methotrexate, oral antidiabetic agents, and insulin have increased effects or an increased risk of toxicity when taken with salicylates.
- Probenecid, sulfipyrazone, and spironolactone may have decreased efficacy when taken with salicylates.
- Corticosteroids may decrease the levels of salicylates in plasma (the liquid part of blood). This may increase the risk of ulcers.
- Alkalinizing drugs and antacids may reduce levels of salicylates in the body.
- The antihypertensive effect of angiotensin-converting enzyme (ACE) inhibitors and beta-adrenergic blockers may be reduced when these drugs are combined with salicylates.
- NSAIDs may be less effective when taken with salicylates. Taking NSAIDs and salicylates together may also increase the risk of gastrointestinal effects.



## PROCEED WITH CAUTION

### Adverse Reactions to Salicylates

Adverse reactions for salicylates vary from drug to drug. The most common adverse reactions include:

- gastric distress
- nausea
- vomiting
- bleeding tendencies

## Acetylsalicylic Acid

Acetylsalicylic acid is better known as ASA or aspirin. It's used to treat mild to moderate pain, fever, and inflammation. It may also be used to reduce the risk of heart attack or to prevent blood from clotting. ASA is available over the counter in several dosage forms and many trade names. The most common dosage forms and trade names are:

- chewing gum (Aspergum)
- chewable tablets (Bayer Children's Aspirin, St. Joseph Adult Chewable Aspirin)
- tablets (Bayer)
- enteric-coated tablets (Ecotrin, Halfprin)
- delayed-release tablets Bayer
- extended-release tablets (Extended Release Bayer 8-Hour)

By prescription, ASA is available as tablets (ZORprin, Easprin).

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Aspirin interferes with the ability of blood platelets to gather and form clots. For this reason, physicians often recommend a dose between 75 and 100 mg of aspirin daily to reduce the chance of heart attack or angina.

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In tablet form, ASA may be enteric-coated to reduce gastric irritation. In delayed-release forms, the ASA is formulated so that it takes longer to begin acting, which reduces gastric irritation. Extended-release forms are formulated so the effects last for longer periods of time.

ASA is also available over the counter in buffered forms. Buffered aspirin (Ascriptin, Bufferin) contains small amounts of antacids to decrease GI irritation. Buffered forms of aspirin have similar dosages as other tablet forms of aspirin. Because they are absorbed more slowly, they are often used for the treatment of long-term conditions, such as arthritis.

ASA may have adverse effects that are not found with other salicylates:

- **leukopenia** (decrease in white blood cells)
- prolonged bleeding time
- **thrombocytopenia** (decrease in blood platelets)



## AT THE COUNTER

## Where's the Aspirin for Babies?

*A customer is having trouble finding "baby aspirin." You help her locate it. After thanking you for your help, she asks you what the correct dose would be for her three-year-old daughter. What should you tell her?*

Children and teenagers should not use aspirin or other salicylates because these OTC drugs can cause Reye syndrome. Reye syndrome is a potentially serious or fatal disorder that can damage the brain and liver. You should suggest that she talk with the pharmacist to find out what options are available for her daughter.

## Choline Magnesium Trisalicylate

Choline magnesium trisalicylate is available by prescription. It's used to treat osteoarthritis, rheumatoid arthritis, and acute painful shoulder syndrome. This drug is administered by mouth in tablet or oral liquid form.

## Diflunisal and Salsalate

Diflunisal (Dolobid) is used to treat osteoarthritis and rheumatoid arthritis. It may also be used to relieve mild to

moderate pain. It is not used to reduce fever. Diflunisal is available by prescription in an oral tablet form. It is usually taken with food, water, or milk. This drug may greatly increase levels of acetaminophen and other NSAIDs. Patients should be advised not to use these drugs while taking diflunisal.

Salsalate (Argesic-SA) is used to treat mild pain and to reduce fever. It may also be used to treat pain and inflammation caused by arthritis. Salsalate comes in tablet form to be taken by mouth.

## Acetaminophen

**Acetaminophen** belongs to a group of drugs called paracetamol (APAP) derivatives. Acetaminophen is an OTC drug that has analgesic (pain-relieving) and antipyretic (fever-reducing) properties. Similar to salicylates, acetaminophen affects the central nervous system. Although the way it works is not completely known, it is believed to stop the body from making prostaglandin. It relieves fever by acting on the hypothalamus.

Unlike salicylates, acetaminophen does not have an anti-inflammatory effect. It also does not affect the way blood platelets work to form clots. Acetaminophen is used to treat the following:

- fever
- headache
- muscle ache
- general pain

Acetaminophen is also the preferred drug for treating fever and flu-like symptoms in children. The American Arthritis Association notes that acetaminophen is an effective pain reliever for some types of arthritis.

Acetaminophen can interact with several other drugs. Patients should be aware of the following interactions:

- The effects of oral anticoagulants and thrombolytic drugs such as warfarin may be slightly increased when taken with acetaminophen.
- The risk of liver toxicity is increased when acetaminophen is combined with long-term alcohol use, phenytoin, barbiturates, carbamazepine, or isoniazid. Therefore, dosages should be monitored in long-term use, and the maximum daily dose of acetaminophen for adults is four grams.
- The effects of some drugs may be reduced when taken with acetaminophen. These drugs include lamotrigine, loop diuretics, and zidovudine.

**Beware of acetaminophen in disguise! Many OTC and prescription medications contain acetaminophen in combination with other drugs. Patients need to take this into account when they manage their total daily dose.**

Acetaminophen is absorbed quickly from the GI tract (when taken orally) or from the mucous layer of the rec-



## PROCEED WITH CAUTION

## Salicylates for Special Populations

Because of the way salicylates affect the body, there may be some concerns with administering them to certain populations, including:

- **Children and teenagers.** Aspirin or salicylates should not be used to treat flu-like symptoms or chickenpox. These drugs can trigger **Reye syndrome**, a potentially fatal disease in children.
- **Pregnant women.** Aspirin is classified as pregnancy risk category D, meaning it has been proven to cause risk to the fetus. Other salicylates are classified as category C. These drugs pose less risk than category D drugs; however, risk to the fetus cannot be eliminated. Salicylates also appear in breast milk.
- **Surgical patients.** Patients should stop using aspirin, if possible, one week before surgery, including dental surgery. This will reduce the risk of postoperative bleeding.
- **Patients with asthma.** These patients may have a higher- than-normal sensitivity to aspirin. This may lead to bronchospasm (narrowing of breathing passages), **urticaria** (hives), **angioedema** (swelling beneath the skin), or shock.



tum (when administered rectally). Forms and common trade names of acetaminophen include:

- tablets (Aspirin Free Anacin, Tylenol)
- chewable tablets
- delayed-release tablets (Tylenol)
- orally dissolving tablets (Tylenol)
- elixir
- drops (Tylenol)
- rectal suppositories (Acephen, Feverall)
- oral suspension (Tylenol)
- oral solution (Comtrex, Tylenol)
- capsules

Oral liquid forms such as drops or elixir are used for children and patients who have difficulty swallowing. It is important to note that infant formulations (concentrated drops) are highly concentrated; therefore, the amount of medication that must be swallowed is less than the equivalent of an oral liquid. This is helpful for caregivers who are administering acetaminophen to infants, who have difficulty swallowing a great deal of liquid at a time.

For example, when administering 80 mg of Tylenol Infants' Drops, the infant would receive one dropper, which is 0.8 mL. The equivalent dose of Children's Tylenol liquid would be 1/2 teaspoon, or 2.5 mL. If the liquid dose of the concentrated drops were given instead, the infant would receive 200 mg, which is indicated for an infant weighing twice as much. Clarifying the difference between concentrated drops and liquid forms of acetaminophen is key in helping prevent an infant from receiving an overdose.

Children should not receive more than five doses of acetaminophen in a 24-hour period. In adults who have a history of alcohol abuse, their use of this drug should be limited to two grams per day. The maximum daily dose for long-term therapy is four grams, unless the patient is closely monitored by a health care provider.

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Doses of APAP higher than four grams per day can cause liver toxicity, so you will need to check the dosing on all APAP prescriptions that you receive. If a patient is receiving a prescription medication with APAP, you'll need to pay close attention to any other prescription or OTC medications the patient consumes at the same time, to see if they contain additional APAP.

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## Nonsteroidal Anti-Inflammatory Drugs

NSAIDs are typically used to combat inflammation. Their anti-inflammatory effect is equal to aspirin. Similar to salicylates, NSAIDs have analgesic and antipyretic effects. NSAIDs may affect blood platelets, but unlike aspirin, their effects are temporary. Some NSAIDs are available over the counter, and others are available only by prescription.

NSAIDs have been useful in treating the following conditions:

- ankylosing spondylitis (an inflammatory joint disease that affects the spine)
- moderate to severe rheumatoid arthritis (an inflammatory disease of the peripheral joints)
- osteoarthritis (a degenerative joint disease) in the hip, shoulder, or other large joints
- acute gouty arthritis (urate deposits in the joints)
- dysmenorrhea (severe pain and cramping during menstruation)
- migraine headaches
- bursitis and tendonitis
- mild to moderate pain

All NSAIDs are absorbed through the GI tract. They're mostly metabolized in the liver and are excreted primarily by the kidneys. NSAIDs work by acting on enzymes known as cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2). Enzymes are special proteins that trigger chemical reactions in the body. COX-1 and COX-2 enzymes convert arachidonic acid, one of the essential fatty acids, into prostaglandins. The prostaglandin made by COX-1 maintains the stomach lining. Prostaglandin produced by COX-2, however, causes inflammation. When NSAIDs stop COX-1 and COX-2 from making prostaglandins, they reduce inflammation.

There are two types of NSAIDs:

- Nonselective NSAIDs block both COX-1 and COX-2. Because COX-1 makes prostaglandins that maintain the stomach lining, nonselective NSAIDs may cause adverse GI effects.
- Selective NSAIDs are sometimes called COX-2 inhibitors. They block only the prostaglandins made by COX-2. They relieve pain and inflammation without causing significant GI effects.

People who take NSAIDs may have a higher risk of having a heart attack or a stroke than people who don't take these medications. Manufacturers of NSAIDs typically include warnings about the risk of cardiac effects on the labels. This risk may be greater for patients who take NSAIDs over long periods of time or for patients with cardiovascular conditions. NSAIDs also stop the body from making renal prostaglandins and may affect kidney function. Patients with kidney, heart, or liver conditions are at higher risk for kidney damage when taking NSAIDs.

## Nonselective Nonsteroidal Anti-Inflammatory Drugs

Many nonselective NSAIDs are available over the counter. They are used to treat the pain and inflammation of osteoarthritis and rheumatoid arthritis.

Nonselective NSAIDs may interact with other medications. Patients need to be aware of the following interactions:

- Nonselective NSAIDs may decrease the antihypertensive effects of ACE inhibitors.

- Taking antacids with nonselective NSAIDs may reduce the level of NSAIDs in the body.
- Nonselective NSAIDs taken with aspirin may increase the patient's risk of developing ulcers. Patients need to be monitored for signs of gastrointestinal bleeding.
- Taking lithium with some nonselective NSAIDs may increase lithium levels in the body.
- Nonselective NSAIDs taken with warfarin or anticoagulants may increase bleeding complications.
- Nonselective NSAIDs may increase levels of methotrexate, digoxin, and cyclosporine, leading to toxicity.

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Remind patients to follow package/prescription directions about the dose and duration of treatment of NSAIDs, especially since there are potential cardiovascular and GI risks involved.

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### Diclofenac

Diclofenac sodium (Voltaren, Voltaren XR, Solaraze) and diclofenac potassium (Cataflam) are used in the treatment of:

- ankylosing spondylitis
- actinic keratosis
- osteoarthritis
- rheumatoid arthritis
- dysmenorrhea
- pain



### PROCEED WITH CAUTION

#### Adverse Reactions to Nonselective Nonsteroidal Anti-Inflammatory Drugs

Because nonselective NSAIDs inhibit COX-1 and COX-2 enzymes, they may also cause unwanted GI effects, such as bleeding or increased risk of ulcers.

There are also many other adverse reactions associated with NSAIDs. However, most patients experience few adverse effects. The adverse reactions to nonselective NSAIDs include:

- constipation
- diarrhea
- dizziness
- drowsiness
- GI upset or pain
- GI bleeding
- ulcers
- headache
- nausea
- rash
- visual disturbances
- vomiting

Diclofenac is available by prescription. It comes in tablets to be taken by mouth. The tablets are available in delayed-release or extended-release forms. This drug is also available as a topical gel and ophthalmic solution.

### Etodolac, Fenoprofen, and Flurbiprofen

Etodolac is available by prescription for managing the pain and inflammation of osteoarthritis and rheumatoid arthritis, as well as for acute pain. It is available in capsule, tablet, and extended-release tablet forms.

Fenoprofen (Nalfon) is used for long-term management of mild to moderate pain. It's also used in the treatment of rheumatoid arthritis and osteoarthritis. This drug is available by prescription as capsules or tablets.

Flurbiprofen is used in treating the signs and symptoms of rheumatoid arthritis and osteoarthritis. It is also prescribed for treating ankylosing spondylitis. It is available by prescription in tablet form and ophthalmic solution.

### Ibuprofen

Ibuprofen is commonly used to control fever in adults and children. It's also used to treat mild to moderate pain and menstrual pain, in addition to treating symptoms of osteoarthritis and rheumatoid arthritis. Ibuprofen is available by prescription and over the counter in several different forms:

- tablets (Advil, Motrin IB, Midol Cramps and Body Aches Formula)
- prescription-strength tablets (Motrin)
- chewable tablets (Advil, Motrin)
- caplets (Motrin IB, Advil)
- liquid-gel capsules (Advil, Motrin IB)
- gelcaps (Motrin IB)
- drops (Advil, Motrin)
- oral suspension (Advil, Motrin)

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You need to know which NSAIDs are prescription and which are over the counter. Some NSAIDs are available in prescription and nonprescription strengths. Know the labeling and dosing differences. For example, nonprescription ibuprofen is 200 mg, but the prescription forms of this drug come in 400-mg, 600-mg, and 800-mg strengths.

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### Indomethacin

Indomethacin (Indocin) is available by prescription. It is used to relieve moderate to severe pain for several different chronic conditions, including:

- osteoarthritis
- rheumatoid arthritis
- ankylosing spondylitis
- gouty arthritis
- acute painful shoulder syndrome (bursitis or tendonitis)

Indomethacin may also be prescribed in the treatment of patent ductus arteriosus in newborn babies. This is a heart problem involving abnormal blood circulation. In babies, indomethacin is given by IV injection. For other conditions, the drug is available in several different forms:

- capsules
- sustained-release capsules
- oral suspension
- suppositories

Dosages vary with the form of the drug. Capsules, sustained-release capsules, and oral suspensions should be taken with food, milk, or antacids to prevent GI upset.

Like other NSAIDs, indomethacin may interact with many other drugs. In addition to the interactions that may affect all drugs in this class, you need to be aware of the following possible interactions for indomethacin:

- Indomethacin taken with bisphosphonates may increase the patient's risk of GI ulcer formation.
- Taking diflunisal or probenecid with indomethacin may increase levels of indomethacin.
- Indomethacin may increase levels of penicillamine, increasing the risk of toxic effects.
- Taking indomethacin with triamterene may cause damage to the kidneys. This combination should be avoided.

### Ketoprofen, Ketorolac, and Meloxicam

Prescription ketoprofen is used to treat pain and inflammation from osteoarthritis and rheumatoid arthritis. It may also be prescribed to treat painful menstruation. It is available in capsules and extended-release capsules.

Ketorolac is prescribed for short-term management of severe, acute pain. It may be administered as a single-dose treatment by mouth or by IM or IV injection. Ketorolac may also be given as a multiple-dose treatment in the form of tablets, injection, or ophthalmic solution. Ketorolac stops platelets from gathering to form clots. In addition to the adverse reactions that are typical of other nonselective NSAIDs, patients taking ketorolac have an increased risk of prolonged bleeding time for up to 48 hours after taking the drug.

Meloxicam (Mobic) may be used in treating juvenile rheumatoid arthritis as well as osteoarthritis and rheumatoid arthritis. It is available by prescription. Meloxicam is taken by mouth as an oral suspension or as tablets.

### Nabumetone

Nabumetone is available by prescription in tablet form. Fewer adverse reactions are associated with nabumetone than with many other NSAIDs. Nabumetone also has fewer reported interactions with other drugs than the other NSAIDs in this class. You should be aware of the following drug interactions:

- Taking nabumetone with diuretics may decrease the effectiveness of the diuretics.

- Nabumetone may cause adverse reactions when taken with warfarin or other highly protein-bound drugs.

### Naproxen

Naproxen and naproxen sodium are used to treat osteoarthritis and rheumatoid arthritis as well as many other conditions, including:

- ankylosing spondylitis
- painful menstruation
- tendonitis
- bursitis
- juvenile arthritis
- acute gout
- mild to moderate pain

Naproxen is available by prescription in several different forms, including:

- extended-release tablets (EC-Naprosyn)
- tablets (Naprosyn)
- oral suspension (Naprosyn)

Over the counter, naproxen sodium is available in the form of tablets, caplets, and gels (Aleve) and extended-release tablets (Midol Extended Relief). Naproxen sodium is also available by prescription. This drug comes in the form of tablets (Anaprox) and extended-release tablets (Naprelan).

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Similar to aspirin, naproxen may protect the heart by preventing blood from clotting.

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In addition to the adverse reactions typical of other drugs in this class, patients using naproxen may have an increased risk of the following:

- edema
- prolonged bleeding time
- palpitations
- **tinnitus** (ringing in the ears)

Taking probenecid with naproxen may decrease the body's ability to eliminate naproxen. This increases the risk of toxicity.

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Most NSAIDs should be taken with food or milk to protect the stomach. When filling prescriptions for these drugs, be sure to place a "Take with food" auxiliary label on the vial.

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### Oxaprozin, Piroxicam, and Sulindac

Oxaprozin (Daypro) is used to treat osteoarthritis and rheumatoid arthritis in adults and juvenile arthritis in children older than six years of age. It is available by prescription in tablet form.

Piroxicam (Feldene) is available by prescription for treating symptoms of osteoarthritis and rheumatoid arthritis. It's administered by mouth as a capsule. In addition to



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### Concerns About Nonselective Nonsteroidal Anti-Inflammatory Drugs

Before distributing nonsteroidal anti-inflammatory drugs, you need to be aware of some concerns for special groups:

- *Children.* Some nonselective NSAIDs are not recommended for use in children. However, ibuprofen is commonly used for reducing fever in children.
- *Elderly patients.* The risk of ulcers increases with age.
- *Pregnant women.* Some nonselective NSAIDs are pregnancy risk category B drugs, meaning there is no evidence of risk in humans. These include diclofenac, ketoprofen, and naproxen. Other nonselective NSAIDs are classified as pregnancy risk category C drugs, such as etodolac, ketorolac, meloxicam, nabumetone, oxaprozin, and piroxicam. Most NSAIDs appear in breast milk. It is best to advise patients who are breastfeeding not to use these drugs.

the adverse reactions of other drugs in this class, patients using piroxicam may have an increased risk of prolonged bleeding.

Sulindac (Clinoril) is used in the treatment of bursitis, tendonitis, and acute gouty arthritis, as well as for symptoms of osteoarthritis and rheumatoid arthritis. It's available by prescription in tablet form.

### Misoprostol

Misoprostol (Cytotec) is available in tablet form and is manufactured alone or in combination with nonselective NSAIDs to help protect the stomach from NSAID-induced gastric ulcers. Because this drug can cause abortion, premature birth, or birth defects, it should not be taken by pregnant women to reduce the risk of NSAID-induced ulcers.

### Selective Nonsteroidal Anti-Inflammatory Drugs

Selective NSAIDs are better known as COX-2 inhibitors, because they block only the prostaglandins made by COX-2 enzymes. This reduces the possibility of some adverse GI effects, such as ulcers, compared to nonselective NSAIDs.

The only COX-2 inhibitor currently available is celecoxib (Celebrex). This drug is used to relieve pain and inflammation associated with the following:

- osteoarthritis
- rheumatoid arthritis
- ankylosing spondylitis

Celecoxib is also effective for relieving pain associated with dysmenorrhea and as part of the treatment program for familial adenomatous polyposis (an inherited condition in which small polyps form in the colon). Celecoxib is available by prescription only and comes in capsule form. Celecoxib should always include the use of a **black box warning**.

(A black box warning lists any serious or life-threatening adverse reactions to the drug.)

In recent years, several COX-2 inhibitors have been withdrawn from the market. Because prostaglandins are involved in regulating blood pressure, COX-2 inhibitors may cause adverse cardiovascular effects. The use of COX-2 inhibitors also increases the risk of serious GI bleeding.

COX-2 inhibitors are classified as pregnancy risk category C drugs; most appear in breast milk. They are not recommended for women who are breastfeeding.

Similar to nonselective NSAIDs, COX-2 inhibitors may interact with other drugs. Some drug interactions that you should be aware of include the following:

- Taking COX-2 inhibitors with ACE inhibitors may lead to blood pressure difficulties.
- Antacids containing aluminum and magnesium may decrease the level of COX-2 inhibitors. These medications should be taken at separate times.
- Taking COX-2 inhibitors with aspirin leads to an increased risk of ulcers. Patients need to be monitored for GI bleeding.
- Fluconazole may have the effect of increasing the level of COX-2 inhibitors.
- Furosemide and thiazides taken with COX-2 inhibitors may increase sodium retention. This results in a higher risk of swelling and increased blood pressure.
- Taking lithium with COX-2 inhibitors may increase lithium levels.
- COX-2 inhibitors taken with warfarin increases anticoagulant effects and may lead to bleeding complications.

### Phenazopyridine Hydrochloride

**Phenazopyridine hydrochloride** is a dye used in commercial coloring that helps relieve symptoms associated with urinary tract infections, including:



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### Adverse Reactions to COX-2 Inhibitors

COX-2 inhibitors may cause the following adverse reactions:

- dyspepsia
- nausea
- vomiting
- GI ulcers (to a lesser degree than with nonselective NSAIDs)
- hypertension
- fluid retention
- peripheral edema
- dizziness
- headache





## AT THE COUNTER

## Stain Savvy

*A patient picks up two prescriptions for a urinary tract infection: SMZ-TMP and phenazopyridine. The patient remembers that one of the medications will change the color of her urine, but she cannot remember which one. What should you tell her?*

Tell the patient that phenazopyridine turns urine an orange or brownish color. Remind her that the urine will stain anything it touches, including clothing and possibly the toilet seat.

- pain
- burning
- urgency
- frequency

Taken orally, only 35 percent of phenazopyridine is metabolized by the liver. The rest is excreted unchanged in the urine. This causes the patient's urine to turn an orange or brown color.

Phenazopyridine is available over the counter (Azo-Gesic, Azo-Standard) and by prescription (Pyridium). It comes as a tablet to be taken by mouth. Phenazopyridine is usually taken three times a day after meals with a full glass of water. Phenazopyridine should not be taken for more than two days.

Phenazopyridine is sometimes included in combination with other drugs and does not cause any significant food or drug interactions. However, patients need to be aware of the following possible adverse reactions:

- If this drug builds up in the body, the patient's skin and sclera (whites of the eyes) may take on a yellow tinge. If this occurs, the patient may need to discontinue use of the drug.
- Acute renal or hepatic failure may occur.

## OPIOID AGONIST AND ANTAGONIST DRUGS

The word **opioid** refers to derivatives of the opium plant (also known as opiates) or to synthetic drugs that imitate natural narcotics.

- **Opioid agonists** are controlled substances used to relieve or decrease pain without causing the patient to lose consciousness. These drugs are sometimes called **narcotic agonists**.
- **Opioid antagonists** are drugs that work against opioid agonists to block their effects and reverse adverse reactions, such as respiratory and CNS depression, produced by those drugs.

Some drugs are classified as **mixed opioid agonist-antagonists**. These drugs act like agonists *and* antagonists by relieving pain and reducing the risk of adverse reactions.

Opioids are typically used in treating moderate to severe acute pain and in treating chronic pain resulting from cancer and other diseases.

### Opioid Agonists

Opioid agonists are mainly used to manage moderate to severe acute and chronic pain. They work by binding with opiate receptors in the central and peripheral nervous systems. When these drugs stimulate the receptors, they mimic the effects of **endorphins**. Endorphins are naturally occurring opiates that are part of the body's pain relief system. In binding with the receptors, opioid agonists provide pain control. The binding process also has the following effects on the body:

- antidiarrheal action (controlling diarrhea)
- contraction of the bladder and ureters (causing the urge to urinate more frequently)
- constriction of the bronchial muscles (reducing respiration rate)
- dilation of blood vessels, especially in the face, head, and neck
- slowing of intestinal peristalsis, or the contractions that move food along the digestive tract (resulting in constipation)
- suppression of the cough center in the brain

Opioid agonists may be administered in many different ways. Opioid agonists administered by IV injection provide the most rapid and immediate pain relief. Subcutaneous and intramuscular injections may delay the absorption of the drug, especially in patients with poor circulation. Also, many of these opioids are available as bulk powders for compounding purposes. Because opioid agonists are metabolized in the liver, the levels of the drug in the body may build up in patients with liver failure. This can cause an increased risk of **neurotoxicity** (damage to the nervous system) and seizures.

Opioid agonists have specific interactions with other drugs. Patients need to be aware of the following:

- Opioid agonists decrease breathing rate and depth. The use of opioid agonists with other drugs that also decrease respiration, such as alcohol, sedatives, hypnotics, and anesthetics, increases the patient's risk of severe respiratory depression, which can be fatal.
- Taking tricyclic antidepressants, phenothiazines, or anticholinergics with opioid agonists may cause severe constipation or urine retention.
- Drugs that may affect the analgesic effect of opioid agonists include amitriptyline, diazepam, phenytoin, protease inhibitors, and rifampin.
- Drugs that may be affected by opioid analgesics include carbamazepine, warfarin, beta-adrenergic blockers, and calcium-channel blockers.



## PROCEED WITH CAUTION

### Adverse Reactions to Opioid Agonists

One of the most common adverse reactions to opioid agonists is decreased rate and depth of breathing that worsens as the dose of the opioid is increased. This may cause periodic, irregular breathing or may trigger asthmatic attacks in susceptible patients. Other adverse reactions include:

- constipation
- flushing
- orthostatic hypotension
- pupil constriction

### Codeine

Codeine is a Schedule II controlled substance, which indicates that it has a high potential for abuse and dependence. Codeine phosphate is available as a subcutaneous injection. Codeine sulfate is available in tablet form. Codeine is also available in combination with other drugs, such as codeine with acetaminophen (Tylenol with Codeine), which is a Schedule III controlled substance. Because codeine acts directly on the cough center in the brain, it can suppress the cough reflex. Cough medications that contain codeine, such as promethazine and guaifenesin, are Schedule V controlled substances. Depending on state law, Schedule V controlled substances may or may not require a prescription. This drug is also used for relief of mild to moderate pain. Taking oral doses of codeine with food or milk can reduce potential GI discomfort.

In addition to the drug interactions that occur with all opioid agonists in this class, codeine may also cause the following interactions:

- Taking codeine with cimetidine or sodium oxybate (GHB) increases the risk of drowsiness, breathing difficulties, and seizures.
- Naltrexone or quinidine may reduce the effects of codeine.

You need to know which pain medications are controlled substances and which are not. Always double-check controlled substances when dispensing to make sure no errors are made. You can also circle and initial the quantity on the label and the hard copy to help prevent errors and keep patients from seeking additional medication when it isn't necessary.

### Fentanyl Citrate

Fentanyl citrate is also a Schedule II controlled substance. This drug is prescribed to manage moderate to severe chronic pain. Administration of fentanyl citrate may be

transmucosal (in which the drug is placed in the mouth between the cheek and gum for absorption), transdermal, or by injection.

- For transmucosal administration, fentanyl comes as buccal tablets to be inserted between the cheek and gum (Fentora) or as a flavored lozenge on a stick (Actiq). Transmucosal fentanyl is typically used for treating breakthrough cancer pain.
- For transdermal administration, fentanyl (Dura-gesic) comes as a patch to be applied to the skin. Transdermal fentanyl is generally used to manage moderate to severe chronic pain in patients who need 24-hour pain control. The patch is worn for 72 hours before it should be removed.

In addition to the adverse effects noted for all opioid agonists in this class, fentanyl may result in muscle rigidity or paralysis.

### Hydrocodone

Similar to codeine and fentanyl, hydrocodone is a Schedule II controlled substance, although it is classified as Schedule III substance when in combination form. Aside from a bulk powder for compounding, this drug is currently available only in combination with other drugs to treat coughs and acute pain. Although hydrocodone may be combined with NSAIDs, these drug combinations are not typically used to treat osteoarthritis, rheumatoid arthritis, or other chronic conditions. The dosage form of hydrocodone depends on the drug combination.

- The combination drug hydrocodone and acetaminophen (DuoCet, Lorcet, Lortab, Norco, Xodol, Co-Gesic, Lorcet Plus, Maxidone, Vicodin, Vicodin ES, Vicodin HP, Zydane, Hycet, Liquicet, Zamicet Dolorex Forte, Margesic H, Stagesic) is available in the form of tablets, capsules, oral solution, and elixir.
- Hydrocodone and ibuprofen (Reprexain, Vicoprofen) are available as coated tablets.

These drug combinations generally have interactions with drugs that affect either or both drugs in the combina-



## ON THE FRONTLINE

### Understanding Orders

*You receive an order in the pharmacy for hydrocodone/APAP. You notice that the order also includes a stool softener. Why?*

Opioid agonists like hydrocodone slow intestinal peristalsis, the action of the intestinal muscles during digestion. Long-term use of hydrocodone will result in constipation. Increasing fiber in the diet or taking a stool softener will help prevent constipation.



## HOW IT WORKS

### How Opioid Agonists Control Pain

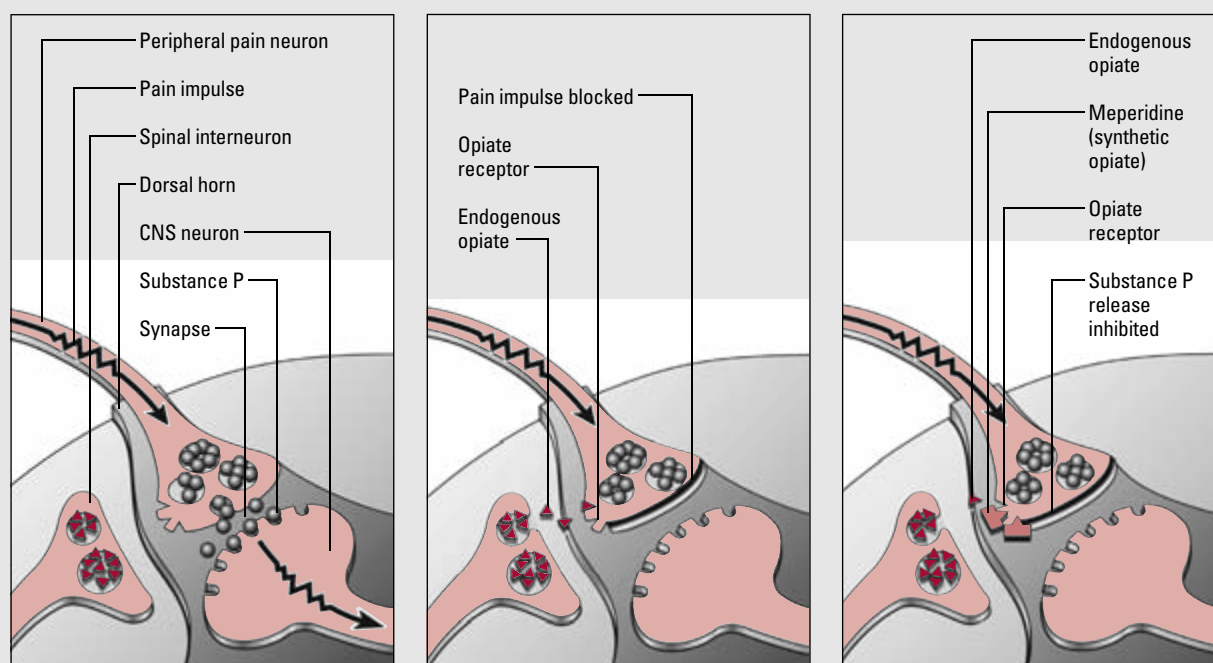
Opioid agonists, such as meperidine, block pain by mimicking the way the body naturally controls pain (figure 4-1).

In the spinal cord, pain neurons from the limbs and trunk meet the neurons of the CNS (first panel of figure). At the synapse (the junction where the signal is passed from one neuron to another), the pain neuron releases substance P (a pain neurotransmitter). Substance P helps transfer pain impulses to the CNS neurons. The CNS neurons carry those impulses to the brain.

Neurons in the spine release natural opiates. When a natural opiate in the body binds to the pain neuron, it stops the

pain neuron from releasing substance P. This slows the movement of the pain impulse to the CNS neuron and the brain (second panel of figure).

Synthetic opiates or opioid agonists add to this pain-blocking effect by binding with open opiate receptors. This stops the release of substance P and slows the transmission of the pain impulse (third panel of figure). Opioid agonists also alter a patient's consciousness of pain, but how this mechanism works remains unknown.



**FIGURE 4-1** How opioid agonists control pain. (From *Clinical Pharmacology Made Incredibly Easy*. 2nd Ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005.)

tion. For example, taking a hydrocodone and aspirin combination drug with warfarin increases the risk of gastric bleeding.

Hydrocodone/APAP comes in a variety of strengths. Always triple-check the prescription with the product from the shelf to make sure the appropriate product has been pulled.

### Hydromorphone

Hydromorphone is also a Schedule II controlled substance. Hydromorphone (Dilaudid) is used in treating moderate to severe pain and cough. It is available in several forms, including:

- oral tablets
- oral solution
- injection
- rectal suppositories

### Levorphanol

Levorphanol (Levo-Dromoran) is prescribed for relieving moderate to severe pain. This drug is another Schedule II controlled substance. It is available as a tablet or as an injection. In addition to the adverse effects noted for all opioid agonists in this class, taking levorphanol increases the risk of visual disturbances, cardiovascular events, and effects on the central nervous system (for example, nervousness or abnormal dreams).

## Meperidine

Meperidine (Demerol, Meperitab) is a Schedule II controlled substance. This drug is available by prescription for the treatment of moderate to severe pain. It may also be used as an adjunct to anesthesia or before surgery.

Meperidine can be given by mouth, as a tablet or oral solution, and by injection. This drug is less effective when given orally. Dosage is adjusted depending on the needs of the patient.

In addition to the adverse effects typical of drugs in this class, other adverse reactions to meperidine may include:

- tremors
- palpitations
- tachycardia
- delirium

## Methadone

Similar to the opioid agonists discussed previously, methadone is a Schedule II controlled substance. Methadone (Dolophine, Methadose) is used in treating severe acute and chronic pain. It is also used in treating opioid dependence. Methadone comes in the form of tablets, tablets for oral suspension, oral solution, and as an injection. Oral administration is less effective than administration by injection. Dosage is adjusted to meet the needs of each patient.

The action of methadone is different from the action of other opioid agonists. Pain relief from methadone usually does not occur until the patient has received treatment for three to five days. Respiratory effects of methadone last longer and occur later than the drug's analgesic effects.

Methadone has the following interactions with other drugs that are not typical of other opioid agonists in this class:

- Methadone therapy increases the level of desipramine in the blood.
- Patients who are taking opioid agonist-antagonists with methadone therapy may experience withdrawal symptoms.
- Taking rifampin with methadone may decrease levels of methadone in the body.

## Morphine

Morphine is a Schedule II controlled substance. It is the most potent opioid analgesic. This drug relieves shortness of breath in patients with pulmonary edema (fluid in the lungs) and left-sided heart failure (a condition in which the heart can't pump enough blood to meet the needs of the body). The effects of other opioid agonists are often compared to morphine. Morphine dilates peripheral blood vessels. This keeps more blood in the parts of the body away from the spinal cord and brain and decreases the load on the heart.

Morphine comes in several different forms:

- tablets
- extended-release tablets (MS Contin, Oramorph)
- extended-release capsules (Avinza, Kadian)
- oral solution (Roxanol)
- injection (Astramorph, DepoDur, Duramorph PF, Infumorph PF)
- rectal suppositories

Patients should be aware that morphine in capsule form must be swallowed whole or sprinkled on applesauce. Chewing or crushing the capsules would allow a large dose of the drug to be released quickly into the body, causing serious adverse effects. In addition to the drug interactions that occur with all opioid agonists in this class, morphine may cause the following interactions:

- Taking morphine with cimetidine may result in breathing difficulties, confusion, and muscle twitching.
- The effects of skeletal muscle relaxants may be increased when taken with morphine.
- The analgesic effect of morphine is increased when taken with neostigmine.
- Morphine may increase the effects of anticoagulant drugs.
- Reserpine blocks the pain-relieving effect of morphine.

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Be sure to double-check abbreviations. The abbreviation for the drug morphine sulfate ( $\text{MSO}_4$ ) can be confused with the abbreviation for magnesium sulfate ( $\text{MgSO}_4$ ). Because these abbreviations are easily confused, many facilities do not use them. However, it's important to be familiar with these abbreviations in case you do see them.

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## Oxycodone

Oxycodone is also a Schedule II controlled substance. It is prescribed for the relief of moderate to severe pain. Oxycodone is administered in several different forms:

- capsules (OxyIR)
- concentrated solution (ETH-Oxydose, OxyFast, Roxicodone)
- tablets (Roxicodone)
- extended-release tablets (OxyContin)
- oral solution (Roxicodone)

The patient should be aware that oxycodone tablets are to be swallowed whole. Chewing or crushing the tablets can lead to toxicity. Extended-release tablets are used when around-the-clock pain relief is needed over a period of time.

Oxycodone also comes in combination with other drugs:



- oxycodone and acetaminophen (Percocet, Roxicet, Tylox, Magnacet, Endocet)
- oxycodone and aspirin (Percodan, Endodan)
- oxycodone and ibuprofen (Combunox)

These combinations also require a prescription.

### Oxymorphone

Oxymorphone, another Schedule II controlled substance, is used in the treatment of moderate to severe pain. It comes as oral tablets (Opana), extended-release tablets (Opana ER), a solution for injection (Numorphan, Opana), and a rectal suppository (Numorphan). Oxymorphone tablets, both the immediate and extended-release formulations, must be swallowed whole, rather than chewed or crushed, to avoid administering a potentially fatal dose. In addition to the typical adverse reactions associated with other opioid agonists in this class, some patients experience **pruritus** (itching).

### Propoxyphene

Propoxyphene is a Schedule IV controlled substance, meaning it has less potential for abuse than Schedule III drugs and limited potential for dependence. This drug is used to treat mild to moderate pain. Propoxyphene is administered orally in the form of tablets (Darvon, Darvon-N 100).

Propoxyphene is also included in combination with other drugs, such as propoxyphene and acetaminophen (Balacet 325, Darvocet A500, Darvocet-N 100, Darvocet-N 50). This combination drug relieves fever as well as pain.

Patients should be aware that taking propoxyphene with food or milk will minimize GI upset. In addition to drug interactions noted for other opioid agonists, propoxyphene may increase levels of carbamazepine when these two drugs are taken together.

### Remifentanyl

Remifentanyl (Ultiva) is a Schedule II controlled substance. This drug is used in inducing and maintaining anesthesia during surgery. It's also used after surgery for pain management. Remifentanyl is administered by IV injection only.

### Sufentanil

Sufentanil (Sufenta), also a Schedule II controlled substance, is used for pain relief during administration of general anesthesia in patients who are intubated and ventilated. Additionally, sufentanil is used as an anesthetic in patients undergoing surgery or as an adjunct to anesthesia.

Epidural administration may be used in combination with a low dose of bupivacaine during labor and delivery. Sufentanil is given by IV injection only. In addition to the adverse reactions associated with other opioid agonists in this class, sufentanil may cause muscle rigidity. Giving

benzodiazepines with sufentanil may lead to decreased arterial pressure.

## Mixed Opioid Agonist-Antagonists

Mixed opioid agonist-antagonists relieve pain while reducing toxic effects and dependency. Similar to opioid agonists, mixed opioid agonist-antagonists affect the CNS. It is believed that these drugs act in two different ways at the same time:

- At some opiate receptor sites, mixed opioid agonist-antagonists bind with the receptor and produce a pain relief effect similar to other opioids.
- At other opiate receptor sites, these drugs block the agonist action, reducing the adverse effects.

Mixed opioid agonist-antagonists are used for pain relief during childbirth and after surgery. They are sometimes prescribed instead of opioid agonists because they have a lower risk of drug dependence. However, patients with a history of opioid abuse shouldn't take these drugs because they could cause symptoms of withdrawal.

Because mixed opioid agonist-antagonists affect the CNS, they may interact with other CNS depressants, such as barbiturates or alcohol.

Mixed opioid agonist-antagonists are listed as pregnancy risk category C drugs. Their safety and use in breastfeeding women haven't been established.

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Mixed opioid agonist-antagonists are less likely to cause respiratory depression and constipation than opioid agonists.

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### Buprenorphine

Buprenorphine is a Schedule III controlled substance, which indicates that it has less abuse potential than Schedule II drugs and a potential for moderate physical or psychological dependence. Buprenorphine is administered as a sublingual tablet (Subutex) to treat opioid dependence. The combination drug buprenorphine and naloxone (Suboxone) also comes in sublingual tablet form for the same



## PROCEED WITH CAUTION

### Adverse Reactions to Mixed Opioid Agonist-Antagonists

The most common adverse reactions to mixed opioid agonist-antagonists are:

- euphoria
- lightheadedness
- nausea
- vomiting
- sedation

use. In addition, buprenorphine is available by injection (Buprenex) to relieve moderate to severe pain.

Buprenorphine may affect opiate receptors in the limbic system (the part of the brain involved in emotions). It seems to release slowly from receptor binding sites compared with other drugs in this class. That means the pain relief effects of buprenorphine last for longer periods of time.

Adverse reactions to buprenorphine include a decrease or increase in pulse rate and blood pressure. Buprenorphine may interact with several other drugs.

- Taking buprenorphine with diazepam may lead to respiratory and cardiovascular collapse.
- Administration of naloxone may not reverse buprenorphine's adverse respiratory effects as it does for other opioids.
- Drugs that block the action of CYP3A4 enzyme, such as erythromycin, azole antifungal agents, and protease inhibitors, may decrease the elimination of buprenorphine from the body.
- Rifampin, carbamazepine, and phenytoin may increase the clearance of buprenorphine.

### Butorphanol and Nalbuphine

Butorphanol (Stadol), a Schedule IV controlled substance, is used to treat moderate to severe pain. It may also be used before surgery to supplement balanced anesthesia and for pain relief during childbirth. Butorphanol is administered by IM or IV injection. It's also available as a nasal spray.

Nalbuphine, which is not a controlled substance, is used to relieve moderate to severe pain. In addition, it's used before surgery to supplement balanced anesthesia and for pain relief during childbirth. Nalbuphine is administered by SubQ, IM, or IV injection.

### Pentazocine

Pentazocine is a Schedule IV controlled substance. Pentazocine lactate injection (Talwin) is used to treat moderate to severe pain. It may be used before surgery or anesthesia and as a supplement to anesthesia during surgery. The injection can be given subcutaneously, intramuscularly, or intravenously.

Pentazocine is also available for oral administration in combination with other drugs. These combinations are:

- pentazocine and acetaminophen (Talacen)
- pentazocine and naloxone (Talwin NX)

### Opioid Antagonists

Opioid antagonists counteract the effects of opioids. When the opioid antagonist enters the central nervous system, it has a strong attraction for opiate receptors. However, opioid antagonists don't stimulate those receptors. Instead, the antagonist fills up the receptor sites so that the opioid (natural or synthetic) can't bind with them. The antagonist may also take the place of the opioid that binds with them. This

process, called **competitive inhibition**, stops the opioid receptors from acting and blocks their effects.

### Naloxone

Naloxone is used to reverse the effects of opioids such as respiratory depression, sedation, and lowered blood pressure. In addition, it's used to treat opioid overdose. As you read earlier in this chapter, naloxone is available in combination with buprenorphine (Suboxone) to treat opioid dependence. This drug is also available in combination with pentazocine (Talwin NX) to treat moderate to severe pain.

Naloxone is given as a SubQ, IM, or IV injection and is not a controlled substance. It is also available in a bulk powder for compounding purposes. It works by competing for the receptor sites that are used by opioid agonists. You need to be aware of the following:

- Naloxone does not produce agonist effects such as depressed breathing, hallucinations and delusions, or constricted pupils.
- Naloxone may not be effective in reversing respiratory depression associated with the use of buprenorphine.
- Because naloxone may also reverse the analgesic effect of opioids, patients taking naloxone may complain of pain or withdrawal symptoms.
- Naloxone has no significant drug interactions.

The adverse effects of naloxone are different from those of other opioid antagonists. The most common adverse reactions are nausea and vomiting. Occasionally, patients may experience hypertension and tachycardia.

### Naltrexone

Naltrexone is used to block the effects of opioids in patients with opioid dependence and in the treatment of alcohol dependence. When administered with morphine or other opioids, naltrexone blocks physical dependence on these opioids. Naltrexone is believed to work by competing for the receptor sites that are used by opioids. Naltrexone is available as tablets (ReVia) or as an extended-release injection (Vivitrol) and is not a controlled substance.

There have been no studies to test possible interactions between naltrexone and drugs other than opiates. Naltrexone should not be given to a patient who is receiving an opioid agonist or is an opioid addict.

Naltrexone may cause a variety of adverse reactions, including:

- edema, hypertension, palpitations, **phlebitis** (inflammation of a vein), or shortness of breath
- anxiety, depression, disorientation, dizziness, headache, mood changes, or nervousness
- anorexia, diarrhea, constipation, nausea, thirst, GI pain, cramps, or vomiting
- urinary frequency
- liver toxicity

## ANESTHETIC DRUGS

**Anesthetic drugs** block the perception of pain or cause a loss of feeling. They allow an individual to undergo surgery or other medical procedures without distress and pain. There are three main groups of anesthetic drugs: general anesthetics, local anesthetics, and topical anesthetics. General anesthetic drugs are further subdivided into two main types: those given by inhalation and those given intravenously.

### Inhalation Anesthetics

**Inhalation anesthetics** are used for surgery. They allow precise and quick control of the depth of the anesthesia. Most inhalation anesthetics are liquids at room temperature. Liquid anesthetics are **volatile**—they evaporate when exposed to air, changing into gas form. Liquid anesthetics require a vaporizer (a device that changes the liquid to a gas) and a special delivery system. As a gas, anesthetics are combined with oxygen. They usually enter the patient's body through a mask or tube.

Inhalation anesthetic drugs move from the lungs into the blood. The blood distributes the drug to other tissues. The drug will be distributed most rapidly to organs with high blood flow, such as the brain, liver, kidneys, and heart.

Inhalation anesthetics are mainly eliminated from the body by the lungs. Some inhalation anesthetics (enflurane, sevoflurane) are also eliminated by the liver. Metabolites are excreted in the urine.

Inhalation anesthetics work by depressing the CNS. The effects of inhalation anesthetics on the CNS are:

- loss of consciousness
- loss of responsiveness to sensory stimulation
- muscle relaxation

Inhalation anesthetics are contraindicated in the patient with a known hypersensitivity to the drug, a liver disorder, or malignant hyperthermia (a potentially fatal complication of anesthesia characterized by muscle rigidity and high fever).

Inhalation anesthetics may interact with other drugs that affect the cardiac, respiratory, or central nervous systems. These interactions may result in the following reactions:

- CNS depression
- cardiac arrhythmias
- depressed respirations

Some inhalation anesthetics, such as enflurane, increase the effects of nondepolarizing relaxants.

### Desflurane

Desflurane (Suprane) is a volatile liquid used to induce or maintain anesthesia. This drug isn't recommended for inducing anesthesia in children because of the risk of adverse



## PROCEED WITH CAUTION

### Adverse Reactions to Inhalation Anesthetics

The most common adverse reaction to inhalation anesthetics is an exaggerated response to a normal dose. After surgery, patients may experience reactions similar to those seen with other CNS depressants, including:

- **ataxia** (loss of coordination)
- confusion
- depressed breathing and circulation
- hypothermia
- nausea
- sedation
- vomiting

effects related to the upper airway. However, desflurane can be used to maintain anesthesia in children. Desflurane is administered using a special vaporizer to avoid irritating the respiratory tract.

Desflurane may reduce the effectiveness of some neuromuscular blocking drugs, including atracurium, pancuronium, and succinylcholine.

### Enflurane, Isoflurane, and Sevoflurane

Enflurane (Ethrane, Compound 347) is a volatile liquid used to induce and maintain general anesthesia. It may also be used to provide pain relief during childbirth. For delivery by Caesarean section, lower concentrations of enflurane are used to avoid increased uterine relaxation and uterine bleeding. Enflurane works quickly to induce anesthesia, and patients recover quickly.

Isoflurane (Terrell) is a volatile liquid inhalation anesthetic. It's used to induce and maintain general anesthesia.

Sevoflurane (Ultane) is used to induce and maintain general anesthesia in adults and children. It is used during inpatient and outpatient surgery. This drug can be inhaled using a mask and has a neutral odor.

### Nitrous Oxide

Nitrous oxide is a commonly used anesthetic drug that is administered in the form of a gas. Nitrous oxide is used in dental surgery to reduce patient anxiety. In dentistry, the gas is administered using a mask placed over the nose. Because the anesthetic effects of nitrous oxide are weak, for medical surgery, nitrous oxide is typically used in combination with other anesthetic drugs. Nitrous oxide has anesthetic and analgesic effects. However, it doesn't result in muscle relaxation.

### Intravenous Anesthetics

**Intravenous anesthetics** are typically used when the patient needs general anesthesia for a short period of time, such

as during outpatient surgery. They're also used to help induce general anesthesia more rapidly or to supplement inhalation anesthetics.

Different types of drugs used as intravenous anesthetics include:

- barbiturates
- benzodiazepines
- dissociatives
- hypnotics
- opiates

Intravenous anesthetics work in different ways, depending on the type of drug.

### Methohexital

Methohexital (Brevital) is a Schedule IV controlled substance. This drug is a barbiturate that is used as an anesthetic in several different situations, including:

- to induce anesthesia before other anesthetic drugs are administered
- as an adjunct to other inhalation anesthetic drugs for short surgical procedures
- with opioid analgesics, to supplement other inhalation anesthetics for longer surgical procedures
- to induce a hypnotic state (adults only)

Methohexital may be administered by IV injection, IV continuous drip, or IM injection. Methohexital sodium may be administered rectally for young children. Dosage concentration varies depending on the situation.

Taking methohexital over a long period of time will result in cumulative effects. Long-term administration of barbiturates or phenytoin before taking methohexital reduces the effectiveness of methohexital.

### Thiopental

Thiopental (Pentothal), a Schedule III controlled substance, is a barbiturate that acts quickly on the CNS to induce hypnosis and anesthesia. Thiopental has several different uses:

- to provide anesthesia for short surgical procedures (15 minutes)
- to supplement regional anesthesia
- to provide hypnosis with other pain relievers or muscle relaxants
- to control convulsions during inhalation anesthesia

Thiopental is administered by IV injection only. Dosage varies depending on the patient and the situation. Using slow injection minimizes respiratory depression.

You should be aware of several drug interactions with thiopental:

- Probenecid taken with thiopental will result in longer than normal action of thiopental.
- Taking diazoxide and thiopental together leads to hypotension.

- Zimelidine and aminophylline reduce the effects of thiopental.
- Midazolam taken with thiopental may increase the effect of thiopental.

Adverse reactions associated with thiopental include:

- respiratory depression
- hiccups, coughing, and muscle twitching
- depressed cardiac function and peripheral dilation

### Midazolam

Midazolam is a Schedule IV controlled substance. Midazolam is a benzodiazepine that works quickly to induce anesthesia. It's used to induce general anesthesia or is administered before other anesthetic drugs. Midazolam is also administered before or during diagnostic, therapeutic, or endoscopic procedures. Procedures during which midazolam is used include the following:

- bronchoscopy
- cystoscopy
- angiography
- oncology procedures
- radiology procedures
- sutures

Midazolam is administered by IM injection or by IV sedation before surgery. It also comes in the form of flavored syrup to be administered orally before inducing anesthesia in children. It should not be administered by rapid injection in neonates because of the risk of severe hypotension. Midazolam isn't used for epidural or intrathecal (injection into the spinal canal) administration.

Drug interactions specific to midazolam include the following:

- Taking midazolam with other CNS depressants increases the risk of hypoventilation, airway obstruction, or apnea.
- Midazolam taken with cimetidine, erythromycin, diltiazem, verapamil, ketoconazole, or itraconazole may result in longer than normal sedation effects.
- In neonates, taking midazolam with fentanyl increases the risk of severe hypotension.

Adverse reactions to midazolam may include:

- CNS and respiratory depression
- hypotension
- dizziness

### Ketamine

Ketamine (Ketalar), a Schedule III controlled substance, is a dissociative drug. It is used before the administration of other general anesthetics and to supplement other low-potency anesthetics such as nitrous oxide. Ketamine is also used as an anesthetic for surgical procedures that don't require muscle relaxation. Some examples of procedures in which ketamine is used include:



- skin grafting and débridement
- procedures related to the eye, ear, nose, and mouth
- procedures of the pharynx, larynx, or bronchial tree
- sigmoidoscopy
- orthopedic procedures

Ketamine is well suited for use for short periods of time, but it can be used over longer periods by giving additional doses. Ketamine is administered by IV or IM injection. Slow administration of ketamine (over periods greater than 60 seconds) reduces the chance of respiratory depression or increased blood pressure.

Ketamine acts directly on the cortex and limbic system in the brain. As a result, it produces a sense of dissociation from the environment. Patients should not drive or operate machinery for 24 hours after taking ketamine.

Ketamine may cause the following interactions with other drugs:

- Administering ketamine together with halothane increases the risk of hypotension and reduces cardiac output (the amount of blood pumped by the heart each minute).
- Giving ketamine and nonpolarizing drugs together increases neuromuscular effects, resulting in prolonged respiratory depression.
- Using barbiturates or opioids with ketamine may prolong recovery time after anesthesia.
- Ketamine plus theophylline may promote seizures.
- Ketamine and thyroid hormones may cause hypertension and tachycardia (rapid heart rate).

Adverse reactions to ketamine may include:

- prolonged recovery
- irrational behavior
- excitement
- disorientation
- delirium, hallucinations
- increased heart rate
- hypertension

## Etomidate

Etomidate (Amidate) is a hypnotic drug used to induce general anesthesia. It may also be used to supplement weak anesthetics, such as nitrous oxide, during short surgical procedures. Etomidate doesn't have analgesic effects.

In terms of drug interactions, the effects of etomidate are enhanced by verapamil, causing respiratory depression and apnea. Adverse reactions to etomidate may include hiccups, coughing, and muscle twitching.

## Propofol

Propofol (Diprivan) is a hypnotic drug that is used to induce or maintain anesthesia in surgical procedures. It may also be used for sedation in the following situations:

- diagnostic procedures
- procedures that require a local anesthetic

- intubated or respiratory-controlled patients in intensive care centers

Propofol is not recommended for inducing anesthesia in patients under the age of three years or during pregnancy.

In addition to the adverse reactions associated with etomidate, propofol may also cause respiratory depression.

## Fentanyl

Fentanyl (Sublimaze), a Schedule II controlled substance, is an opioid analgesic. (You read about this drug previously under opioid agonists.) Opiates work by binding with receptor cells scattered throughout the CNS. They stop the cells from sending signals to release neurotransmitters from sensory nerves entering the CNS. Fentanyl is used as an adjunct to general or regional anesthesia. It may also be used to maintain anesthesia and for postoperative pain and restlessness. Fentanyl may be used in combination with a neuroepileptic, such as droperidol, to produce a tranquilizing effect and pain relief for surgical procedures.

Fentanyl is administered by IM or IV injection. It has several drug interactions that are not found with other intravenous anesthetics.

- Tranquilizers such as droperidol used with fentanyl may result in decreases in blood pressure or, less commonly, increases in blood pressure.
- Diazepam with fentanyl may result in cardiovascular depression.
- The use of MAOIs with fentanyl increases the risk of hypertension.

Adverse reactions associated with fentanyl include:

- CNS and respiratory depression
- hypoventilation
- cardiac arrhythmias
- muscle rigidity

## Sufentanil

Like fentanyl, sufentanil (Sufenta) is a Schedule II controlled substance and an opioid analgesic. It's used as an anesthetic in patients undergoing surgery or as an adjunct to anesthesia. It may also be used in epidural administration along with a low dose of bupivacaine during labor and delivery. Sufentanil is given by slow IV injection. In addition to the injection formulation, sufentanil is also available as a bulk powder for compounding purposes.

In terms of drug interactions, giving benzodiazepines with sufentanil may lead to decreased arterial pressure.

## Local Anesthetics

**Local anesthetics** are administered to prevent or relieve pain in a specific area of the body. In addition, local anesthetic drugs are often used as an alternative to general anesthesia for elderly or debilitated patients.

There are two main groups of local anesthetics:

- “amide” drugs (with nitrogen in the molecular chain)
- “ester” drugs (with oxygen in the molecular chain)

The absorption of local anesthetics varies depending on the drug and the area of the body. However, distribution occurs throughout the body. Esters and amides are metabolized differently, but they both yield metabolites that are excreted in the urine.

Local anesthetics work by blocking nerve signals at the point where different nerves meet. As the local anesthetic accumulates, it causes the membrane of each nerve cell to expand. When the cell membrane expands, the nerve cell loses its ability to depolarize, which is necessary to send the nerve signal.

These drugs may be used:

- to prevent and relieve pain from medical procedures, disease, or injury
- to treat severe pain that topical anesthetics or analgesics can't relieve
- as an alternative to general anesthetics in surgery for older patients
- as an alternative to general anesthetics in surgery for patients with disorders that affect respiratory function, such as chronic obstructive pulmonary disease or **myasthenia gravis** (a disease that causes skeletal muscle fatigue)

For some procedures, a local anesthetic is combined with a drug that constricts blood vessels, such as epinephrine. Vasoconstriction helps control local bleeding and reduces absorption of the anesthetic. Reduced absorption prolongs the anesthetic's action at the site and limits its distribution and CNS effects.



## PROCEED WITH CAUTION

### Adverse Reactions to Local Anesthetics

Dose-related CNS reactions include:

- shivering
- positional headache
- pain

Dose-related reactions related to the cardiovascular system may include:

- bradycardia (slow heart rate)
- hypotension

Local anesthetic solutions that contain vasoconstrictors such as epinephrine can also produce CNS and cardiovascular reactions. These reactions include the following:

- anxiety
- restlessness
- palpitations
- tachycardia

Local anesthetics produce few significant interactions with other drugs. They can, however, produce adverse reactions.

### “Amide” Drugs

In general, amide local anesthetics are less prone to allergic reactions than their ester cousins. However, some amide drugs, such as lidocaine and bupivacaine, contain preservatives that can cause allergic reactions.

It's important to be aware that the effects of amide drugs are additive.

#### Bupivacaine

Bupivacaine (Marcaine, Sensorcaine) is available as an injection to produce local anesthesia for dental procedures and oral surgery. It's also administered for medical surgery, diagnostic and therapeutic procedures, and, in lower concentrations, for obstetrical procedures. Bupivacaine is also available in formulations that contain epinephrine.

#### Lidocaine

Lidocaine (Xylocaine) is administered for local anesthesia by infiltration methods (where the drug is administered by SubQ injection near nerve endings) and as a nerve block, such as a caudal or **epidural block**. It may also be administered by IV injection to control cardiac arrhythmias. Lidocaine may be administered with or without epinephrine.

Lidocaine has the following interactions with other drugs:

- Administration of lidocaine with beta-blockers may result in increased levels of lidocaine.
- Cimetidine administered with lidocaine may increase the risk of lidocaine toxicity.
- Administration of procainamide with lidocaine may result in additive effects that may depress cardiovascular function.
- Administration of lidocaine with succinylcholine may prolong the neuromuscular effects of succinylcholine.

#### Mepivacaine

Mepivacaine (Carbocaine, Polocaine) is typically administered as a nerve block or by infiltration for dental procedures. Mepivacaine is also administered as a block in several other situations, including:

- for peripheral nerves
- during obstetrical procedures (for example, epidural block)
- for pain management

The concentration of the solution varies depending on the purpose of the block.

#### Prilocaine

Prilocaine (Citanest) is used in dental procedures. It's administered by injection as a nerve block or by infiltration.

Prilocaine may be administered with epinephrine for longer procedures or without epinephrine for shorter procedures (15 minutes or less).

### Ropivacaine

Ropivacaine (Naropin) is administered through an IV infusion or bolus after surgery or labor to treat acute pain. Additionally, this drug is used as a local anesthetic for surgery, as an epidural block for Caesarean section, and as a major nerve block. Ropivacaine may also be administered by infiltration.

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You can recognize local anesthetics by their names: most end with the letters - *caine*.

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### “Ester” Drugs

Some “ester” types of local anesthetics are formulated with a preservative called aminobenzoic acid. Some examples of esters that include this preservative are procaine and tetracaine.

Ester drugs containing aminobenzoic acid should not be used if the patient is taking sulfonamide drugs. Aminobenzoic acid blocks the action of the sulfonamides and may lead to infection.

Chloroprocaine (Nesacaine) is used by infiltration and as a peripheral nerve block when formulated with the preservative methylparaben. Without the preservative, chloroprocaine is administered by infiltration and as peripheral and central nerve blocks.

Procaine (Novocain) is used for spinal anesthesia and for local anesthesia by local infiltration or peripheral nerve block methods. Appropriate concentrations vary. For spinal anesthesia, full anesthesia occurs about five minutes after administration.

Tetracaine (Pontocaine) is used to induce and maintain spinal anesthesia for procedures that last for long periods of time (two to three hours).

### Topical Anesthetics

**Topical anesthetics** are applied directly to unbroken skin or mucous membranes to prevent or relieve minor pain. Some injectable local anesthetics, such as lidocaine and tetracaine, are also topically effective. In addition, some topical anesthetics, such as lidocaine, are combined in other products.

Most topical anesthetics produce little systemic absorption. However, systemic absorption may occur if the patient receives frequent or high-dose applications to the eye or large areas of burned or injured skin.

Many topical anesthetics work by blocking nerve signals. Like local anesthetics, topical anesthetic accumulates in the nerve cell membranes. This causes the cell membrane to expand and lose its ability to depolarize. When the nerve signals are blocked, the patient experiences a loss of feeling or analgesic effect in the area.



### PROCEED WITH CAUTION

#### Adverse Reactions to Topical Anesthetics

Topical anesthetics can cause a hypersensitivity reaction, which may include:

- a rash
- itching
- hives
- swelling of the mouth and throat
- breathing difficulty

Topical anesthetics aren't well absorbed into systemic circulation. As a result, topical anesthetics have few interactions with other drugs.

### Lidocaine

Lidocaine is an amide anesthetic that comes in a variety of different dosage forms. It is available over the counter.

Topical forms of the drug include:

- spray
- cream
- gel
- liquid
- ointment
- pads
- swabs

For oral administration, lidocaine is available in the following dosage forms:

- spray
- cream
- gel
- liquid
- drops
- lozenges
- ointment
- paste
- swabs
- wax

Lidocaine is also available as a rectal ointment for treating hemorrhoids and as an otic solution for treating ear ache/pain.

### Tetracaine

Tetracaine (Pontocaine, Viractin, TetraVisc) is used as an ophthalmic anesthesia for short procedures such as:

- cataract removal
- diagnostic procedures involving the eye
- removing sutures or foreign bodies from the eye

### Benzocaine

Benzocaine is available over the counter to relieve topical pain and itching from minor cuts and scrapes, sunburn,

and insect bites. It may also be used to numb mucosal tissues inside the nose, mouth, rectum, or vagina to reduce pain during minor medical procedures.

Benzocaine comes in a variety of different dosage forms and strengths. Different forms of the drug may have different uses.

- Some liquids, gels, or ointments are used to relieve pain from cold sores and fever blisters.
- Other liquids are in lotion form to relieve pain and itching from scrapes, cuts, insect bites, sunburn, or other skin irritations.
- Gels, sprays, or liquid forms of benzocaine are used to reduce mouth pain associated with teething or dental procedures.
- Some sprays are used for oral or mucosal anesthesia. They control pain and suppress the gag reflex.
- Other sprays are used for soothing minor skin irritations such as minor cuts and scrapes, insect bites, or sunburns.
- Several forms of benzocaine are designed to relieve pain and itching from hemorrhoids. These formulations are creams, ointments, or sprays.
- Benzocaine is used with other drugs in several ear preparations. For example, it's used with antipyrine in a drug that's used to treat ear infections.
- Benzocaine may also be formulated in combination with dextromethorphan in lozenges to relieve symptoms of the common cold, such as sore throat or cough.

## Cocaine

Cocaine, a Schedule II controlled substance, is available as a topical solution or as a powder to mix as solution. Cocaine is also available as a bulk powder for compounding purposes. The solution can be administered in several different ways:

- using cotton applicators or packs
- dripped into a cavity
- as a spray

Topical cocaine shouldn't be used for ophthalmic procedures, because it can damage the cornea of the eye.

## Dyclonine and Dibucaine

Dyclonine is used as a topical anesthetic for mucous membranes. It is available over the counter in lozenges or solution. It is commonly used in combination products as well.

Dibucaine (Nupercainal) is an amide anesthetic used for rectal anesthesia. It is available as an ointment for relief of pain and itching due to hemorrhoids. It is available over the counter.

## Pramoxine

Pramoxine is available over the counter in several forms:

- cream (AmLactin AP, Prax, Tronothane, Sarna, Campho-Phenique)

- lotion (Prax, Sarn, Dermarest, Eczemaa)
- gel (PraxeGel, Itch-X)
- spray (Itch-X)
- wipes (Bactine)
- aerosol foam (ProctoFoam) for hemorrhoids

Pramoxine creams, gels, lotions, sprays, and wipes are mainly used to relieve itching and pain for minor skin irritations and burns. Pramoxine lotion may also be used to cleanse the anogenital area after rectal surgery and to relieve pain and itching from hemorrhoids. Pramoxine for rectal use comes in the form of foam, creams, or ointments.

Pramoxine also comes in combination with hydrocortisone. This combination drug has anesthetic and anti-inflammatory effects. It is used to treat a variety of skin conditions.

## Aromatic Compounds

Some topical anesthetics are aromatic compounds, such as benzyl alcohol and clove oil. These chemicals seem to stimulate nerve endings. This stimulation causes irritation that interferes with the perception of pain.

Benzyl alcohol can cause topical reactions such as skin irritation.

Clove oil contains eugenol, a substance that may have analgesic and antiseptic effects. Clove oil has been used in dental materials such as cements or fillers. When used topically, clove oil may have a mild anesthetic effect. Clove oil is sometimes combined with other pain-reducing products, such as lidocaine or prilocaine.

## Cooling Effect

Other topical anesthetics produce a cooling effect. Ethyl chloride spray superficially freezes the tissue, stimulating the cold-sensation receptors and blocking the nerve endings in the frozen area. However, because ethyl chloride is a refrigerant, it may produce frostbite in areas where it has been applied.

Menthol selectively stimulates the sensory nerve endings for cold, causing a cool sensation and some local pain relief. Menthol is often used in combination with other topical anesthetics in OTC preparations to treat cold sores, cold symptoms, nasal congestion, itching, minor skin irritations, and minor aches and pains.

## QUICK QUIZ

Answer the following multiple-choice questions.

1. Which of the following characteristics of acetylsalicylic acid allows it to protect the heart?
  - a. antipyretic
  - b. anti-inflammatory
  - c. anticoagulant
  - d. analgesic



2. Which of the following is *not* a possible drug interaction associated with nonselective NSAIDs?
  - a. The antihypertensive effects of ACE inhibitors are decreased.
  - b. There is an increased risk of bleeding complications with anticoagulants.
  - c. Pramoxine may cause increased levels of NSAIDs in the body, resulting in hyperventilation.
  - d. Antacids may reduce the level of NSAIDs in the body.
3. Which of the following is *not* a nonopioid analgesic drug?
  - a. salsalate
  - b. etodolac
  - c. phenazopyridine hydrochloride
  - d. sufentanil
4. Which of the following drugs can be administered to depress the CNS, resulting in loss of consciousness and muscle relaxation?
  - a. naproxen
  - b. oxaprozin
  - c. isoflurane
  - d. tetracaine
5. Which route of administration is commonly used for the drugs prilocaine and procaine?
  - a. oral solution
  - b. nerve block injection
  - c. spray
  - d. suppository

Please answer each of the following questions in one to three sentences.

1. What is the difference between selective and nonselective NSAIDs?

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2. How do opioid agonists work in the body to relieve pain? Briefly describe their mechanism of action.

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3. How do opioid antagonists counteract the effects of opioid agonists?

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4. Briefly explain the differences between general anesthesia, local anesthesia, and topical anesthesia.

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5. List three uses of topical anesthetic drugs.

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Answer the following questions as either true or false.

1. \_\_\_ Similar to salicylates, acetaminophen has an anti-inflammatory effect.
2. \_\_\_ Opioid agonists like hydrocodone slow intestinal peristalsis.
3. \_\_\_ Enflurane is an inhalation anesthetic that may be used to provide pain relief during childbirth.
4. \_\_\_ A common adverse reaction to mixed opioid agonist-antagonists is fever.
5. \_\_\_ Topical anesthetics work by causing the membranes of cells to expand and depolarize.

Match the generic name of each drug in the left column with the correct trade name from the right column.

- |               |              |
|---------------|--------------|
| 1. diflunisal | a. Pentothal |
| 2. meperidine | b. Sublimaze |
| 3. prilocaine | c. Dolobid   |
| 4. thiopental | d. Citanest  |
| 5. fentanyl   | e. Demerol   |

## DRUG CLASSIFICATION TABLE

Classification	Generic Name	Trade Name(s)
Salicylates	aspirin <i>ass'-pur-in</i>	<i>chewing gum (OTC)</i> : Aspergum <i>tablets (OTC)</i> : Bayer <i>chewable tablets (OTC)</i> : Bayer Children's Aspirin, St. Joseph Adult Chewable Aspirin <i>delayed-release tablets (OTC)</i> : Bayer <i>enteric-coated tablets (OTC)</i> : Ecotrin, Halfprin <i>extended-release tablets (OTC)</i> : Extended Release Bayer 8-Hour <i>extended-release tablets (Rx)</i> : ZORprin <i>rectal suppositories (OTC)</i> : (no longer marketed under trade name)
	buffered aspirin <i>ass'-pur-in</i>	<i>tablets</i> : Ascriptin, Aspir-Mox, Bufferin
	choline magnesium trisalicylate <i>co'-leenmag-nee'-see-um-trye-sal-ih'-sah-late</i>	<i>tablets</i> : (no longer marketed under trade name) <i>oral solution</i> : (no longer marketed under trade name)
	diflunisal <i>dye-floo'-ni-sal</i>	<i>tablets</i> : Dolobid
	salsalate <i>sal'-sa-late</i>	<i>tablets</i> : Argesic-SA
Nonsalicylates	acetaminophen <i>a-sea-tah-min'-oh-fen</i>	<i>chewable tablets</i> : (no longer marketed under trade name) <i>dissolving tablets</i> : Tylenol <i>elixir</i> : (no longer marketed under trade name) <i>drops</i> : Tylenol <i>rectal suppositories</i> : Acephen, Feverall, <i>oral suspension</i> : Tylenol <i>tablets</i> : Aspirin Free Anacin, Panadol, Tylenol <i>delayed-release tablets</i> : Tylenol 8 Hour, Tylenol Arthritis Pain <i>oral solution</i> : Comtrex Sore Throat, Tylenol <i>capsules</i> : (no longer marketed under trade name)
NSAIDs	diclofenac sodium <i>dye-kloe'-fen-ak</i>	<i>delayed-release tablets</i> : Voltaren <i>extended-release tablets</i> : Voltaren XR <i>topical gel</i> : Solaraze <i>ophthalmic solution</i> : Voltaren
	diclofenac potassium <i>dye-kloe-fen'-ak</i>	<i>tablets</i> : Cataflam
	etodolac <i>ee-toe-doe'-lak</i>	<i>capsules</i> : (no longer marketed under trade name) <i>tablets</i> : (no longer marketed under trade name) <i>extended-release tablets</i> : (no longer marketed under trade name)
	fenoprofen <i>fen-oh-proe'-fen</i>	<i>capsules</i> : Nalfon <i>tablets</i> : (no longer marketed under trade name)
	flurbiprofen <i>flure-bi'-proe-fen</i>	<i>tablets</i> : (no longer marketed under trade name) <i>ophthalmic solution</i> : Ocufen
	ibuprofen <i>eye'-byoo-proe-fen</i>	<i>chewable tablets</i> : Advil, Motrin <i>caplets</i> : Motrin IB, Advil <i>liquid-gel capsules</i> : Advil, Motrin IB

continued

**DRUG CLASSIFICATION TABLE** (continued)

Classification	Generic Name	Trade Name(s)
NSAIDs (continued)		<i>gelcaps</i> : Motrin IB <i>drops</i> : Advil, Motrin <i>oral suspension</i> : Advil, Motrin <i>tablets (Rx)</i> : Motrin <i>tablets</i> : Advil, Motrin IB, Midol Cramps and Body Aches Formula
	indomethacin <i>in-doe-meth'-a-sin</i>	<i>injection</i> : Indocin <i>oral suspension</i> : Indocin <i>capsules</i> : (no longer marketed under trade name) <i>sustained-release capsules</i> : Indocin SR <i>rectal suppositories</i> : Indocin
	ketoprofen <i>kee-toe-proe'-fen</i>	<i>tablets</i> : (no longer marketed under trade name) <i>capsules</i> : (no longer marketed under trade name) <i>extended-release capsules</i> : (no longer marketed under trade name)
	ketorolac <i>ket-ór-o-lac</i>	<i>ophthalmic solution</i> : Acular <i>tablets</i> : (no longer marketed under trade name) <i>injection</i> : (no longer marketed under trade name)
	meloxicam <i>mel-ox'-i-kam</i>	<i>tablets</i> : Mobic <i>oral suspension</i> : Mobic
	nabumetone <i>nah-byew'-meh-tone</i>	<i>tablets</i> : (no longer marketed under trade name)
	naproxen <i>na-prox'-en</i>	<i>extended-release tablets</i> : EC-Naprosyn <i>tablets</i> : Naprosyn <i>oral suspension</i> : Naprosyn
	naproxen sodium <i>na-prox'-en</i>	<i>caplets (OTC)</i> : Aleve <i>gelcaps (OTC)</i> : Aleve <i>tablets (OTC)</i> : Aleve <i>extended-release tablets (OTC)</i> : Midol Extended Relief <i>tablets (Rx)</i> : Anaprox <i>extended-release tablets</i> : Naprelan
	oxaprozin <i>oks-a-pro'zin</i>	<i>tablets</i> : Daypro
	piroxicam <i>peer-ox'-i-kam</i>	<i>capsules</i> : Feldene
	sulindac <i>sul-in'-dak</i>	<i>tablets</i> : Clinoril
	misoprostol <i>my'-so-prahst'-ole</i>	<i>tablets</i> : Cytotec
	misoprostol and diclofenac <i>my'-so-prahst'-ole dye-kloe'-fen-ak</i>	<i>delayed-release tablets</i> : Arthrotec
	celecoxib <i>sell-ah-cocx'-ib</i>	<i>capsules</i> : Celebrex
Other pain relievers	phenazopyridine hydrochloride <i>fen-az-oh-peer'-i-deen</i>	<i>tablets (Rx)</i> : Pyridium <i>tablets (OTC)</i> : Azo-Gesic, Azo-Standard
Opioid agonists	codeine <i>koe'-deen</i>	<i>injection</i> : (no longer marketed under trade name) <i>tablets</i> : (no longer marketed under trade name)

continued

**DRUG CLASSIFICATION TABLE** (continued)

Classification	Generic Name	Trade Name(s)
Opioid agonists (continued)	codeine and acetaminophen <i>koe'-deen a-sea-tah-min'-oh-fen</i>	<i>elixir</i> : (no longer marketed under trade name) <i>oral solution</i> : (no longer marketed under trade name) <i>oral suspension</i> : Capital and Codeine <i>tablets</i> : Tylenol #3, Tylenol #4
	fentanyl citrate <i>fen'-ta-nil</i>	<i>lollipops/lozenges</i> : Actiq <i>extended-release transdermal patch</i> : Duragesic <i>buccal tablets</i> : Fentora <i>injection (IV anesthetic)</i> : Sublimaze
	hydrocodone and acetaminophen <i>hy-droe-coe-done a-sea-tah-min'-oh-fen</i>	<i>tablets</i> : DuoCet, Lorcet, Lortab, Norco, Xodol, Co-Gesic, Lorcet Plus, Maxidone, Vicodin, Vicodin ES, Vicodin HP, Zydone <i>oral solution</i> : Hycet, Liquicet, Zamicet <i>capsules</i> : Dolorex Forte, Margesic H, Stagesic <i>elixir</i> : Lortab
	hydrocodone and ibuprofen <i>hy-droe-coe-done eye'-byoo-proe-fen</i>	<i>tablets</i> : Reprexain, Vicoprofen
	hydromorphone <i>hy-droe-mor'-fone</i>	<i>injection</i> : Dilaudid <i>tablets</i> : Dilaudid <i>oral solution</i> : Dilaudid <i>rectal suppositories</i> : (no longer marketed under trade name)
	levorphanol <i>lee-vor'-fa-nole</i>	<i>tablets</i> : (no longer marketed under trade name) <i>injection</i> : Levo-Dromoran
	meperidine <i>me-per-i'-deen</i>	<i>injection</i> : Demerol <i>oral solution</i> : (no longer marketed under trade name) <i>tablets</i> : Demerol, Meperitab
	methadone <i>meth'-a-doa</i> n	<i>oral solution</i> : Methadose <i>injection</i> : (no longer marketed under trade name) <i>tablets</i> : Dolophine, Methadose <i>tablet for oral suspension</i> : (no longer marketed under trade name)
	morphine <i>mor'-feen</i>	<i>extended-release capsules</i> : Kadian, Avinza <i>extended-release tablets</i> : MS Contin, Oramorph <i>injection</i> : Astramorph, DepoDur, Infumorph PF, Duramorph PF <i>oral solution</i> : Roxanol <i>tablets</i> : (no longer marketed under trade name) <i>suppositories</i> : (no longer marketed under trade name)
	oxycodone <i>ox-ee-koe'-done</i>	<i>capsules</i> : OxyIR <i>concentrated solution</i> : ETH-Oxydose, OxyFast, Roxicodone <i>tablets</i> : Roxicodone <i>extended-release tablets</i> : OxyContin <i>solution</i> : Roxicodone

continued



**DRUG CLASSIFICATION TABLE** (continued)

Classification	Generic Name	Trade Name(s)
Opioid agonists (continued)	oxycodone and acetaminophen <i>ox-ee-koe'-done a-sea-tah-min'-oh-fen</i>	<i>capsules:</i> Tylox <i>oral solution:</i> Roxicet <i>tablets:</i> Percocet, Roxicet, Perloxx, Narvox, Magnacet, Endocet
	oxycodone and aspirin <i>ox-ee-koe'-done ass'-pur-in</i>	<i>tablets:</i> Percodan, Endodan
	oxycodone and ibuprofen <i>ox-ee-koe'-done eye'-byoo-proe-fen</i>	<i>tablets:</i> Combunox
	oxymorphone <i>ox-ee-mor'-phone</i>	<i>injection:</i> Numorphan, Opana <i>rectal suppositories:</i> Numorphan <i>tablets:</i> Opana <i>extended-release tablets:</i> Opana ER
	propoxyphene <i>proe-pox'-i-feen</i>	<i>tablets:</i> Darvon-N 100 <i>capsules:</i> Darvon
	propoxyphene and acetaminophen <i>proe-pox'-i-feen a-sea-tah-min'-oh-fen</i>	<i>tablets:</i> Balacet 325, Darvocet A500, Darvocet-N 100, Darvocet-N 50
	remifentanil <i>reh-mih-fen'-tah'-nil</i>	<i>injection:</i> Ultiva
	sufentanil <i>soo-fen'-ta-nil</i>	<i>injection:</i> Sufenta
Mixed opioid agonist-antagonists	buprenorphine <i>byoo-pren-nor'-feen</i>	<i>injection:</i> Buprenex <i>sublingual tablets:</i> Subutex
	buprenorphine and naloxone <i>byoo-pren-nor'-feen nal-ox'-ohn</i>	<i>sublingual tablets:</i> Suboxone
	butorphanol <i>byoo-to'-fa-nole</i>	<i>injection:</i> Stadol <i>nasal spray:</i> (no longer marketed under trade name)
	nalbuphine <i>nal'-byoo-feen</i>	<i>injection:</i> (no longer marketed under trade name)
	pentazocine <i>pen-taz'-oh-seen</i>	<i>injection:</i> Talwin
	pentazocine and acetaminophen <i>pen-taz'-oh-seen a-sea-tah-min'-oh-fen</i>	<i>tablets:</i> Talacen
	pentazocine and naloxone <i>pen-taz'-oh-seen nal-ox'-ohn</i>	<i>tablets:</i> Talwin NX
Opioid antagonists	naloxone <i>nal-ox'-ohn</i>	<i>injection:</i> (no longer marketed under trade name)
	naltrexone <i>nal-trex'-ohn</i>	<i>tablets:</i> ReVia <i>injection:</i> Vivitrol
Inhalation anesthetics	desflurane <i>des'-floo-rane</i>	<i>inhalation liquid:</i> Suprane
	enflurane <i>en'-floo-rane</i>	<i>inhalation liquid:</i> Compound 347, Ethrane
	nitrous oxide <i>nye'-trus</i>	<i>inhalation gas:</i> (no longer marketed under trade name)
	sevoflurane <i>see-vo-floo'-rane</i>	<i>inhalation liquid:</i> Ultane
Intravenous anesthetics	methohexital <i>meth-oh-hex'-i-tal</i>	<i>injection:</i> Brevital
	thiopental <i>thye-oh-pen'-tal</i>	<i>injection:</i> Pentothal

continued

**DRUG CLASSIFICATION TABLE** (continued)

Classification	Generic Name	Trade Name(s)
Intravenous anesthetics (continued)	midazolam <i>med-zool'-ham</i>	<i>injection:</i> (no longer marketed under trade name) <i>syrup:</i> (no longer marketed under trade name)
	ketamine <i>keet'-a'-meen</i>	<i>injection:</i> Ketalar
	etomidate <i>e-tom'-i-date</i>	<i>injection:</i> Amidate
	propofol <i>proe'-po-fole</i>	<i>injection:</i> Diprivan
	fentanyl <i>fen'-ta-nil</i>	<i>injection:</i> Sublimaze <i>lollipops/lozenges (pain):</i> Actiq <i>extended-release transdermal patch (pain):</i> Duragesic <i>buccal tablets (pain):</i> Fentora
	sufentanil <i>soo-fen'-ta-nil</i>	<i>injection:</i> Sufenta
Local anesthetics	bupivacaine <i>byoo-piv'-a-kane</i>	<i>injection:</i> Marcaine, Sensorcaine
	lidocaine <i>lye'-doe-kane</i>	<i>injection:</i> Xylocaine
	mepivacaine <i>me-piv'-a-kane</i>	<i>injection:</i> Carbocaine, Polocaine
	prilocaine <i>pril'-oh-kane</i>	<i>injection:</i> Citanest
	ropivacaine <i>roe-piv'-a-kane</i>	<i>injection:</i> Naropin
	chloroprocaine <i>klor-oh-proe'-kane</i>	<i>injection:</i> Nesacaine
	procaine <i>proe'-kane</i>	<i>injection:</i> Novocain
	tetracaine <i>tet'-ra-kane</i>	<i>injection:</i> Pontocaine
Topical anesthetics	lidocaine <i>lye'-doe-kane</i>	(available in many different dosage forms under a variety of trade names)
	tetracaine <i>tet'-ra-kane</i>	<i>injection:</i> Pontocaine <i>topical solution:</i> Pontocaine <i>topical gel:</i> Viractin <i>ophthalmic solutions:</i> TetraVisc
	benzocaine <i>ben'-zoe-kane</i>	(available in many different dosage forms under a variety of trade names)
	antipyrine and benzocaine <i>an-tee-pye'-reen ben'-zoe-kane</i>	<i>otic solution/drops:</i> A/B Otic, Aurodex, Dolotic, OtoCare, Otoalgan, Pro-Otic
	cocaine <i>ko'-kane</i>	<i>topical solution:</i> (no longer marketed under trade name)
	dyclonine <i>dye'-clone-een</i>	(marketed under a large number of trade names, including combination products)
	pramoxine <i>pra-mox'-een</i>	<i>cream:</i> AmLactin AP, Prax, Tronothane, Sarna, Campho-Phenique <i>lotion:</i> Prax, Sarna, Dermarest Eczema <i>gel:</i> PrameGel, Itch-X <i>spray:</i> Itch-X <i>wipes:</i> Bactine <i>aerosol foam:</i> ProctoFoam

continued

**DRUG CLASSIFICATION TABLE** (continued)

Classification	Generic Name	Trade Name(s)
Topical anesthetics (continued)	pramoxine and hydrocortisone <i>pra-mox'-een</i>	<i>cream</i> : Analpram HC, Pramosone <i>lotion</i> : Analpram HC <i>ointment</i> : Pramosone <i>gel</i> : Novacort <i>rectal foam</i> : Proctofoam HC <i>topical foam</i> : Epifoam
	dibucaine <i>dye-byoo'-kane</i>	<i>ointment</i> : Nupercainal
	benzyl alcohol <i>ben'-zil al-ko-hal</i>	(marketed under a large number of trade names, including combination products)
	clove oil <i>klov oil</i>	
	ethyl chloride spray <i>eth'-ill klor'-ide</i>	
	menthol <i>men'-thol</i>	(marketed under a large number of trade names, including combination products)