OPIOID (NARCOTIC) ANALGESICS (Systemic)

Introduction

This monograph includes information on the following:1) Anileridine a; 2) Butorphanol b; 3) Codeine; 4) Hydrocodone c a; 5) Hydromorphone ; 6) Levorphanol ; 7) Meperidine ; 8) Methadone ; 9) Morphine ; 10) **Nalbuphine** ; 11) Opium; 12) Oxycodone ; 13) Oxymorphone ; 14) Pentazocine ; 15) Propoxyphene .

Meperidine ¾Pethidine
Propoxyphene¾Dextropropoxyphene
VA CLASSIFICATION (Primary/Secondary)
Anileridine¾CN101/CN206
Butorphanol¾CN101/
Codeine
  Oral¾CN101/; GA400
  Parenteral¾CN101/
Hydrocodone¾CN101/
Hydromorphone
  Oral¾CN101/
  Parenteral¾CN101/; RE301
  Rectal¾CN101
Levorphanol
  Oral¾CN101
  Parenteral¾CN101/
Meperidine
  Oral¾CN101
  Parenteral¾CN101/
Methadone¾CN101/; RE301
Morphine
  Oral¾CN101/; GA400
  Parenteral¾CN101/; RE301; GA400
  Rectal¾CN101/
Nalbuphine¾CN101/
Opium
  Oral¾GA400/
  Parenteral¾CN101
Oxycodone¾CN101
Oxymorphone
  Parenteral¾CN101/
  Rectal¾CN101
Pentazocine
  Oral¾CN101
  Parenteral¾CN101/
Propoxyphene¾CN101

Note: Controlled substance classification¾

Drug	U.S.	Canada
Anileridine		N
Butorphanol	II	g
Codeine	II	N
Hydrocodone	h	N
Hydromorphone	II	N
Levorphanol	II	N
Meperidine	II	N
Methadone	II	N i
Morphine	II	N
Nalbuphine	f	C
Opium	II	N
Oxycodone	II	N
Oxymorphone	II	N
Pentazocine	IV	N
Propoxyphene	IV	N

f Not a controlled substance in the U.S.

gNot commercially available in Canada.

h Commercially available in the U.S. only in combination with other active ingredients.

i Available in Canada only through practitioners authorized to treat opioid addicts.

Commonly used brand name(s):64215; Astramorph PF9; Cotanal-6515; Darvon15; Darvon-N15; Demerol7; Dilaudid5; Dilaudid-55; Dilaudid-HP5; Dolophine8; Duramorph9; Epimorph9; Hycodan4; Hydrostat IR5; Kadian9; Leritine1; Levo-Dromoran6; M S Contin9; M-Eslon9; M.O.S9; M.O.S.-S.R9; MSIR9; MS/L9; MS/L Concentrate9; MS/S9; MSIR9; Methadose8; Morphine Extra-Forte9; Morphine Forte9; Morphine H.P9; Morphitec9; Nubain10; Numorphan13; OMS Concentrate9; Oramorph SR9; OxyContin12; PMS-Hydromorphone5; PMS-Hydromorphone Syrup5; PP-Cap15; Pantopon11; Paveral3; RMS Uniserts9; Rescudose9; Robidone4; Roxanol9; Roxanol 1009; Roxanol UD9; Roxicodone12; Roxicodone Intensol12; Stadol2; Statex9; Statex Drops9; Supeudol12; Talwin14; Talwin-Nx14.
Other commonly used names are: Dextropropoxyphene Propoxyphene .

, Dihydromorphinone Hydromorphone.

, Laudanum Opium Tincture.

, Levorphan Levorphanol.

, Pethidine Meperidine.

, Papaveretum Opium (Parenteral).

c Commercially available in the U.S. only in combination with other active ingredients. See Cough/Cold Combinations (Systemic) , Opioid (Narcotic) Analgesics and Acetaminophen (Systemic), and Opioid (Narcotic) Analgesics and Aspirin (Systemic) .

Note: For a listing of dosage forms and brand names by country availability, see Dosage Forms section(s).

a Not commercially available in the U.S.

b Not commercially available in Canada.

Category

Note: All of the opioid analgesics have similar pharmacologic actions; however, clinical uses among specific agents may vary because of actual pharmacokinetic differences, differences in potential for causing adverse effects, lack of specific testing, and/or lack of clinical-use data.Analgesic¾Anileridine a; Butorphanol b; Codeine; Hydrocodone; Hydromorphone; Levorphanol; Meperidine; Methadone; Morphine; Nalbuphine; Opium; Oxycodone; Oxymorphone; Pentazocine; Propoxyphene.

Note: Butorphanol, nalbuphine, and pentazocine are opioid agonist/antagonist analgesics; the other agents in this group are opioid agonist analgesics.
Anesthesia adjunct (opioid analgesic)¾Parenteral dosage forms only: Butorphanol; Hydromorphone; Levorphanol; Meperidine; Morphine; Nalbuphine; Oxymorphone; Pentazocine.

Note: For other opioids used primarily as anesthesia adjuncts, see Fentanyl Derivatives (Systemic) .
Antidiarrheal¾Codeine; Morphine; Opium Tincture.

Note: For other opioids used only as antidiarrheals, see individual monograph listings for Difenoxin and Atropine , Diphenoxylate and Atropine, Loperamide, and Paregoric .
Antitussive¾Codeine (oral dosage forms only); Hydrocodone; Hydromorphone; Methadone; Morphine.

Note: For use of hydromorphone as an antitussive, see Cough-Cold Combinations (Systemic)¾Hydromorphone and Guaifenesin .
Suppressant (narcotic abstinence syndrome)¾Methadone; Opium Tincture.

Pulmonary edema therapy adjunct¾Morphine.

Indications

Note: Bracketed information in the Indications section refers to uses that are not included in U.S. product labeling.

Accepted

Pain (treatment)¾Morphine, methadone, and parenteral opium are indicated for relief of severe pain; codeine and propoxyphene are indicated for relief of mild to moderate pain; and the other opioid analgesics are indicated for relief of moderate to severe pain.
Epidural or intrathecal administration of small doses of opioid analgesics may provide prolonged pain relief. Although administration via these routes may decrease the risk of some side/adverse effects, respiratory depression may occur. Solutions containing a preservative must not be used. Only morphine sulfate is currently commercially available in a dosage form that is FDA-approved for administration via these routes.
For relief of pain due to acute myocardial infarction, morphine is usually considered the drug of choice. Butorphanol and pentazocine are less desirable than other opioid analgesics for this purpose because they have cardiovascular effects that tend to increase cardiac work. Although nalbuphine has not been reported to adversely affect cardiovascular function in patients with acute myocardial infarction (and may be less likely than morphine to cause hypotension), its effects in patients with severely compromised cardiac function caused by acute myocardial infarction have not been fully determined. Therefore, these agents should be used with caution in such patients.
Parenterally administered opioid analgesics (except for methadone) are indicated to provide obstetrical analgesia.
Controlled clinical studies have shown that intrathecal, but not epidural, administration of opioid analgesics provides adequate relief of labor pain. Only a preservative-free solution should be used. Morphine sulfate is the only opioid analgesic currently commercially available in a dosage form that is FDA-approved for administration via these routes.

Anesthesia, general or local, adjunct¾Parenteral dosage forms of butorphanol, [hydromorphone] , levorphanol, meperidine, morphine, nalbuphine, oxymorphone, and pentazocine are indicated to supplement general, regional, or local anesthesia 90.

During surgery, they are often used in conjunction with other agents, such as a combination of an ultrashort-acting barbiturate, a neuromuscular blocking agent, and an inhalation anesthetic (usually nitrous oxide), for the maintenance of "balanced" anesthesia.
Parenteral dosage forms of most opioid analgesics are indicated to provide analgesic, antianxiety, and sedative effects as presurgical medication. However, other medications, such as benzodiazepines, are more commonly used if the patient is not in pain.

Diarrhea (treatment)¾[Codeine] *, [morphine] , and opium tincture are indicated for treatment of diarrhea. In diarrhea caused by poisoning, these agents should not be used until the toxic material has been eliminated from the gastrointestinal tract.

Cough (treatment)¾Although only codeine (oral dosage forms), hydrocodone, and hydromorphone are indicated as antitussives, all opioid analgesics depress the cough reflex. Meperidine, oxymorphone, and propoxyphene have relatively less antitussive activity than other opioid analgesics, especially in low or moderate doses.
[Methadone and morphine are sometimes used as antitussives when severe pain is present and coughing cannot be relieved by other means.]

Opioid (narcotic) abstinence syndrome (prophylaxis and treatment); or

Opioid (narcotic) drug use, illicit (treatment)¾ Methadone is indicated as a suppressant to permit detoxification. Oral methadone is also indicated as maintenance therapy to discourage addicts from returning to illicit use of other opioid drugs.

Edema, pulmonary, acute (treatment adjunct)¾Morphine is indicated as adjunctive therapy in the treatment of acute pulmonary edema secondary to left ventricular failure.
Oxymorphone is also FDA-approved as an adjunct in the treatment of acute pulmonary edema. However, oxymorphone is rarely if ever used for this indication; morphine is the preferred medication.

[Opioid (narcotic) dependence, neonatal (treatment)]¾Opium tincture is used in diluted form in the treatment of neonatal opioid dependence.

Unaccepted

Methadone is not recommended for obstetrical analgesia because its long duration of action increases the risk of neonatal respiratory depression.

* Not included in Canadian product labeling.

Pharmacology/Pharmacokinetics

See Table 1.

See Table 2.

Physicochemical characteristics:

Molecular weight¾Anileridine: 352.46 90

Butorphanol tartrate: 477.55
Codeine phosphate: 406.37 (hemihydrate); 397.36 (anhydrous)
Codeine sulfate: 750.86 (trihydrate); 696.81 (anhydrous)
Hydrocodone bitartrate: 494.50 (hydrate); 449.46 (anhydrous)
Hydromorphone hydrochloride: 321.80
Levorphanol tartrate: 443.49 (dihydrate); 407.46 (anhydrous)
Meperidine hydrochloride: 283.80
Methadone hydrochloride: 345.91
Morphine sulfate: 758.83 (pentahydrate); 668.76 (anhydrous)
Nalbuphine hydrochloride: 393.91
Oxycodone hydrochloride: 351.83
Oxymorphone hydrochloride: 337.80
Pentazocine hydrochloride: 321.89
Pentazocine lactate: 375.51
Propoxyphene hydrochloride: 375.94
Propoxyphene napsylate: 565.72 (monohydrate); 547.71 (anhydrous)

Mechanism of action/Effect:

Opioid analgesics bind with stereospecific receptors at many sites within the central nervous system (CNS) to alter processes affecting both the perception of pain and the emotional response to pain. Although the precise sites and mechanisms of action have not been fully determined, alterations in release of various neurotransmitters from afferent nerves sensitive to painful stimuli may be partially responsible for the analgesic effects. When these medications are used as adjuncts to anesthesia, analgesic actions may provide dose-related protection against hemodynamic responses to surgical stress.

It has been proposed that there are multiple subtypes of opioid receptors, each mediating various therapeutic and/or side effects of opioid drugs. The actions of an opioid analgesic may therefore depend upon its binding affinity for each type of receptor and on whether it acts as a full agonist or a partial agonist or is inactive at each type of receptor.

At least two types of opioid receptors (mu and kappa) mediate analgesia. A third type of receptor (sigma) may not mediate analgesia; actions at this receptor may produce the subjective and psychotomimetic effects characteristic of pentazocine and, to a lesser extent, butorphanol and nalbuphine. Morphine and other opioid agonists exert their agonist activity primarily at the mu receptor, whereas buprenorphine, nalbuphine, and pentazocine exert agonist activity at the kappa and sigma receptors. Mu receptors are widely distributed throughout the CNS, especially in the limbic system (frontal cortex, temporal cortex, amygdala, and hippocampus), thalamus, striatum, hypothalamus, and midbrain as well as laminae I, II, IV, and V of the dorsal horn in the spinal cord. Kappa receptors are localized primarily in the spinal cord and in the cerebral cortex.

Nalbuphine and pentazocine may displace opioids having only agonist activity from their receptor binding sites and competitively inhibit their actions. The medications may therefore precipitate withdrawal symptoms in patients who are physically dependent on such agonists. Butorphanol appears to have no significant antagonist activity at the mu receptor; in some studies, it failed to produce withdrawal symptoms in patients physically dependent on morphine. However, butorphanol does not substitute for mu-receptor agonists sufficiently to prevent or attenuate withdrawal symptoms caused by abrupt discontinuation of these agonists in physically dependent patients. Also, opioid agonist/antagonist drugs share several pharmacologic actions that differ from those of opioids having only agonist activity; i.e., different respiratory depressant, subjective, psychotomimetic, and hemodynamic effects; lower dependence liability; and reduced severity of withdrawal symptoms produced when they are discontinued after prolonged use.

Antidiarrheal¾

Act locally and possibly centrally to alter intestinal motility.

Antitussive¾

Suppress the cough reflex by a direct central action, probably in the medulla or pons.

Suppressant (narcotic abstinence syndrome)¾

Substitute for other opioid drugs when administered orally and prevent or attenuate withdrawal symptoms during detoxification. Withdrawal symptoms that may occur when the substituted opioid is discontinued are usually greatly reduced in severity. With continued administration, methadone may produce cross-tolerance to the euphoric effects of other opioid drugs, thereby reducing the patient"s desire for such drugs.

Biotransformation:

Hepatic; also in intestinal mucosa.

Precautions to Consider

Pregnancy/Reproduction

Pregnancy¾Risk-benefit must be considered because opioid analgesics cross the placenta. Regular use during pregnancy may cause physical dependence in the fetus, leading to withdrawal symptoms (convulsions, irritability, excessive crying, tremors, hyperactive reflexes, fever, vomiting, diarrhea, sneezing, and yawning) in the neonate. Use of methadone by pregnant women participating in methadone maintenance programs has also been associated with fetal distress in uteroand low birth weight.
For butorphanol, nalbuphine, pentazocine, and propoxyphene: Although studies in humans have not been done, studies in animals have not shown that these agents cause adverse effects on fetal development (Pentazocine and naloxone tablets¾FDA Pregnancy Category C).
For codeine, hydrocodone, hydromorphone, morphine, and opium: Although teratogenic effects in humans have not been documented, controlled studies have not been done. Studies in animals have shown codeine (single dose of 100 mg per kg) to cause delayed ossification in mice and (in doses of 120 mg per kg) increased resorptions in rats, and hydrocodone, hydromorphone, and morphine to be teratogenic in very high doses (FDA Pregnancy Category C).
For anileridine, levorphanol, meperidine, methadone, oxycodone, and oxymorphone: Although teratogenic effects in humans have not been documented, controlled studies have not been done 90.

Labor and delivery¾Opioid analgesics, including epidurally or intrathecally administered opioids, readily enter the fetal circulation when used during labor and may cause respiratory depression in the neonate, especially the premature neonate. These agents should be used with caution, if at all, during the delivery of a premature infant. Methadone is not recommended for obstetrical analgesia because its long duration of action increases the risk of neonatal respiratory depression. Also, morphine, hydromorphone, codeine, and possibly other opioids may prolong labor. Intrathecal administration of up to 1 mg of morphine sulfate has little effect on the first stage of labor but may prolong the second stage of labor.

Breast-feeding

Problems in humans with most opioid analgesics have not been documented. Butorphanol, codeine, meperidine, methadone, morphine, and propoxyphene are distributed into breast milk. Information concerning the distribution of other opioid analgesics into breast milk is lacking. With usual analgesic doses, concentrations of those drugs known to be distributed into breast milk are generally low. However, risk-benefit must be considered when methadone is administered to a nursing mother in a methadone maintenance program because use of maintenance doses may cause physical dependence in the infant.

Pediatrics

Children up to 2 years of age may be more susceptible to the effects, especially the respiratory depressant effects, of these medications.
Paradoxical excitation is especially likely to occur in pediatric patients receiving opioid analgesics.

Geriatrics

Geriatric patients may be more susceptible to the effects, especially the respiratory depressant effects, of these medications. Also, geriatric patients are more likely to have prostatic hypertrophy or obstruction and age-related renal function impairment, and are therefore more likely to be adversely affected by opioid-induced urinary retention. In addition, geriatric patients may metabolize or eliminate these medications more slowly than younger adults. Lower doses or longer dosing intervals than those usually recommended for adults may be required, and are usually therapeutically effective, for these patients.

Dental

Opioid analgesics may decrease or inhibit salivary flow, thus contributing to the development of caries, periodontal disease, oral candidiasis, and discomfort.

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):
See Table 3.

Laboratory value alterations

The following have been selected on the basis of their potential clinical significance (possible effect in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):
With diagnostic test results

Gastric emptying studies

(opioid analgesics delay gastric emptying, thereby invalidating test results)

Hepatobiliary imaging using technetium Tc 99m disofenin

(delivery of technetium Tc 99m disofenin to the small bowel may be prevented because opioid analgesics [except for butorphanol] may cause constriction of the sphincter of Oddi and increased biliary tract pressure; these actions result in delayed visualization and thus resemble obstruction of the common bile duct)

With physiology/laboratory test values

Cerebrospinal fluid (CSF) pressure

(may be increased; effect is secondary to respiratory depression-induced carbon dioxide retention)

Plasma amylase activity and

Plasma lipase activity

(may be increased because opioid analgesics [except butorphanol] can cause contractions of the sphincter of Oddi and increased biliary tract pressure; the diagnostic utility of determinations of these enzymes may be compromised for up to 24 hours after the medication has been given)

Serum alanine aminotransferase (ALT [SGPT]) and

Serum alkaline phosphatase and

Serum aspartate aminotransferase (AST [SGOT]) and

Serum bilirubin and

Serum lactate dehydrogenase (LDH)

(activity may be increased in patients receiving propoxyphene)

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)¾ not necessarily inclusive (>> = major clinical significance).
Except under special circumstances, this medication should not be used when the following medical problems exist

For all opioid analgesic usage

>> Diarrhea associated with pseudomembranous colitis caused by cephalosporins, lincomycins (possibly including topical clindamycin), or penicillins or

>> Diarrhea caused by poisoning, until toxic material has been eliminated from gastrointestinal tract

(opioid analgesics may slow elimination of toxic material, thereby worsening and/or prolonging the diarrhea)

>> Respiratory depression, acute

(may be exacerbated)

For epidural or intrathecal administration

>> Any condition that precludes epidural or intrathecal administration, such as:
>> Coagulation defects caused by anticoagulant therapy or hematologic disorders

(trauma to a blood vessel during administration may result in uncontrollable CNS or soft tissue hemorrhage)

>> Infection at or near site of administration

(risk of spreading the infection into the CNS)

Risk-benefit should be considered when the following medical problems exist

For all opioid analgesics

Abdominal conditions, acute

(diagnosis or clinical course may be obscured)

Allergic reaction to the opioid analgesic considered for use, history of

>> Asthma, acute attack or

>> Respiratory impairment or disease, chronic

(opioids may decrease respiratory drive and increase airway resistance in patients with these conditions)

Cardiac arrhythmias or

Convulsions, history of

(may be induced or exacerbated by opioids; meperidine and propoxyphene may be especially likely to induce or exacerbate convulsions; with meperidine, the proconvulsant activity of its metabolite normeperidine may be responsible)

Drug abuse or dependence, current or history of, including alcoholism, or

Emotional instability or

Suicidal ideation or attempts

(patient predisposition to drug abuse)

Gallbladder disease or gallstones

(opioids [except butorphanol] may cause biliary contraction)

Gastrointestinal tract surgery, recent

(opioids may alter gastrointestinal motility)

Head injury or

Increased intracranial pressure, pre-existing or

Intracranial lesions

(risk of respiratory depression and further elevation of cerebrospinal fluid pressure is increased; also, opioids may cause sedation and pupillary changes that may obscure clinical course of head injury)

Hepatic function impairment

(opioids metabolized in liver)

Hypothyroidism

(risk of respiratory depression and prolonged CNS depression is greatly increased)

>> Inflammatory bowel disease, severe

(risk of toxic megacolon may be increased, especially with repeated dosing)

Prostatic hypertrophy or obstruction or

Urethral stricture or

Urinary tract surgery, recent

(opioids may cause urinary retention)

Renal function impairment

(increased risk of convulsions [with meperidine] or other adverse effects because opioids and/or their metabolites excreted primarily via kidneys; also, opioids may cause urinary retention)

Caution is also advised in administration to very young, elderly, or very ill or debilitated patients, who may be more sensitive to the effects, especially the respiratory depressant effects, of these medications.

For butorphanol, nalbuphine, or pentazocine only (in addition to those medical problems listed above)

Dependence on opioid agonist analgesics, current

(nalbuphine and pentazocine may precipitate, and butorphanol does not prevent occurrence of, withdrawal symptoms)

Hypertension

(butorphanol may increase blood pressure in these patients when used as presurgical medication)

>> Myocardial infarction, acute

(pentazocine and butorphanol may increase cardiac work; effects of nalbuphine in patients with severely compromised cardiac function have not been fully evaluated)

For epidural or intrathecal administration (in addition to those medical problems listed above as applying to all opioid analgesics)

Dependence on opioid analgesics, current

(low doses of opioids administered via epidural or intrathecal injection will not prevent withdrawal symptoms from occurring in a physically dependent patient)

Patient monitoring

The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on condition; >> = major clinical significance):
>> Respiratory function

(monitoring recommended for at least 24 hours following epidural or intrathecal injection because delayed respiratory depression may occur up to 24 hours after administration via these routes)

Side/Adverse Effects

See Table 4.

Note: Physical dependence, with or without psychological dependence, may occur with chronic administration of opioid analgesics; an abstinence syndrome may occur when these drugs are discontinued. Specific withdrawal symptoms that may occur, and their severity, depend upon the specific drug used, the abruptness of withdrawal, and the degree to which dependence has developed. Butorphanol, nalbuphine, and pentazocine have lower dependence liability and potential for abuse than opioid agonists; codeine and propoxyphene have lower dependence liability and potential for abuse than other agonists because of their comparatively lower potency with usual doses.
Epidural or intrathecal administration does not eliminate the risk of severe side effects common to systemic opioid analgesics. Respiratory depression may occur shortly after administration because of direct venous redistribution to the respiratory centers in the CNS. Also, delayed respiratory depression may occur up to 24 hours after administration, possibly as the result of rostral spread of the medication. Intrathecal administration and/or injection into thoracic sites are more likely to cause respiratory depression than epidural administration and/or injection into lumbar sites.
Following epidural or intrathecal administration of morphine, urinary retention occurs very frequently (incidence about 90% in males and somewhat lower in females) and may persist for 10 to 20 hours following injection. Catheterization may be required. Also, dose-related generalized pruritus occurs frequently. Excessive sedation is uncommon, and loss of motor, sensory, or sympathetic function does not occur.

Those indicating possible withdrawal and the need for medical attention if they occur after medication is discontinued

Body aches; diarrhea ; fast heartbeat; fever, runny nose, or sneezing; gooseflesh; increased sweating; increased yawning; loss of appetite; nausea or vomiting; nervousness, restlessness, or irritability; shivering or trembling; stomach cramps; trouble in sleeping; unusually large pupils; weakness

Note: The signs and symptoms of withdrawal listed above are characteristic of the abstinence syndrome produced by abrupt discontinuation of mu-receptor agonists such as morphine. The milder abstinence syndrome produced by abrupt discontinuation of opioids having mixed agonist/antagonist activity may also include some of these signs and symptoms.
It has been proposed that adverse effects (such as tachycardia, hypertension, hyperpnea, hyperalgesia, nausea, and vomiting) occurring (rarely) after naloxone is administered for postoperative reversal of opioid effects following a lengthy surgical procedure may be manifestations of an induced abstinence syndrome in acutely dependent individuals. However, other symptoms more commonly associated with an opioid withdrawal syndrome have not been reported.

Overdose

For specific information on the agents used in the management of opioid (narcotic) analgesics overdose, see:
· Naloxone (Systemic) monograph.
For more information on the management of overdose or unintentional ingestion, contact a Poison Control Center (see Poison Control Center Listing).

Clinical effects of overdose

The following effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:
Acute and chronic

Cold, clammy skin; confusion; convulsions; dizziness, severe; drowsiness, severe; low blood pressure; nervousness or restlessness, severe; pinpoint pupils of eyes; slow heartbeat; slow or troubled breathing; unconsciousness; weakness, severe

Note: Convulsions are more likely to occur with meperidine or propoxyphene than with other opioids.

Treatment of overdose

To decrease absorption¾Emptying the stomach via induction of emesis or gastric lavage (if the opioid was taken orally). However, treatment of respiratory depression or other potentially life-threatening adverse effects must take precedence.
Specific treatment¾Administering the opioid antagonist naloxone. However, larger doses of naloxone may be required for treatment of overdose with butorphanol, nalbuphine, pentazocine, or propoxyphene. Naloxone injections may be repeated at two- to three-minute intervals as needed. The fact that naloxone may also antagonize the analgesic actions of opioid analgesics and may precipitate withdrawal symptoms in physically dependent patients must be kept in mind. For reversal of postoperative opioid depression, dosage of naloxone must be carefully titrated to avoid interference with control of postoperative pain or causing other adverse effects; hypertension and tachycardia, sometimes resulting in left ventricular failure and pulmonary edema, have occurred following naloxone administration in these circumstances (especially in cardiac patients). See the package insert or Naloxone (Systemic) for specific dosing guidelines for use of this product.
Monitoring¾Continuing to monitor the patient (mandatory because the duration of action of the opioid analgesic may exceed that of the antagonist) and administering additional naloxone as needed.

Alternatively, initial treatment may be followed by continuous intravenous infusion of naloxone, with the rate of infusion being adjusted according to patient response.
Supportive care¾Establishing adequate respiratory exchange through provision of a patent airway and institution of assisted or controlled respiration. Administering intravenous fluids and/or vasopressors and using other supportive measures as needed. Patients in whom intentional overdose is confirmed or suspected should be referred for psychiatric consultation.

Patient Consultation

As an aid to patient consultation, refer to Advice for the Patient, Narcotic Analgesics¾For Pain Relief (Systemic),Narcotic Analgesics¾For Surgery and Obstetrics (Systemic), and Opium Preparations (Systemic) .
In providing consultation, consider emphasizing the following selected information (>> = major clinical significance):
Before using this medication

>> Conditions affecting use, especially:

Sensitivity to the opioid considered for use, history of
Pregnancy¾Opioids cross the placenta; regular use by pregnant women may cause physical dependence in the fetus and withdrawal symptoms in the neonate
Breast-feeding¾Butorphanol, codeine, meperidine, methadone, morphine, and propoxyphene are known to be distributed into breast milk; high-dose methadone may cause dependence in nursing infants
Use in children¾Children up to 2 years of age are more susceptible to the effects of opioids, especially respiratory depression; also, children may be more likely to experience paradoxical CNS excitation during therapy
Use in the elderly¾Geriatric patients are more susceptible to the effects of opioids, especially respiratory depression
Dental¾May cause dryness of mouth, which can lead to caries, periodontal disease, oral candidiasis, and discomfort
Other medications, especially alcohol or other CNS depressants, monoamine oxidase inhibitors, naltrexone, rifampin, and zidovudine
Other medical problems, especially diarrhea caused by antibiotics or poisoning, asthma or other respiratory problems, and severe inflammatory bowel disease
Proper use of this medication

Proper administration of

>> Injections (if dispensed to the patient for home use)

>> Meperidine syrup¾Mixing with 1/2 glass (4 ounces) of water to lessen numbing effect in mouth and throat

>> Methadone oral concentrate¾Diluting with water to at least 1 ounce before taking, unless premixed at a methadone treatment center

>> Methadone dispersible tablets¾Must be dissolved in water or fruit juice before taking

Morphine oral liquid¾May be mixed with fruit juice to improve taste

>> Morphine extended-release tablets¾Swallowing tablets whole; not breaking, crushing, or chewing

Suppository dosage forms¾Proper administration technique

Proper administration of opium tincture

Medication may be diluted in water, which will cause it to turn milky

Taking with food or meals if gastrointestinal irritation occurs

>> Importance of not taking more medication than the amount prescribed because of danger of overdose and habit-forming potential

>> Not increasing dose if medication is less effective after a few weeks; checking with physician

Missed dose (if on scheduled dosing): Taking as soon as possible; not taking if almost time for next dose; not doubling doses
>> Proper storage
Precautions while using this medication

Regular visits to physician to check progress during long-term therapy

>> Avoiding use of alcoholic beverages or other CNS depressants during therapy, unless prescribed or otherwise approved by physician

>> Caution if dizziness, drowsiness, lightheadedness, or false sense of well-being occurs

>> Caution when getting up suddenly from a lying or sitting position

Lying down if nausea or vomiting, or dizziness or lightheadedness occurs

Need to inform physician or dentist of use of medication if any kind of surgery (including dental surgery) or emergency treatment is required

Possible dryness of mouth; using sugarless gum or candy, ice, or saliva substitute for relief; checking with dentist if dry mouth continues for more than 2 weeks

>> Checking with physician before discontinuing medication after prolonged use of high doses; gradual dosage reduction may be necessary to avoid withdrawal symptoms

>> Suspected overdose: Getting emergency help at once

For opium tincture when used as antidiarrheal only

>> Consulting physician if diarrhea continues and/or fever develops

Side/adverse effects

Signs of potential side effects, especially respiratory depression or impairment; allergic reactions; confusion, convulsions, hallucinations, mental depression, or other signs of CNS toxicity; hepatotoxicity; hypertension; and paradoxical CNS excitation, especially in children

General Dosing Information

These medications may suppress respiration, especially in very young, elderly, very ill, or debilitated patients and those with respiratory problems. Lower doses may be required for these patients. However, elderly patients may also be more sensitive to the analgesic effects of these medications so that lower doses or an increased dosing interval may be sufficient to provide effective analgesia.
Dosage and dosing intervals should be individualized on the basis of the potency and duration of action of the specific drug used, the severity of pain, the condition of the patient, other medications given concurrently, and patient response.
Concurrent administration of a nonopioid analgesic (such as aspirin or other salicylates, other nonsteroidal anti-inflammatory analgesics, or acetaminophen) with opioid analgesics provides additive analgesia and may permit lower doses of the opioid analgesic to be utilized.
Some clinicians recommend that patients in severe chronic pain receive opioid analgesics on a fixed dosage schedule so that they remain free of pain rather than on an as needed basis after pain recurs. The medication should be given orally if possible.
Tolerance to many of the effects of these medications may develop with repeated administration. The first sign of tolerance is usually a decrease in the duration of adequate analgesia. Tolerance to the respiratory depressant effects of opioid analgesics develops concurrently with tolerance to their analgesic effects. Careful adjustment of dosage as required to provide adequate analgesia is not likely to increase the risk of respiratory depression. Patients who become tolerant to one of these agents may be partially cross-tolerant to the others. However, when an alternate opioid analgesic is substituted for one to which tolerance has developed, it is recommended that one-half of the equianalgesic dose of the new medication be used initially. Dosage of the new medication may then be adjusted as necessary.
Psychological and physical dependence may occur with chronic administration of opioid analgesics, including epidurally or intrathecally administered opioid analgesics; an abstinence syndrome may occur when these drugs are discontinued. Physical dependence in patients receiving prolonged therapy for severe chronic pain rarely leads to true addiction, i.e., a desire to continue taking the drug (for its euphoric effect) after it is no longer required for treatment. Fear of causing addiction should not result in failure to provide adequate pain relief, although caution is advised if patient predisposition toward drug abuse is known or strongly suspected. Gradual withdrawal may minimize the development of withdrawal symptoms following prolonged use.
For parenteral dosage forms only

Rapid intravenous injection of most opioid analgesics has caused anaphylactoid reactions, severe respiratory depression, hypotension, peripheral circulatory collapse, and cardiac arrest. It is recommended that when an opioid analgesic must be given intravenously, dosage should be reduced and a dilute solution should be injected slowly over a period of several minutes. An opioid antagonist and equipment for artificial ventilation should be available.
When an opioid analgesic is administered parenterally, the patient usually should be lying down and should remain recumbent for a period of time to minimize side effects such as hypotension, dizziness,

lightheadedness, nausea, and vomiting. If these side effects occur in an ambulatory patient, they may be relieved if the patient lies down.
In patients with shock, impaired perfusion may prevent complete absorption following intramuscular or subcutaneous injection. Repeated administration may result in overdose due to an excessive amount suddenly being absorbed when circulation is restored.
Opioid analgesics may not provide sufficient analgesia to prevent or overcome hemodynamic responses to surgical stress when used as the sole intravenous supplement to nitrous oxide for the maintenance of balanced anesthesia. Concurrent use of other medications, such as a benzodiazepine, an ultrashort-acting barbiturate, or a potent hydrocarbon inhalation anesthetic, may be required.
Epidural or intrathecal administration of opioid analgesics should be performed only by physicians experienced in these techniques. Solutions containing a preservative must not be injected via these routes. Resuscitative equipment and medications should be immediately available for management of respiratory depression or other complications that may arise from inadvertent intrathecal or intravascular administration. Also, facilities for adequate monitoring of the patient's respiratory status must be available.
For epidural or intrathecal administration, injection into the lumbar area may be preferred because of the increased risk of respiratory depression with injection into the thoracic area. Also, the epidural route is preferred, whenever possible, because of the increased risk of respiratory depression with intrathecal administration.
Prior to epidural administration, proper placement of the needle or catheter in the epidural space must be verified. Aspiration to check for blood in the cerebrospinal fluid may be performed; however, the fact that intravascular administration is possible even when aspiration for blood is negative must be kept in mind. Alternatively, administration of 5 mL (3 mL for obstetrical patients) of preservative-free 1.5% lidocaine hydrochloride with epinephrine 1:200,000 injection may be used to verify placement in the epidural space. Tachycardia occurring after injection of the test medication indicates that the medication has entered the circulation; sudden onset of segmental anesthesia indicates that the medication has been administered intrathecally.
Following epidural or intrathecal injection of an opioid analgesic, administration of low doses of naloxone via continuous intravenous infusion for 24 hours may decrease the incidence of potential side effects without interfering with the analgesic effectiveness of the medication.

ANILERIDINE

Summary of Differences

Pharmacology/pharmacokinetics:¾
Equivalence¾:
75 mg via oral administration therapeutically equivalent to 10 mg of intramuscular morphine. 90

Biotransformation¾:
Metabolized mostly in the liver 90.

Onset of action¾:
Oral: 15 minutes 90

Duration of action¾:
2 or 3 hours 90

Excretion¾:
Very little is excreted in the urine 90.

Oral dosage forms

ANILERIDINE HYDROCHLORIDE TABLETS USP

Usual adult dose

Analgesic¾
Oral, 25 to 50 mg (base) every 6 hours as needed 90.

Usual pediatric dose

Analgesic¾
Dosage in patients up to 12 years of age has not been established 90.

Strength(s) usually available
U.S.¾Not commercially available.
Canada¾25 mg (base) (Rx)[Leritine 90]

Packaging and storage:

Store between 15 and 30 °C (59 and 86 °F). Protect from light 90.

Note: Controlled substance in Canada.

BUTORPHANOL

Summary of Differences

Indications¾
Caution required when used as analgesic to relieve pain due to acute myocardial infarction because of cardiovascular effects that tend to increase cardiac work.

Pharmacology/pharmacokinetics¾
Mechanism of action/effect:
An opioid agonist/antagonist analgesic.
Agonist: Has agonist activity at the kappa and sigma receptors.
Antagonist: Probably has no direct antagonist activity at the mu receptor; antagonist effects may result from failure to substitute for mu-receptor agonists sufficiently to prevent or attenuate withdrawal symptoms in physically dependent patients.

Equivalence:
2 mg via intramuscular injection therapeutically equivalent to 10 mg of intramuscular morphine.

Protein binding:
High.

Half-life:
2.5-4 hours.

Onset of action:
Intramuscular: 10-30 minutes.
Intravenous: 2-3 minutes.

Time to peak concentration:
0.5-1 hour.

Peak plasma concentration:
2.2 nanograms/mL.

Time to peak effect:
Intramuscular: 30-60 minutes.
Intravenous: 30 minutes.

Duration of action (nontolerant patients only; decreases as tolerance develops during chronic therapy):
Intramuscular: 3-4 hours.
Intravenous: 2-4 hours.

Elimination:
72% Renal, < 5% as unchanged buprenorphine; 15% biliary.

Precautions¾
Laboratory value alterations:
Does not interfere with hepatobiliary imaging.
Does not increase plasma amylase or lipase activity.

Medical considerations/contraindications:
Caution not required in gallbladder disease or gallstones.
Also, should be used with caution in patients physically dependent on opioid agonists, in hypertensive patients (when used preoperatively), and in patients with acute myocardial infarction.

Side/adverse effects¾
Less likely to cause constipation than most other opioids.
Biliary spasm has not been reported.
Rarely, may cause subjective and psychotomimetic effects characteristic of sigma receptor agonists.
Has lower dependence liability than opioid agonists.
Withdrawal symptoms less severe than those produced by opioid agonist analgesics.

Parenteral Dosage Forms

BUTORPHANOL TARTRATE INJECTION USP

Usual adult dose

Analgesic¾
Intramuscular, 1 to 4 mg (usually 2 mg) every three to four hours as needed.
Intravenous, 500 mcg (0.5 mg) to 2 mg (usually 1 mg) every three to four hours as needed.
Anesthesia adjunct¾
Preoperative¾
Intravenous, usually 2 mg sixty to ninety minutes prior to surgery, although dosage must be individualized 1.

Balanced anesthesia¾
Intravenous, initially 1 to 4 mg, 2 followed by supplemental doses of 500 mcg (0.5 mg) to 1 mg as needed 1, 2.

Note:
Dosage must be individualized. Supplemental doses of up to 60 mcg (0.06 mg) per kg of body weight may be necessary in some patients 1.

The total quantity of butorphanol required during surgery usually ranges between 60 and 180 mcg (0.06 and 0.18 mg) per kg of body weight.

Usual pediatric dose

Dosage in patients up to 18 years of age 11 has not been established.

Strength(s) usually available

U.S.¾With preservative (benzethonium chloride 0.1 mg/mL)

2 mg per mL (Rx)[Stadol 19]

Without preservative

1 mg per mL (Rx)[Stadol 19]

2 mg per mL (Rx)[Stadol 19]

Canada¾Not commercially available.

Packaging and storage:

Store between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from light. Protect from freezing.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.

Note: Controlled substance in the U.S.

CODEINE

Summary of Differences

Indications¾
Oral dosage forms also indicated as antitussive.
Also, used as antidiarrheal.

Pharmacology/pharmacokinetics¾
Mechanism of action/effect:
An opioid agonist analgesic; exerts agonist activity primarily at the mu receptor, but with usual doses is relatively weak.

Equivalence:
120 mg via intramuscular injection or 200 mg via oral administration therapeutically equivalent to 10 mg of intramuscular morphine.

Protein binding:
Very low.

Half-life:
2.5-4 hours.

Biotransformation:
Hepatic; about 10% demethylated to morphine.

Onset of action:
Analgesic¾
Intramuscular¾10-30 minutes.
Subcutaneous¾10-30 minutes.
Oral¾30-45 minutes.

Time to peak effect:
Analgesic¾
Intramuscular¾30-60 minutes.
Oral¾1-2 hours.

Duration of action:
Analgesic (in nontolerant patients only; decreases as tolerance develops during chronic therapy): Intramuscular, subcutaneous, or oral¾4 hours.
Antitussive: Oral¾4-6 hours.

Elimination:
Renal, 5-15% as unchanged codeine and 10% as unchanged or conjugated morphine.

Side/adverse effects¾

More likely than most other opioids to cause constipation, especially during chronic therapy.
Has lower dependence liability than most other opioid agonists.
Withdrawal symptoms less severe than those produced by stronger opioid agonist analgesics.

Additional Dosing Information

See also General Dosing Information.

For parenteral dosage forms only

Local tissue irritation, pain, and induration may occur with repeated subcutaneous injection.

Oral Dosage Forms

Note: Bracketed uses in the Dosage Forms section refer to categories of use and/or indications that are not included in U.S. product labeling.

CODEINE PHOSPHATE ORAL SOLUTION

Usual adult dose

Analgesic¾
Oral, 15 to 60 mg (usually 30 mg) every three to six hours as needed.
[Antidiarrheal] *¾
Oral, 30 mg up to four times a day.
Antitussive¾
Oral, 10 to 20 mg every four to six hours.

Usual adult prescribing limits

Antitussive¾
Up to 120 mg in twenty-four hours.

Usual pediatric dose

Analgesic¾
Premature infants: Use is not recommended.
Newborn infants: Dosage has not been established.
Infants and children: Oral, 500 mcg (0.5 mg) per kg of body weight or 15 mg per square meter of body surface every four to six hours as needed.
[Antidiarrheal] *¾
Oral, 500 mcg (0.5 mg) per kg of body weight up to four times a day.
Antitussive¾
Children up to 2 years of age¾
Use is not recommended.

Children 2 to 5 years of age¾

Oral, 1 mg per kg of body weight per day, administered in four equal divided doses, or for

Children 2 years of age (average body weight 12 kg)¾Oral, 3 mg every four to six hours, not to exceed 12 mg per day.

Children 3 years of age (average body weight 14 kg)¾Oral, 3.5 mg every four to six hours, not to exceed 14 mg per day.

Children 4 years of age (average body weight 16 kg)¾Oral, 4 mg every four to six hours, not to exceed 16 mg per day.

Children 5 years of age (average body weight 18 kg)¾Oral, 4.5 mg every four to six hours, not to exceed 18 mg per day.

Children 6 to 12 years of age¾

Oral, 5 to 10 mg every four to six hours, not to exceed 60 mg per day.

Note: Use of a calibrated measure is recommended to prevent possible overdosage in children up to 6 years of age.

Strength(s) usually available

U.S.¾15 mg per 5 mL (Rx) 20

Canada¾10 mg per mL (Rx)[Paveral 21]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a tight, light-resistant container, unless otherwise specified by manufacturer. Protect from freezing.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in both the U.S. and Canada.

CODEINE PHOSPHATE TABLETS USP

Usual adult dose

Analgesic¾
Oral, 15 to 60 mg (usually 30 mg) every three to six hours as needed.
[Antidiarrheal] *¾
Oral, 30 mg up to four times a day.
Antitussive¾
Oral, 10 to 20 mg every four to six hours.

Usual adult prescribing limits

Antitussive¾
Up to 120 mg in twenty-four hours.

Usual pediatric dose

Analgesic¾
Premature infants: Use is not recommended.
Newborn infants: Dosage has not been established.
Infants and children: Oral, 500 mcg (0.5 mg) per kg of body weight or 15 mg per square meter of body surface every four to six hours as needed.
[Antidiarrheal] *¾
Oral, 500 mcg (0.5 mg) per kg of body weight up to four times a day.
Antitussive¾
Children up to 2 years of age¾
Use is not recommended.

Children 2 to 5 years of age¾
Oral, 1 mg per kg of body weight per day, administered in four equal divided doses, or for
Children 2 years of age (average body weight 12 kg)¾Oral, 3 mg every four to six hours, not to exceed 12 mg per day.
Children 3 years of age (average body weight 14 kg)¾Oral, 3.5 mg every four to six hours, not to exceed 14 mg per day.
Children 4 years of age (average body weight 16 kg)¾Oral, 4 mg every four to six hours, not to exceed 16 mg per day.
Children 5 years of age (average body weight 18 kg)¾Oral, 4.5 mg every four to six hours, not to exceed 18 mg per day.

Children 6 to 12 years of age¾
Oral, 5 to 10 mg every four to six hours, not to exceed 60 mg per day.

Strength(s) usually available

U.S.¾30 mg (Rx) [Generic] 20

60 mg (Rx) [Generic] 20

Canada¾15 mg (Rx) [Generic] 22

30 mg (Rx) [Generic] 22

Note: Strengths of commercially available tablets do not correspond to recommended antitussive doses.

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F). Store in a well-closed, light-resistant container.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in both the U.S. and Canada.

CODEINE SULFATE TABLETS USP

Usual adult dose

Analgesic¾
Oral, 15 to 60 mg (usually 30 mg) every three to six hours as needed.
[Antidiarrheal]¾
Oral, 30 mg up to four times a day.
Antitussive¾
Oral, 10 to 20 mg every four to six hours.

Usual pediatric dose

Analgesic¾
Premature infants: Use is not recommended.
Newborn infants: Dosage has not been established.
Infants and children: Oral, 500 mcg (0.5 mg) per kg of body weight or 15 mg per square meter of body surface every four to six hours as needed.
[Antidiarrheal]¾
Oral, 500 mcg (0.5 mg) per kg of body weight up to four times a day.
Antitussive¾
Children up to 2 years of age¾
Use is not recommended.

Children 2 to 5 years of age¾
Oral, 1 mg per kg of body weight per day, administered in four equal divided doses, or for
Children 2 years of age (average body weight 12 kg)¾Oral, 3 mg every four to six hours, not to exceed 12 mg per day.
Children 3 years of age (average body weight 14 kg)¾Oral, 3.5 mg every four to six hours, not to exceed 14 mg per day.
Children 4 years of age (average body weight 16 kg)¾Oral, 4 mg every four to six hours, not to exceed 16 mg per day.
Children 5 years of age (average body weight 18 kg)¾Oral, 4.5 mg every four to six hours, not to exceed 18 mg per day.

Children 6 to 12 years of age¾
Oral, 5 to 10 mg every four to six hours, not to exceed 60 mg per day.

Strength(s) usually available

U.S.¾15 mg (Rx) [Generic] 20

30 mg (Rx) [Generic] 20

60 mg (Rx) [Generic] 20

Canada¾Not commercially available.

Note: Strengths of commercially available tablets do not correspond to recommended antitussive doses.

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F). Store in a well-closed container.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Parenteral Dosage Forms

CODEINE PHOSPHATE INJECTION USP

Usual adult dose

Analgesic¾
Intramuscular, intravenous, or subcutaneous, 15 to 60 mg (usually 30 mg) every four to six hours as needed.

Usual pediatric dose

Analgesic¾
Premature infants: Use is not recommended.
Newborn infants: Dosage has not been established.
Infants and children: Intramuscular or subcutaneous, 500 mcg (0.5 mg) per kg of body weight or 15 mg per square meter of body surface every four to six hours as needed.

Strength(s) usually available

U.S.¾With preservative

30 mg per mL (Rx) [Generic] 20

60 mg per mL (Rx) [Generic] 20

Canada¾30 mg per mL (Rx) [Generic] 23

60 mg per mL (Rx) [Generic] 23

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from light. Protect from freezing.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in both the U.S. and Canada.

CODEINE PHOSPHATE SOLUBLE TABLETS

Usual adult dose

Analgesic¾
Intramuscular or subcutaneous, 15 to 60 mg (usually 30 mg) every four to six hours as needed.

Usual pediatric dose

Analgesic¾
Premature infants: Use is not recommended.
Newborn infants: Dosage has not been established.
Infants and children: Intramuscular or subcutaneous, 500 mcg (0.5 mg) per kg of body weight or 15 mg per square meter of body surface every four to six hours as needed.

Strength(s) usually available

U.S.¾30 mg (Rx) [Generic] 24

60 mg (Rx) [Generic] 24

Canada¾Not commercially available.

Packaging and storage:

Store between 15 and 30 °C (59 and 86 °F), in a tight, light-resistant container, unless otherwise specified by manufacturer.

Preparation of dosage form:

For parenteral administration¾Dissolve the required number of tablets in a suitable volume of sterile water for injection, then filter through a 0.22-micron membrane filter. 12

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in the U.S.

CODEINE SULFATE SOLUBLE TABLETS

Usual adult dose

Analgesic¾
Intramuscular or subcutaneous, 15 to 60 mg (usually 30 mg) every four to six hours as needed.

Usual pediatric dose

Analgesic¾
Premature infants: Use is not recommended.
Newborn infants: Dosage has not been established.
Infants and children: Intramuscular or subcutaneous, 500 mcg (0.5 mg) per kg of body weight or 15 mg per square meter of body surface every four to six hours as needed.

Strength(s) usually available

U.S.¾30 mg (Rx) [Generic] 25

60 mg (Rx) [Generic] 25

Canada¾Not commercially available.

Packaging and storage:

Store between 15 and 30 °C (59 and 86 °F), in a tight, light-resistant container, unless otherwise specified by manufacturer.

Preparation of dosage form:

For parenteral administration¾Dissolve the required number of tablets in a suitable volume of sterile water for injection, then filter through a 0.22-micron membrane filter. 13

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in the U.S.

HYDROCODONE

Summary of Differences

Indications¾
Also, indicated as an antitussive.
Pharmacology/pharmacokinetics:

Mechanism of action/effect:
An opioid agonist analgesic; exerts agonist activity primarily at the mu receptor.

Half-life:
3.8 hours.

Onset of action:
Analgesic: Oral 10-30 minutes.

Time to peak effect:
Analgesic: Oral 30-60 minutes.

Duration of action:
Analgesic (nontolerant patients only; decreases as tolerance develops during chronic therapy): Oral¾4-6 hours.
Antitussive: Oral¾4-6 hours.

Elimination:
Renal.

Side/adverse effects¾
More likely than most other opioids to cause side effects associated with histamine release.

Oral Dosage Forms

HYDROCODONE BITARTRATE SYRUP

Usual adult dose

Antitussive¾
Oral, 5 mg every four to six hours as needed.

Usual pediatric dose

Dosage has not been established.

Strength(s) usually available

U.S.¾Not commercially available.
Canada¾5 mg per 5 mL (Rx)[Hycodan 26 (sucrose)] [Robidone 27 (alcohol 3.2%) (sugar)]

Note: In Canada, Hycodan contains only hydrocodone bitartrate; in the U.S., Hycodan contains homatropine in addition to hydrocodone bitartrate.

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a well-closed container, unless otherwise specified by manufacturer. Protect from freezing.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in Canada.

HYDROCODONE BITARTRATE TABLETS USP

Usual adult dose

Analgesic¾
Oral, 5 to 10 mg every four to six hours as needed.
Antitussive¾
Oral, 5 mg every four to six hours as needed.

Usual pediatric dose

Analgesic¾
Oral, 150 mcg (0.15 mg) per kg of body weight every six hours as needed.

Strength(s) usually available

U.S.¾Not commercially available.
Canada¾5 mg (Rx)[Hycodan 26 (scored) (lactose)]

Note: In Canada, Hycodan contains only hydrocodone bitartrate; in the U.S., Hycodan contains homatropine in addition to hydrocodone bitartrate.

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F). Store in a tight, light-resistant container.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in Canada.

HYDROMORPHONE

Summary of Differences

Indications¾
Also, indicated as an antitussive; see also Cough/Cold Combinations (Systemic)¾Hydromorphone and Guaifenesin .

Pharmacology/pharmacokinetics¾
Mechanism of action/effect:
An opioid agonist analgesic; exerts agonist activity primarily at the mu receptor.

Equivalence:
1.5 mg via intramuscular injection, 7.5 mg via oral administration, or 3 mg via rectal administration therapeutically equivalent to 10 mg of intramuscular morphine.

Half-life:
2.6-4 hours.

Onset of action:
Intramuscular: 15 minutes.
Intravenous: 10-15 minutes.
Oral: 30 minutes.
Subcutaneous: 15 minutes.

Time to peak effect:
Intramuscular: 30-60 minutes.
Intravenous: 15-30 minutes.
Oral: 90-120 minutes.
Subcutaneous: 30-90 minutes.

Duration of action (nontolerant patients only; decreases as tolerance develops during chronic therapy):
Intramuscular: 4-5 hours.

Intravenous: 2-3 hours.
Oral: 4 hours.
Subcutaneous: 4 hours.

Elimination:
Renal.

Oral Dosage Forms

HYDROMORPHONE HYDROCHLORIDE ORAL SOLUTION

Usual adult dose

Analgesic¾
Oral, 2.5 to 10 mg every three to six hours, depending on the severity of pain and patient tolerance. 28

Usual pediatric dose

Dosage must be individualized by physician, depending on the severity of pain and the patient"s age, size, and opioid tolerance.

Strength(s) usually available

U.S.¾5 mg per 5 mL[Dilaudid-5 28]

Canada¾5 mg per 5 mL[Dilaudid 29 (sucrose)] [PMS-Hydromorphone Syrup 30]

HYDROMORPHONE HYDROCHLORIDE TABLETS USP

Usual adult dose

Analgesic¾
Oral, 2 mg every three to six hours as needed.

Note: Dosage may be increased to 4 mg or more every four to six hours, depending on the severity of pain and patient tolerance.

Usual pediatric dose

Dosage must be individualized by physician, depending on the severity of pain and the patient"s age, size, and opioid tolerance.

Strength(s) usually available

U.S.¾1 mg (Rx)[Hydrostat IR 31]

2 mg (Rx)[Dilaudid 32 (lactose)] [Hydrostat IR 31] [Generic] 20

3 mg (Rx)[Hydrostat IR 31]

4 mg (Rx)[Dilaudid 32 (lactose)] [Hydrostat IR 31] [Generic] 20

8 mg (Rx)[Dilaudid 28]

Canada¾1 mg (Rx)[Dilaudid 29] [PMS-Hydromorphone 30]

2 mg (Rx)[Dilaudid 29] [PMS-Hydromorphone 30] [Generic] 33

4 mg (Rx)[Dilaudid 29] [PMS-Hydromorphone 30] [Generic] 33

8 mg (Rx)[Dilaudid 29] [PMS-Hydromorphone 30]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight, light-resistant container.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in both the U.S. and Canada.

Parenteral Dosage Forms

HYDROMORPHONE HYDROCHLORIDE INJECTION USP

Usual adult dose

Analgesic¾
Intramuscular or subcutaneous, 1 to 2 mg every three to six hours as needed; may be increased to 3 or 4 mg every four to six hours if pain is severe.

Note: For opioid-tolerant patients requiring high-dose therapy, the 10-mg-per-mL concentration may be substituted for lower strengths of hydromorphone hydrochloride injection or for other opioid analgesics. 7 Dosage must be individualized, depending on the severity of pain, opioid requirements at the time therapy with the high-potency injection is initiated, and patient response. Although patients who have become tolerant to another opioid may be at least partially cross-tolerant to hydromorphone also, it is recommended that one-half of the equianalgesic dose of hydromorphone be used initially, then adjusted as necessary. 8

Intravenous, 500 mcg (0.5 mg) to 1 mg every three hours as needed; administered slowly.

Usual pediatric dose

Dosage must be individualized by physician on the basis of patient"s age and size.

Strength(s) usually available

U.S.¾With preservatives

1 mg per mL (Rx) [Generic] 20

2 mg per mL (Rx)[Dilaudid 32 (methylparaben and propylparaben)] [Generic] 20

3 mg per mL (Rx) [Generic] 20

4 mg per mL (Rx) [Generic] 20

Without preservative

1 mg per mL (Rx)[Dilaudid 32]

2 mg per mL (Rx)[Dilaudid 32]

4 mg per mL (Rx)[Dilaudid 32]

10 mg per mL (Rx)[Dilaudid-HP 34]

Canada¾Without preservative

2 mg per mL (Rx)[Dilaudid 29]

10 mg per mL (Rx)[Dilaudid-HP 35]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from light. Protect from freezing.

Auxiliary labeling:

- May cause drowsiness.
- Avoid alcoholic beverages.
- May be habit-forming.

Note: Controlled substance in both the U.S. and Canada.

Rectal Dosage Forms

HYDROMORPHONE HYDROCHLORIDE SUPPOSITORIES

Usual adult dose

Analgesic¾
Rectal, 3 mg every four to eight hours as needed.

Usual pediatric dose

Dosage has not been established.

Strength(s) usually available

U.S.¾3 mg (Rx)[Dilaudid 32]

Canada¾3 mg (Rx)[Dilaudid 29] [PMS-Hydromorphone 30]

Packaging and storage:

Store between 2 and 8 °C (36 and 46 °F), in a well-closed container, unless otherwise specified by manufacturer. Protect from freezing.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.
· Store in refrigerator.

Note: Controlled substance in both the U.S. and Canada.

LEVORPHANOL

Summary of Differences

Pharmacology/pharmacokinetics¾
Mechanism of action/effect:
An opioid agonist analgesic; exerts agonist activity primarily at the mu receptor.

Equivalence:
2 mg via intramuscular injection or 4 mg via oral administration therapeutically equivalent to 10 mg of intramuscular morphine.

Protein binding:
Moderate.

Onset of action:

Oral: 10-60 minutes.

Time to peak effect:
Intramuscular: 60 minutes.
Intravenous: Within 20 minutes.
Oral: 90-120 minutes.
Subcutaneous: 60-90 minutes.

Duration of action (nontolerant patients only; duration decreases as tolerance develops during chronic therapy):
Intramuscular, intravenous, oral, or subcutaneous: 4-5 hours.

Elimination:
Renal.

Oral Dosage Forms

LEVORPHANOL TARTRATE TABLETS USP

Usual adult dose

Analgesic¾
Oral, 2 mg; may be increased to 3 or 4 mg if pain is severe.

Usual pediatric dose

Dosage must be individualized by physician on the basis of patient"s age and size.

Strength(s) usually available

U.S.¾2 mg (Rx)[Levo-Dromoran 36 (scored) (lactose)] [Generic] 20

Canada¾2 mg (Rx)[Levo-Dromoran 37 (scored) (lactose)]

Packaging and storage:

Store between 15 and 30 °C (59 and 86 °F), in a light-resistant container, unless otherwise specified by manufacturer. Store in a well-closed container.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in both the U.S. and Canada.

Parenteral Dosage Forms

LEVORPHANOL TARTRATE INJECTION USP

Usual adult dose

Analgesic¾
Subcutaneous, 2 mg; may be increased to 3 mg if pain is severe.

Note: The medication may also be given intravenously.
For preoperative analgesia¾Subcutaneous, 1 to 2 mg ninety minutes prior to surgery. 4

Usual pediatric dose

Dosage must be individualized by physician on the basis of patient"s age and size.

Strength(s) usually available

U.S.¾With preservatives

2 mg per mL (Rx)[Levo-Dromoran 36 (methylparaben and propylparaben [1-mL ampuls]) (or 0.45% phenol [10-mL vials])]

Canada¾With preservatives

2 mg per mL (Rx)[Levo-Dromoran 37 (0.45% phenol)]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from freezing.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in both the U.S. and Canada.

MEPERIDINE

Summary of Differences

Pharmacology/pharmacokinetics¾
  Mechanism of action/effect:
    An opioid agonist analgesic; exerts agonist activity primarily at the mu receptor.

Equivalence:

75 mg via intramuscular injection or 300 mg via oral administration therapeutically equivalent to 10 mg of intramuscular morphine.

Protein binding:

High.

Half-life:

2.4-4 hours.

Biotransformation:

Metabolized to normeperidine, which is active and toxic.

Onset of action:

Intramuscular: 10-15 minutes.
Intravenous: 1 minute.
Oral: 15 minutes.
Subcutaneous: 10-15 minutes.

Time to peak effect:

Intramuscular: 30-50 minutes.
Intravenous: 5-7 minutes.
Oral: 60-90 minutes.
Subcutaneous: 30-50 minutes.

Duration of action (nontolerant patients only; decreases as tolerance develops during chronic therapy):

Intramuscular, intravenous, oral, or subcutaneous: 2-4 hours.

Elimination:

Renal, 5% as unchanged meperidine.

Precautions¾

Drug interactions and/or related problems:

May increase effects of coumarin- or indandione-derivative anticoagulants.

Contraindicated in patients who have received a monoamine oxidase (MAO) inhibitor within past 14-21 days; concurrent use has produced serious, sometimes fatal, reactions.

Concurrent use with amphetamines, which have some MAO-inhibiting activity, not recommended because of risk of serious reactions similar to those reported with other MAO inhibitors.

Side/adverse effects¾

More likely than most other opioids to cause side effects associated with histamine release, convulsions, or constipation.

Additional Dosing Information

See also General Dosing Information.

For oral dosage forms only

The syrup may be diluted with 1/2 glass (120 mL) of water to prevent a slight topical anesthetic effect on the mucous membranes.
For parenteral dosage forms only

Intramuscular administration is preferred when repeated doses are required. Repeated subcutaneous administration causes local tissue irritation and induration.
Inadvertent injection around a nerve trunk may cause sensory-motor paralysis, which is usually, but not always, transitory.

Oral Dosage Forms

MEPERIDINE HYDROCHLORIDE SYRUP USP

Usual adult dose

Analgesic¾
Oral, 50 to 150 mg (usually 100 mg) every three to four hours as needed.

Usual pediatric dose

Analgesic¾
Oral, 1.1 to 1.76 mg per kg of body weight, not to exceed 100 mg, every three to four hours as needed. Use of a calibrated measure is recommended to prevent possible overdosage in children up to 6 years of age.

Strength(s) usually available

U.S.¾50 mg per 5 mL (Rx)[Demerol 38 (glucose) (saccharin sodium)] [Generic] 20

Canada¾Not commercially available.

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F). Store in a tight, light-resistant container. Protect from freezing.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in the U.S.

MEPERIDINE HYDROCHLORIDE TABLETS USP

Usual adult dose

Analgesic¾
Oral, 50 to 150 mg (usually 100 mg) every three to four hours as needed.

Usual pediatric dose

Analgesic¾
Oral, 1.1 to 1.76 mg per kg of body weight, not to exceed 100 mg, every three to four hours as needed.

Strength(s) usually available

U.S.¾50 mg (Rx)[Demerol 38] [Generic] 20

100 mg (Rx)[Demerol 38] [Generic] 20

Canada¾50 mg (Rx)[Demerol 39 (scored)]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F). Store in a well-closed, light-resistant container.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in both the U.S. and Canada.

Parenteral Dosage Forms

MEPERIDINE HYDROCHLORIDE INJECTION USP

Usual adult dose

Analgesic¾
Intramuscular (preferred) or subcutaneous, 50 to 150 mg (usually 100 mg) every three to four hours as needed.
Intravenous infusion, 15 to 35 mg per hour as required, administered using an infusion pump.

Note: Dosage must be adjusted according to the severity of pain and patient response.
Obstetrical analgesia: Intramuscular (preferred) or subcutaneous, 50 to 100 mg administered when pains become regular. May be repeated at one- to three-hour intervals as needed.

Anesthesia adjunct¾
Preoperative: Intramuscular (preferred) or subcutaneous, 50 to 100 mg thirty to ninety minutes prior to anesthesia.
Intravenous, by repeated slow injection of fractional doses of a solution diluted to 10 mg per mL.
Intravenous infusion, as a solution diluted to 1 mg per mL.

Note: Dosage must be titrated to the needs of the patient, depending on the premedication given, the type of anesthesia, and the nature and duration of the surgical procedure.

Usual pediatric dose

Analgesic¾
Intramuscular (preferred) or subcutaneous, 1.1 to 1.76 mg per kg of body weight, not to exceed 100 mg, every three to four hours as needed.
Preoperative¾
Intramuscular (preferred) or subcutaneous, 1 to 2.2 mg per kg of body weight, not to exceed 100 mg, thirty to ninety minutes prior to anesthesia.

Strength(s) usually available

U.S.¾With preservative

25 mg per mL (Rx) [Generic] 20

50 mg per mL (Rx)[Demerol 38 (metacresol)] [Generic] 20

75 mg per mL (Rx) [Generic] 20

100 mg per mL (Rx)[Demerol 38 (metacresol)] [Generic] 20

Without preservative

10 mg per mL (Rx) [Generic] 20

25 mg per mL (Rx)[Demerol 38] [Generic] 20

50 mg per mL (Rx)[Demerol 38] [Generic] 20

75 mg per mL (Rx)[Demerol 38] [Generic] 20

100 mg per mL (Rx)[Demerol 38] [Generic] 20

Note: In addition to being available in single- or multiple-dose units containing the concentrations listed above, Demerol is available in single-dose ampuls that contain 0.5, 1.5, or 2 mL of the 50 mg per mL concentration (providing 25, 75, or 100 mg of meperidine hydrochloride, respectively). 38

Canada¾With preservative

50 mg per mL (Rx)[Demerol 39 (metacresol)]

100 mg per mL (Rx)[Demerol 39 (metacresol)]

Without preservative

10 mg per mL (Rx) [Generic] 40

25 mg per mL (Rx) [Generic] 40

50 mg per mL (Rx)[Demerol 39] [Generic] 40

75 mg per mL (Rx)[Demerol 39] [Generic] 40

100 mg per mL (Rx)[Demerol 39] [Generic] 40

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from light. Protect from freezing.

Incompatibilities:

Solutions of meperidine are chemically incompatible with aminophylline, barbiturates, heparin, iodides, methicillin, phenytoin, sodium bicarbonate, sulfadiazine, and sulfisoxazole.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in both the U.S. and Canada.

METHADONE

Summary of Differences

Note: In the U.S., methadone may be dispensed for treatment of opioid addiction only through treatment programs that have been approved by the Food and Drug Administration (FDA), Drug Enforcement Administration (DEA), and designated state authorities. Use of methadone in such programs is subject to treatment requirements stipulated in the Code of Federal Regulations. 83

In Canada, methadone is a controlled substance (Classification N). It is available only through physicians who have received special authorization to prescribe the medication for treatment of opioid addiction.
Indications¾
Also, indicated as narcotic abstinence syndrome suppressant.

Also, used as antitussive.
Not recommended for obstetrical analgesia.

Pharmacology/pharmacokinetics¾

Mechanism of action/effect:

An opioid agonist analgesic; exerts agonist activity primarily at the mu receptor.

Equivalence:

10 mg via intramuscular injection or 20 mg via oral administration therapeutically equivalent to 10 mg of intramuscular morphine.

Protein binding:

High.

Half-life:

15-25 hours; increases with repeated administration.

Onset of action:

Intramuscular: 10-20 minutes.
Oral: 30-60 minutes.

Time to peak effect:

Intramuscular: 1-2 hours.
Intravenous: 15-30 minutes.
Oral: 1.5-2 hours.

Duration of action (in nontolerant patients, may increase considerably with chronic use because of accumulation of methadone or active metabolites; may then decrease as tolerance develops during chronic therapy):

Intramuscular: 4-5 hours.
Intravenous: 3-4 hours.
Oral: 4-6 hours.

Elimination:

Primarily renal (rate increased in acidic urine); also some biliary elimination.

Precautions¾

Drug interactions and/or related problems:

Urinary acidifiers may increase methadone elimination, thereby reducing the plasma concentration; withdrawal symptoms may occur in some physically dependent patients.

Phenytoin or rifampin may increase methadone metabolism and precipitate withdrawal symptoms in physically dependent patients.

Side/adverse effects¾

May be more likely than most other opioids to cause constipation.

Additional Dosing Information

See also General Dosing Information.

U.S. Federal regulations permit methadone to be used in detoxification and maintenance treatment programs for opioid addiction. Short-term (up to 30 days) or long-term (up to 180 days) detoxification programs use methadone to alleviate adverse physiological or psychological consequences of withdrawal from illicit opioids, with dosage gradually being decreased until a drug-free state is achieved. After 180 days, patients who have not achieved a drug-free state are considered to be receiving maintenance treatment. Patients 18 years of age or older may also be enrolled directly into a maintenance program without first attempting detoxification. In maintenance treatment programs, relatively stable doses of opioid are given on a continuing basis as a substitute for illicit opioids. 83

Detoxification and comprehensive maintenance programs must include a full range of medical and rehabilitative services in addition to opioid administration. However, patients who are awaiting admission to a comprehensive maintenance program may receive up to 120 days of interim maintenance treatment, which consists only of opioid administration and needed medical services. 83

Oral administration is preferred for detoxification and mandatory for maintenance.
For parenteral dosage forms only

Intramuscular administration is recommended when repeated doses are required. Repeated subcutaneous administration causes local tissue irritation and induration.

Oral Dosage Forms

METHADONE HYDROCHLORIDE ORAL CONCENTRATE USP

Usual adult dose

Analgesic¾
Oral, 5 to 20 mg every four to eight hours. Dosage may be increased or the interval between doses decreased if pain is very severe or if the patient becomes tolerant to the medication.
Suppressant (narcotic abstinence syndrome) ¾
Detoxification: Oral, 15 to 40 mg once a day or as needed to control observed withdrawal symptoms; dosage to be reduced at one- or two-day intervals according to patient response.
Maintenance: Dosage must be individualized.

Usual adult prescribing limits

Up to 120 mg per day.

Usual pediatric dose

Analgesic¾
Dosage must be individualized by physician on the basis of patient"s age and size. Use of a calibrated measure is recommended to prevent possible overdosage in children up to 6 years of age.
Suppressant (narcotic abstinence syndrome) ¾
Dosage must be individualized by physician according to the needs of the specific patient. Dosage must not exceed 120 mg per day. 83

Note: Patients younger than 18 years of age may be admitted to methadone maintenance programs only after two documented attempts at short-term (up to thirty days) detoxification or drug-free treatment have failed. A one-week waiting period is required between a detoxification attempt and admission to a methadone maintenance program. A parent, legal guardian, or other responsible adult designated by the State authority must complete and sign a consent to treatment form for all such minors. 83

Strength(s) usually available

U.S.¾10 mg per mL (Rx)[Methadose 20] [Generic] 20

Packaging and storage:

Store between 15 and 30 °C (59 and 86 °F). Store in a tight container. Protect from light. Protect from freezing.

Preparation of dosage form:

Each dose must be diluted with water or another liquid before administration. For use in the treatment of chronic pain, each dose should be diluted to at least 30 mL. U.S. Federal regulations stipulate that the oral concentrate be diluted with water or other suitable liquid before being administered to a patient undergoing treatment for opioid addiction. 83 It is recommended that each dose be diluted to 90 mL or more as a deterrent to misuse by injection. 85 Treatment centers that dispense both methadone and levomethadyl (which must also be dispensed as a diluted liquid) should use liquids of different colors for preparing each medication, so that they can be readily distinguished from each other. 83

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in the U.S.
When preparing the label, indicate that the medication must be diluted with water or another liquid to 30 mL or more prior to administration.
If the concentrate is being taken home, make sure the patient understands the dilution requirements.

METHADONE HYDROCHLORIDE ORAL SOLUTION USP

Usual adult dose

Analgesic¾
Oral, 5 to 20 mg every four to eight hours. Dosage may be increased or the interval between doses decreased if pain is very severe or if the patient becomes tolerant to the medication.

Usual pediatric dose

Analgesic¾
Dosage must be individualized by physician on the basis of patient"s age and size. Use of a calibrated measure is recommended to prevent possible overdosage in children up to 6 years of age.

Strength(s) usually available

U.S.¾5 mg per 5 mL (Rx) [Generic] 20

10 mg per 5 mL (Rx) [Generic] 20

Canada¾Not commercially available.

Packaging and storage:

Store between 15 and 30 °C (59 and 86 °F). Store in a tight container. Protect from light. Protect from freezing.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in the U.S.

METHADONE HYDROCHLORIDE TABLETS USP

Usual adult dose

Analgesic¾
Oral, 2.5 to 10 mg every three to four hours as needed initially. For chronic use, dose and dosing interval to be adjusted according to patient response.

Usual pediatric dose

Analgesic¾
Dosage must be individualized by physician on the basis of patient"s age and size.

Strength(s) usually available

U.S.¾5 mg (Rx)[Dolophine 41 (lactose) (sucrose)] [Methadose 20] [Generic] 20

10 mg (Rx)[Dolophine 41 (lactose) (sucrose)] [Methadose 20] [Generic] 20

Canada¾Not commercially available.

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F). Store in a well-closed container.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in the U.S.

METHADONE HYDROCHLORIDE TABLETS (DISPERSIBLE) USP

Usual adult dose

Suppressant (narcotic abstinence syndrome) ¾
Detoxification: Oral, 15 to 40 mg once a day or as needed to control observed withdrawal symptoms; dosage to be reduced at one- or two-day intervals according to patient response.
Maintenance: Dosage must be individualized.

Usual adult prescribing limits

Up to 120 mg per day.

Usual pediatric dose

Suppressant (narcotic abstinence syndrome) ¾
Dosage must be individualized by physician according to the needs of the specific patient. Dosage must not exceed 120 mg per day. 83

Note: Patients younger than 18 years of age may be admitted to methadone maintenance programs only after two documented attempts at short-term (up to thirty days) detoxification or drug-free treatment have failed. A one-week waiting period is required between a detoxification attempt and admission to a methadone maintenance program. A parent, legal guardian, or other responsible adult designated by the State authority must complete and sign a consent to treatment form for all such minors. 83

Strength(s) usually available

U.S.¾40 mg (Rx)[Methadose 20] [Generic] 42

Packaging and storage:

Store between 15 and 30 °C (59 and 86 °F). Store in a well-closed container.

Preparation of dosage form:

U.S. Federal regulations stipulate that the tablets must be dispersed in water or other suitable liquid before being administered to the patient. Treatment centers that dispense both methadone and levomethadyl (which must also be dispensed as a diluted liquid) should use liquids of different colors for preparing each medication, so that they can be readily distinguished from each other. 83 The dispersible tablets have been formulated with insoluble excipients as a deterrent to misuse of the medication by injection. 17

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in the U.S.

Parenteral Dosage Forms

METHADONE HYDROCHLORIDE INJECTION USP

Usual adult dose

Analgesic¾
Intramuscular or subcutaneous, 2.5 to 10 mg every three to four hours as needed.
Suppressant (narcotic abstinence syndrome) ¾
For detoxification only: Intramuscular or subcutaneous, 15 to 40 mg once a day or as needed to control observed withdrawal symptoms; dosage to be reduced at one- or two-day intervals according to patient response.

Note: Parenteral administration in a detoxification regimen is recommended only for patients unable to take medication orally.

Usual pediatric dose

Analgesic¾
Dosage must be individualized by physician on the basis of patient"s age and size
Strength(s) usually available

U.S.¾With preservative

10 mg per mL (Rx)[Dolophine 43 (chlorobutanol)]

Without preservative

10 mg per mL (Rx)[Dolophine 43]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a light-resistant container. Protect from freezing.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in the U.S.

MORPHINE

Summary of Differences

Indications¾
Drug of choice to relieve pain due to acute myocardial infarction.
Also, indicated as adjunctive therapy in the treatment of acute pulmonary edema secondary to left ventricular failure.
Also, used as antitussive.

Pharmacology/pharmacokinetics¾
Mechanism of action/effect:
An opioid agonist analgesic; exerts agonist activity primarily at the mu receptor.

Equivalence:
60 mg via oral administration therapeutically equivalent to 10 mg intramuscularly; however, with chronic use on a fixed schedule may decrease to 20-30 mg.

Protein binding:
Low.

Half-life:
2-3 hours.

Onset of action:
Epidural: 15-60 minutes.
Intramuscular: 10-30 minutes.
Intrathecal: 15-60 minutes.
Rectal: 20-60 minutes.
Subcutaneous: 10-30 minutes.

Time to peak effect:
Intramuscular: 30-60 minutes.
Intravenous: 20 minutes.

Oral (immediate-release dosage forms): 1-2 hours.
Subcutaneous: 50-90 minutes.

Duration of action (nontolerant patients only; may decrease as tolerance develops during chronic therapy):
Epidural: Up to 24 hours.
Intramuscular: 4-5 hours.
Intrathecal: Up to 24 hours.
Intravenous: 4-5 hours.
Oral: 4-5 hours with immediate-release dosage forms; 8 or 12 hours (depending on specific product) with extended-release dosage forms.
Subcutaneous: 4-5 hours.

Elimination:
85% Renal, 9-12% as unchanged morphine; 7-10% biliary.

Precautions¾
Drug interactions and/or related problems:
May decrease clearance of zidovudine; toxicity of either or both medications may be potentiated.

Side/adverse effects¾
More likely than most other opioids to cause constipation and to produce symptoms associated with histamine release.

Additional Dosing Information

See also General Dosing Information.

For oral dosage forms only

The oral dosage forms are recommended for administration via a fixed dosage schedule to patients with severe, chronic pain. However, low doses of an immediate-release oral dosage form may be used on an as-needed basis to relieve "breakthrough"" pain that occurs during chronic treatment with an extended-release dosage form. 84

Periodic attempts should be made to reduce the dosage after an initial response has been achieved and maintained for at least 3 days.
The oral liquid may be diluted in a glass of fruit juice just prior to ingestion, if desired, to improve the taste.
The extended-release tablets are to be swallowed whole. They should not be broken, crushed, or chewed.
For parenteral dosage forms only

Intramuscular administration is recommended when repeated doses are required. Repeated subcutaneous administration causes local tissue irritation, pain, and induration.
The 25- or 50-mg-per-mL concentration of morphine sulfate injection available in Canada may be administered undiluted to opioid-tolerant patients requiring high-dose therapy. 9 The 25-mg-per-mL

concentration of morphine sulfate injection available in the U.S. is intended only for the preparation of intravenous infusion solutions and is not to be administered via other parenteral routes. 15

Bioequivalence information

Bioavailability or bioequivalence problems among different brands of Morphine Sulfate Tablets (immediate-release) and different brands of Morphine Sulfate Oral Solution have not been documented. 18

Morphine Sulfate Extended-release Capsules (available in Canada) should not be interchanged with other extended-release dosage forms containing morphine hydrochloride or morphine sulfate. Bioavailability or bioequivalence studies comparing the products have not been done. 58

Oral Dosage Forms

MORPHINE HYDROCHLORIDE SYRUP

Usual adult dose

Analgesic¾
Chronic pain: Dosage and dosing interval must be individualized by the physician according to the severity of pain and patient response. Initial oral doses of 10 to 30 mg every four hours are recommended by most manufacturers of oral morphine products. However, some patients receiving the medication via the recommended fixed dosing schedule may respond to lower doses, while others have required 75 mg or more.

Usual pediatric dose

Analgesic¾
Dosage must be individualized by the physician according to the severity of pain as well as on the basis of the patient"s age and size. Use of calibrated measure is recommended to prevent possible overdosage in children up to 6 years of age.

Strength(s) usually available

U.S.¾Not commercially available.
Canada¾1 mg per mL (Rx)[Morphitec 44 (alcohol 5%) (tartrazine)] [M.O.S 45]

5 mg per mL (Rx)[Morphitec 44 (alcohol 5%) (tartrazine)] [M.O.S 45]

10 mg per mL (Rx)[Morphitec 44 (alcohol 5%) (tartrazine)] [M.O.S 45]

20 mg per mL (Rx)[Morphitec 44 (alcohol 5%) (tartrazine)] [M.O.S 45]

50 mg per mL (Rx)[M.O.S 45]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a well-closed container, unless otherwise specified by manufacturer. Protect from freezing.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in Canada.

MORPHINE HYDROCHLORIDE TABLETS

Usual adult dose

Analgesic¾
Chronic pain: Dosage and dosing interval must be individualized by the physician according to the severity of pain and patient response. Initial oral doses of 10 to 30 mg every four hours are recommended by most manufacturers of oral morphine products. However, some patients receiving the medication via the recommended fixed dosing schedule may respond to lower doses, while others have required 75 mg or more.

Usual pediatric dose

Analgesic¾
Dosage must be individualized by the physician according to the severity of pain as well as on the basis of the patient"s age and size.

Strength(s) usually available

U.S.¾Not commercially available.
Canada¾10 mg (Rx)[M.O.S 45]

20 mg (Rx)[M.O.S 45]

40 mg (Rx)[M.O.S 45]

60 mg (Rx)[M.O.S 45]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a well-closed container, unless otherwise specified by manufacturer. Protect from freezing.

Auxiliary labeling:

· May cause drowsiness.

· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in Canada.

MORPHINE HYDROCHLORIDE EXTENDED-RELEASE TABLETS

Usual adult dose

Analgesic¾
Chronic pain: Dosage must be individualized by the physician according to the severity of pain and patient response.

Usual pediatric dose

Dosage has not been established.

Strength(s) usually available

U.S.¾Not commercially available.
Canada¾30 mg (Rx)[M.O.S.-S.R 46]

60 mg (Rx)[M.O.S.-S.R 46]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a well-closed container, unless otherwise specified by manufacturer.

Auxiliary labeling:

· Swallow tablets whole.
· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in Canada.

MORPHINE SULFATE CAPSULES

Usual adult dose

Analgesic¾
Chronic pain: Dosage and dosing interval must be individualized by the physician according to the severity of pain and patient response. Initial oral doses of 10 to 30 mg every four hours are recommended by most manufacturers of oral morphine products. However, some patients receiving the

medication via the recommended fixed dosing schedule may respond to lower doses, while others have required 75 mg or more.

Usual pediatric dose

Analgesic¾
Dosage must be individualized by the physician according to the severity of pain as well as on the basis of the patient"s age and size.

Strength(s) usually available

U.S.¾15 mg (Rx)[MSIR 47]

30 mg (Rx)[MSIR 47]

Canada¾Not commercially available.

MORPHINE SULFATE EXTENDED-RELEASE CAPSULES

Note: The extended-release capsule dosage form has not been evaluated for bioequivalence with other extended-release dosage forms containing morphine hydrochloride or morphine sulfate and should not be interchanged with them. 58

Usual adult dose

Analgesic¾
Chronic pain: Oral, administer dose every twelve to twenty-four hours 87.

Note: Dosage must be individualized by the physician according to the severity of pain and patient response 87.

Note: Patients being transferred from other opioid analgesics or other morphine dosage forms to the morphine sulfate extended-release capsules should receive a total daily dose of oral morphine sulfate equivalent to the established total daily dose of previously administered medication, administered in divided doses at twelve-hour or twenty-four-hour intervals. The manufacturers" prescribing information contains recommendations for calculating equivalent dosage. 87

Usual pediatric dose

Dosage has not been established.

Strength(s) usually available

U.S.¾20 mg (Rx)[Kadian 87]

50 mg (Rx)[Kadian 87]

100 mg (Rx)[Kadian 87]

Canada¾10 mg (Rx)[M-Eslon]

20 mg (Rx)[Kadian 88]

30 mg (Rx)[M-Eslon]

50 mg (Rx)[Kadian 88]

60 mg (Rx)[M-Eslon]

100 mg (Rx)[Kadian 88] [M-Eslon]

Note: The M-Eslon product has not been compared to any slow-release morphine preparation on the Canadian market, and is therefore not interchangeable 58.

Packaging and storage:

Store between 15 and 30 °C (59 and 86 °F).

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in U.S. and Canada.

MORPHINE SULFATE ORAL SOLUTION

Note: Bioavailability or bioequivalence problems among different brands of Morphine Sulfate Oral Solution have not been documented. 18

Usual adult dose

Analgesic¾
Chronic pain: Dosage and dosing interval must be individualized by the physician according to the severity of pain and patient response. Initial oral doses of 10 to 30 mg every four hours are recommended by most manufacturers of oral morphine products. However, some patients receiving the medication via the recommended fixed dosing schedule may respond to lower doses, while others have required 75 mg or more.

Usual pediatric dose

Analgesic¾

Dosage must be individualized by the physician according to the severity of pain as well as on the basis of the patient"s age and size. Use of calibrated measure is recommended to prevent possible overdosage in children up to 6 years of age.

Strength(s) usually available

U.S.¾10 mg per 2.5 mL (unit dose) (Rx)[Rescudose 48] [Roxanol UD 48]

10 mg per 5 mL (Rx)[MSIR 47 (sucrose)] [MS/L 49] [Generic] 20

20 mg per 5 mL (Rx)[MSIR 47] [Roxanol UD 48] [Generic] 20

20 mg per mL (Rx)[MSIR 47] [MS/L Concentrate 49] [OMS Concentrate 50] [Roxanol 48]

30 mg per 1.5 mL (Rx)[Roxanol UD 48]

100 mg per 5 mL (Rx)[Roxanol 100 48]

Canada¾2 mg per mL (Rx) [Generic] 51

4 mg per mL (Rx) [Generic] 51

20 mg per mL (Rx)[Statex Drops 52]

50 mg per mL (Rx)[Statex Drops 52]

Packaging and storage:

Store between 15 and 30 °C (59 and 86 °F), in a tight, light-resistant container, unless otherwise specified by manufacturer. Protect from freezing.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in both the U.S. and Canada.

MORPHINE SULFATE SYRUP

Usual adult dose

Analgesic¾
Chronic pain: Dosage and dosing interval must be individualized by the physician according to the severity of pain and patient response. Initial oral doses of 10 to 30 mg every four hours are recommended by most manufacturers of oral morphine products. However, some patients receiving the

medication via the recommended fixed dosing schedule may respond to lower doses, while others have required 75 mg or more.

Usual pediatric dose

Analgesic¾
Dosage must be individualized by the physician according to the severity of pain as well as on the basis of the patient"s age and size.

Strength(s) usually available

U.S.¾Not commercially available.
Canada¾1 mg per mL (Rx)[Statex 52]

5 mg per mL (Rx)[Statex 52]

10 mg per mL (Rx)[Statex 52]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a well-closed container, unless otherwise specified by manufacturer. Protect from freezing.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in Canada.

MORPHINE SULFATE TABLETS

Note: Bioavailability or bioequivalence problems among different brands of Morphine Sulfate Tablets have not been documented. 18

Usual adult dose

Analgesic¾
Chronic pain: Dosage and dosing interval must be individualized by the physician according to the severity of pain and patient response. Initial oral doses of 10 to 30 mg every four hours are recommended by most manufacturers of oral morphine products. However, some patients receiving the medication via the recommended fixed dosing schedule may respond to lower doses, while others have required 75 mg or more.

Usual pediatric dose

Analgesic¾
Chronic pain: Dosage must be individualized by the physician according to the severity of pain as well as on the basis of the patient"s age and size.

Strength(s) usually available

U.S.¾15 mg (Rx)[MSIR 47 (scored)] [Generic] 20

30 mg (Rx)[MSIR 47 (scored)] [Generic] 20

Canada¾5 mg (Rx)[MSIR 53 (scored)] [Statex 52 (scored)]

10 mg (Rx)[MSIR 53 (scored)] [Statex 52 (scored)]

15 mg (Rx) [Generic] 51

20 mg (Rx)[MSIR 53 (scored)]

25 mg (Rx)[Statex 52 (scored)]

30 mg (Rx)[MSIR 53 (scored)] [Generic] 51

50 mg (Rx)[Statex 52 (scored)]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a well-closed container, unless otherwise specified by manufacturer.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in both the U.S. and Canada.

MORPHINE SULFATE EXTENDED-RELEASE TABLETS

Usual adult dose

Analgesic¾
Chronic pain: Oral, 30 mg every twelve hours, initially, with dosage and dosing interval then being adjusted according to the requirements of the individual patient.

Note: Patients being transferred from other opioid analgesics or other morphine dosage forms to the morphine sulfate extended-release tablets should receive a total daily dose of oral morphine sulfate

equivalent to the established total daily dose of previously administered medication, administered in divided doses at twelve-hour intervals. The manufacturers" prescribing information contains recommendations for calculating equivalent dosage.

Usual pediatric dose

Dosage has not been established.

Strength(s) usually available

U.S.¾15 mg (Rx)[M S Contin 54] [Generic] 20

30 mg (Rx)[M S Contin 54] [Oramorph SR 55] [Generic] 20

60 mg (Rx)[M S Contin 54] [Oramorph SR 55] [Generic] 20

100 mg (Rx)[M S Contin 54] [Oramorph SR 55] [Generic] 20

200 mg (Rx)[M S Contin 54]

Canada¾15 mg (Rx)[M S Contin 56]

30 mg (Rx)[M S Contin 56] [Oramorph SR 57]

60 mg (Rx)[M S Contin 56] [Oramorph SR 57]

100 mg (Rx)[M S Contin 56] [Oramorph SR 57]

200 mg (Rx)[M S Contin 56 (scored)]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a well-closed container, unless otherwise specified by manufacturer.

Auxiliary labeling:

· Swallow tablets whole.
· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in both the U.S. and Canada.

Parenteral Dosage Forms

MORPHINE SULFATE INJECTION USP

Usual adult dose

Analgesic¾
Intramuscular or subcutaneous, 5 to 20 mg (usually 10 mg, initially) every four hours as needed. For severe, chronic pain the medication may also be administered by subcutaneous infusion, using a portable pump, at a rate titrated to the requirements and response of the individual patient. 64

Note: The recommendation of an initial 10-mg dose is based on a 70-kg person.
In Canada, the 25- or 50-mg-per-mL concentration may be substituted for lower strengths of morphine sulfate injection or for other opioid analgesics in opioid-tolerant patients requiring high-dose therapy. 9
Dosage must be individualized, depending on the severity of pain, opioid requirements at the time therapy with the high-potency injection is initiated, and patient response. Although patients who have become tolerant to another opioid may be at least partially cross-tolerant to morphine also, it is recommended that one-half of the equianalgesic dose of morphine be used initially, then adjusted as necessary. 8

Intravenous, 4 to 10 mg diluted in 4 to 5 mL of sterile water for injection, administered slowly. For severe, chronic pain the medication may also be administered via intravenous infusion at a rate titrated to the requirements and response of the individual patient. 64

Epidural (in the lumbar region), 5 mg.

Note: If adequate pain relief is not achieved within one hour, incremental doses of 1 to 2 mg may be administered at intervals sufficient to assess effectiveness, up to a maximum of 10 mg per twenty-four hours.
Intrathecal, 200 mcg (0.2 mg) to 1 mg as a single dose.

Note: Clinical experience with repeated intrathecal injections is limited. Therefore, repeated administration via this route is not recommended. Alternate routes of administration should be considered for treating recurrent or chronic pain.

Usual pediatric dose

Analgesic¾
Subcutaneous, 100 to 200 mcg (0.1 to 0.2 mg) per kg of body weight every four hours as needed, not to exceed 15 mg per dose.
Intravenous, 50 to 100 mcg (0.05 to 0.1 mg) per kg of body weight, administered very slowly.
Preoperative¾
Intramuscular, 50 to 100 mcg (0.05 to 0.1 mg) per kg of body weight, not to exceed 10 mg per dose.

Strength(s) usually available

U.S.¾With preservative

1 mg per mL (Rx) [Generic] 20

2 mg per mL (Rx) [Generic] 20

4 mg per mL (Rx) [Generic] 20

5 mg per mL (Rx) [Generic] 20

8 mg per mL (Rx) [Generic] 20

10 mg per mL (Rx) [Generic] 20

15 mg per mL (Rx) [Generic] 20

25 mg per mL (Rx) [Generic] 20

50 mg per mL (Rx) [Generic] 20

Without preservative

500 mcg (0.5 mg) per mL (Rx)[Astramorph PF 59] [Duramorph 60] [Generic] 20

1 mg per mL (Rx)[Astramorph PF 59] [Duramorph 60] [Generic] 20

50 mg per mL (Rx) [Generic] 20

Canada¾With preservative

1 mg per mL (Rx) [Generic] 62

2 mg per mL (Rx) [Generic] 62

5 mg per mL (Rx) [Generic] 62

10 mg per mL (Rx) [Generic] 62

15 mg per mL (Rx) [Generic] 62

25 mg per mL (Rx)[Morphine Forte 62]

50 mg per mL (Rx)[Morphine Extra-Forte 62]

Without preservative

500 mcg (0.5 mg) per mL (Rx)[Epimorph 65] [Generic] 62

1 mg per mL (Rx)[Epimorph 65] [Generic] 62, 64

2 mg per mL (Rx) [Generic] 64

25 mg per mL (Rx)[Morphine H.P 63] [Generic] 64

50 mg per mL (Rx)[Morphine H.P 63] [Generic] 64

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from light. Protect from freezing.

Stability:

Do not autoclave the preservative-free injection.
Unused portion of preservative-free injection must be discarded.

Incompatibilities:

Morphine Sulfate Injection USP is incompatible with soluble barbiturates.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in both the U.S. and Canada.

MORPHINE SULFATE SOLUBLE TABLETS

Usual adult dose

Analgesic¾
Intramuscular or subcutaneous, 5 to 20 mg (usually 10 mg, initially) every four hours as needed.

Note: The recommendation of an initial 10-mg dose is based on a 70-kg person.

Usual pediatric dose

Analgesic¾
Subcutaneous, 100 to 200 mcg (0.1 to 0.2 mg) per kg of body weight every four hours as needed, not to exceed 15 mg per dose.

Strength(s) usually available

U.S.¾10 mg (Rx) [Generic] 66

15 mg (Rx) [Generic] 66

30 mg (Rx) [Generic] 66

Canada¾Not commercially available.

Packaging and storage:

Store between 15 and 30 °C (59 and 86 °F), in a tight, light-resistant container, unless otherwise specified by manufacturer.

Preparation of dosage form:

For parenteral administration¾Dissolve the required number of tablets in a suitable volume of sterile water for injection, then filter through a 0.22-micron membrane filter. 14

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in the U.S.

Rectal Dosage Forms

MORPHINE HYDROCHLORIDE SUPPOSITORIES

Usual adult dose

Analgesic¾
Rectal, 20 to 30 mg every four to six hours.

Usual pediatric dose

Analgesic¾
Dosage must be individualized by the physician according to the severity of pain as well as on the basis of the patient"s age and size.

Strength(s) usually available

U.S.¾Not commercially available.
Canada¾10 mg (Rx)[M.O.S 45]

20 mg (Rx)[M.O.S 45]

30 mg (Rx)[M.O.S 45]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a well-closed container, unless otherwise specified by manufacturer. Protect from freezing.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in Canada.

MORPHINE SULFATE SUPPOSITORIES

Usual adult dose

Analgesic¾
Rectal, 10 to 30 mg every four hours or as required.

Note: Dosage must be individualized according to the severity of pain and the response of the patient.

Usual pediatric dose

Analgesic¾
Dosage must be individualized by physician on the basis of the patient"s age and size.

Strength(s) usually available

U.S.¾5 mg (Rx)[MS/S 49] [RMS Uniserts 50] [Roxanol 48] [Generic] 20

10 mg (Rx)[MS/S 49] [RMS Uniserts 50] [Roxanol 48] [Generic] 20

20 mg (Rx)[MS/S 49] [RMS Uniserts 50] [Roxanol 48] [Generic] 20

30 mg (Rx)[MS/S 49] [RMS Uniserts 50] [Roxanol 48] [Generic] 20

Canada¾5 mg (Rx)[Statex 52]

10 mg (Rx)[MSIR 53] [Statex 52]

20 mg (Rx)[MSIR 53] [Statex 52]

30 mg (Rx)[MSIR 53] [Statex 52]

Packaging and storage:

Store between 15 and 30 °C (59 and 86 °F), in a well-closed container, unless otherwise specified by manufacturer. Protect from freezing.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in both the U.S. and Canada.

NALBUPHINE

Summary of Differences

Indications¾
Caution required when used as analgesic to relieve pain in patients with severely compromised cardiac function; cardiovascular effects in these patients have not been fully evaluated.
Pharmacology/pharmacokinetics :

Mechanism of action/effect:
An opioid agonist/antagonist analgesic.
Agonist: Has agonist activity at the kappa and sigma receptors.
Antagonist: Has antagonist activity at the mu receptor; may precipitate withdrawal symptoms in patients who are physically dependent on mu-receptor agonists.

Equivalence:
10 mg via intramuscular injection therapeutically equivalent to 10 mg of intramuscular morphine.

Half-life:
5 hours.

Onset of action:
Intramuscular: Within 15 minutes.
Intravenous: 2-3 minutes.
Subcutaneous: Within 15 minutes.

Time to peak concentration:
Intramuscular: 0.5 hour.

Peak plasma concentration:
48 nanograms per mL.

Time to peak effect:
Intramuscular: 60 minutes.
Intravenous: 30 minutes.

Duration of action (nontolerant patients only; decreases as tolerance develops during chronic therapy):

Intramuscular: 3-6 hours.
Intravenous: 3-4 hours.
Subcutaneous: 3-6 hours.

Elimination:
Renal.

Precautions¾
Drug interactions and/or related problems:
May antagonize effects of mu-receptor agonists.

Medical considerations/contraindications:
Should be used with caution in patients who are physically dependent on opioid agonists.

Side/adverse effects¾
Rarely, may cause subjective and psychotomimetic effects characteristic of sigma receptor agonists.
Respiratory depression subject to a "ceiling effect,"" after which the depth of respiratory depression does not increase with dose.
More likely than most other opioid analgesics to produce symptoms associated with histamine release.
Has lower dependence liability than opioid agonists.
Withdrawal symptoms less severe than those produced by opioid agonist analgesics.

Parenteral Dosage Forms

NALBUPHINE HYDROCHLORIDE INJECTION

Usual adult dose

Analgesic¾
Intramuscular, intravenous, or subcutaneous, 10 mg every three to six hours as needed.

Note: The usual adult dose is based on a 70-kg person.
Anesthesia adjunct (balanced anesthesia) ¾
Initial: Intravenous, 300 mcg (0.3 mg) to 3 mg per kg of body weight, administered over a ten- to fifteen-minute period.
Supplemental: Intravenous, 250 to 500 mcg (0.25 to 0.5 mg) per kg of body weight, as required. 5

Usual adult prescribing limits

For nontolerant patients¾
Up to 20 mg as a single dose and up to 160 mg as a total daily dose.

Usual pediatric dose

Dosage has not been established.

Strength(s) usually available

U.S.¾With preservatives

10 mg per mL (Rx)[Nubain 67 (methylparaben) (propylparaben) (sodium metabisulfite)] [Generic] 20

20 mg per mL (Rx)[Nubain 67 (methylparaben) (propylparaben) (sodium metabisulfite)] [Generic] 20

Without preservatives

10 mg per mL (Rx)[Nubain 67]

20 mg per mL (Rx)[Nubain 67]

Canada¾With preservatives

10 mg per mL (Rx)[Nubain 68 (methylparaben) (propylparaben) (sodium metabisulfite)]

20 mg per mL (Rx)[Nubain 68 (methylparaben) (propylparaben) (sodium metabisulfite)]

Packaging and storage:

Store between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from light. Protect from freezing.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.

Note: Controlled substance in Canada.

OPIUM

Summary of Differences

Indications¾
  Oral dosage form:
    Indicated as antidiarrheal.
    Also, used as narcotic abstinence syndrome suppressant in neonates.

Pharmacology/pharmacokinetics¾
  Mechanism of action/effect:
    An opioid agonist analgesic; has agonist activity primarily at the mu receptor.

  Equivalence:
    13.3 mg parenterally is therapeutically equivalent to 10 mg of intramuscular morphine.

  Elimination:

Renal and biliary.

Additional Dosing Information

See also General Dosing Information.

The effects of opium preparations are due primarily to the morphine component.
For oral dosage form only

Alteration of intestinal motility in patients with traveler"s diarrhea may result in prolonged fever by slowing expulsion of infectious organisms that penetrate intestinal mucosa (for example, Shigella, Salmonella, and certain strains of Escherichia coli).
Opium may produce fluid retention in the bowel, which may mask dehydration and electrolyte depletion caused by severe diarrhea, especially in young children. Patients with severe or prolonged diarrhea should be monitored for signs of dehydration or electrolyte imbalance, and corrective therapy administered as required.
To reduce the risk of toxic megacolon in patients with acute inflammatory bowel disease, treatment with opium tincture should be discontinued promptly if abdominal distention or other gastrointestinal symptoms occur.
Tolerance to the antidiarrheal effects of opium tincture may develop with prolonged use.
Following prolonged administration of high doses, opium tincture should be withdrawn gradually in order to reduce the possibility of withdrawal symptoms.
Many clinicians have recommended use of diluted opium tincture instead of paregoric in the treatment of neonatal narcotic dependence, because of the risks associated with two of the components of the paregoric formulation. Opium tincture is diluted to produce the same concentration of morphine as paregoric and may be administered every 3 hours, with gradual withdrawal over 2 to 4 weeks when symptoms are controlled.
For parenteral dosage form only

This formulation contains all of the alkaloids of opium as the hydrochlorides.

Oral Dosage Forms

OPIUM TINCTURE (Laudanum) USP

Usual adult dose

Antidiarrheal¾
Oral, 0.3 to 1 mL (usually 0.6 mL) (the equivalent of morphine¾3 to 10 mg) four times a day.

Usual adult prescribing limits

A single dose of 1 mL, or a total of 6 mL within twenty-four hours.

Usual pediatric dose

Dosage has not been established.

Strength(s) usually available

U.S.¾10% of opium (the equivalent of 900 mg to 1.1 grams of anhydrous morphine per 100 mL) (Rx) [Generic] (alcohol 17-21%) 20

Canada¾10% of opium (the equivalent of 900 mg to 1.1 grams of anhydrous morphine per 100 mL) (Rx) [Generic] (alcohol 17-21%)

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight, light-resistant container. Avoid exposure to direct sunlight and excessive heat. Protect from freezing.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· Do not take other medicines without your doctor''s advice.
· Keep out of reach of children.
· May be habit-forming.

Note: Caution¾Be careful not to confuse opium tincture with camphorated tincture of opium (paregoric).
Controlled substance in both the U.S. and Canada.
Refrigeration is not recommended because decreased solubility and precipitation of some of the ingredients may occur. If this occurs, the preparation must be discarded.

Parenteral Dosage Forms

OPIUM ALKALOIDS HYDROCHLORIDES INJECTION (Papaveretum)

Usual adult dose

Analgesic¾
Intramuscular or subcutaneous, 5 to 20 mg every four to five hours as needed.

Usual pediatric dose

Dosage has not been established.

Strength(s) usually available

U.S.¾Not commercially available. 69

Canada¾With preservatives

20 mg, as hydrochlorides of opium alkaloids, per mL (Rx)[Pantopon 70 (methylparaben) (propylparaben)]

Note: Contains 10 mg of anhydrous morphine per mL. 70

Packaging and storage:

Store between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from freezing.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in Canada.

OXYCODONE

Summary of Differences

Pharmacology/pharmacokinetics¾
Mechanism of action/effect:
An opioid agonist analgesic; has agonist activity primarily at the mu receptor.

Equivalence:
30 mg via oral administration therapeutically equivalent to 10 mg of intramuscular morphine.

Half-life:
2-3 hours.

Time to peak effect:
Oral: 1 hour.

Duration of action (nontolerant patients only; duration decreases as tolerance develops during chronic therapy):
Oral: 3-4 hours.

Elimination:
Renal.

Oral Dosage Forms

OXYCODONE HYDROCHLORIDE ORAL SOLUTION USP

Usual adult dose

Analgesic¾
Oral, 5 mg every three to six hours as needed; may be increased if severe pain is present.

Usual pediatric dose

Dosage must be individualized by physician on the basis of patient"s age and size. Use of calibrated measure is recommended to prevent possible overdosage in children up to 6 years of age.

Strength(s) usually available

U.S.¾5 mg per 5 mL (Rx)[Roxicodone 71 (alcohol 7-9%)]

20 mg per mL (Rx)[Roxicodone Intensol 71]

Canada¾Not commercially available.

Packaging and storage:

Store between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight, light-resistant container. Protect from freezing.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in the U.S.

OXYCODONE HYDROCHLORIDE TABLETS USP

Usual adult dose

Analgesic¾
Oral, 5 mg every three to six hours or 10 mg three or four times a day 10 as needed; may be increased if severe pain is present.

Usual pediatric dose

Dosage must be individualized by physician on the basis of patient"s age and size.

Strength(s) usually available

U.S.¾5 mg (Rx)[Roxicodone 71 (scored)]

Canada¾5 mg (Rx)[Supeudol 72]

10 mg (Rx)[Supeudol 72]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F). Store in a tight, light-resistant container.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in both the U.S. and Canada.

OXYCODONE HYDROCHLORIDE EXTENDED-RELEASE TABLETS

Usual adult dose

Analgesic¾
Oral, administer dose every twelve hours 86.

Note: Dosage must be individualized by the physician according to the severity of pain and patient response 86.

The 80-mg dose should be used in opioid tolerant patients only 86.

Usual pediatric dose

Safety and efficacy have not been established 86.

Strength(s) usually available

U.S.¾10 mg (Rx)[OxyContin 86]

20 mg (Rx)[OxyContin 86]

40 mg (Rx)[OxyContin 86]

80 mg (Rx)[OxyContin 86]

Canada¾10 mg (Rx)[OxyContin 89]

20 mg (Rx)[OxyContin 89]

40 mg (Rx)[OxyContin 89]

80 mg (Rx)[OxyContin 89]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F). Store in a tight, light-resistant container.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in both the U.S. and Canada.

Rectal Dosage Forms

OXYCODONE HYDROCHLORIDE SUPPOSITORIES

Usual adult dose

Analgesic¾
Rectal, 10 to 40 mg three or four times a day.

Usual pediatric dose

Dosage must be individualized by physician on the basis of patient"s age and size.

Strength(s) usually available

U.S.¾Not commercially available.
Canada¾10 mg (Rx)[Supeudol 72]

20 mg (Rx)[Supeudol 72]

Packaging and storage:

Store between 2 and 8 °C (36 and 46 °F), in a well-closed container, unless otherwise specified by manufacturer. Protect from freezing.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.
· Store in refrigerator. Protect from freezing.

Note: Controlled substance in Canada.

OXYMORPHONE

Summary of Differences

Indications¾

FDA-approved, but rarely if ever used, as adjunctive therapy in the treatment of acute pulmonary edema secondary to left ventricular failure.

Pharmacology/pharmacokinetics¾

Mechanism of action/effect:

An opioid agonist analgesic; has agonist activity primarily at the mu receptor.

Equivalence:

1 mg via intramuscular injection or 10 mg rectally therapeutically equivalent to 10 mg of intramuscular morphine.

Onset of action:

Intramuscular: 10-15 minutes.
Intravenous: 5-10 minutes.
Subcutaneous: 10-20 minutes.
Rectal: 15-30 minutes.

Time to peak effect:

Intramuscular: 30-90 minutes.
Intravenous: 15-30 minutes.
Rectal: 2 hours.

Duration of action (nontolerant patients only; duration decreases as tolerance develops during chronic therapy):

Intramuscular: 3-6 hours.
Intravenous: 3-4 hours.
Subcutaneous: 3-6 hours.
Rectal: 3-6 hours.

Elimination:

Renal.

Parenteral Dosage Forms

OXYMORPHONE HYDROCHLORIDE INJECTION USP

Usual adult dose

Analgesic¾

Intramuscular or subcutaneous, 1 to 1.5 mg every three to six hours as needed.
Intravenous, 500 mcg (0.5 mg).

Note: Doses may be cautiously increased, if necessary, if pain is severe.
For obstetrical analgesia¾Intramuscular, 500 mcg (0.5 mg) to 1 mg.

Usual pediatric dose

Dosage has not been established.

Strength(s) usually available

U.S.¾With preservatives

1 mg per mL (Rx)[Numorphan 20 (methylparaben) (propylparaben)]

1.5 mg per mL (Rx)[Numorphan 20 (methylparaben) (propylparaben)]

Canada¾With preservatives

1.5 mg per mL (Rx)[Numorphan 73 (methylparaben) (propylparaben)]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from light. Protect from freezing.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in both the U.S. and Canada.

Rectal Dosage Forms

OXYMORPHONE HYDROCHLORIDE SUPPOSITORIES USP

Usual adult dose

Analgesic¾
Rectal, 5 mg every four to six hours as needed.

Usual pediatric dose

Dosage has not been established.

Strength(s) usually available

U.S.¾5 mg (Rx)[Numorphan 20]

Canada¾5 mg (Rx)[Numorphan 73]

Packaging and storage:

Store between 2 and 8 °C (36 and 46 °F), in a well-closed container. Protect from freezing.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.
· Store in refrigerator. Protect from freezing.

Note: Controlled substance in both the U.S. and Canada.

PENTAZOCINE

Summary of Differences

Indications¾
Less desirable than morphine or other opioid agonist analgesics for relief of pain due to acute myocardial infarction because of cardiovascular effects that tend to increase cardiac work.

Pharmacology/pharmacokinetics¾
Mechanism of action/effect:
An opioid agonist/antagonist analgesic.
Agonist: Has agonist activity at the kappa and sigma receptors.
Antagonist: Has antagonist activity at the mu receptor; may precipitate withdrawal symptoms in patients who are physically dependent on mu-receptor agonists.

Equivalence:
60 mg via intramuscular injection or 180 mg via oral administration therapeutically equivalent to 10 mg of intramuscular morphine.

Protein binding:
Moderate.

Half-life:
2-3 hours.

Onset of action:
Intramuscular: 15-20 minutes.

Intravenous: 2-3 minutes.
Oral: 15-30 minutes.
Subcutaneous: 15-20 minutes.

Time to peak effect:
Intramuscular: 30-60 minutes.
Intravenous: 15-30 minutes.
Oral: 60-90 minutes.
Subcutaneous: 30-60 minutes.

Duration of action (nontolerant patients only; decreases as tolerance develops during chronic therapy):
Intramuscular: 2-3 hours.
Intravenous: 2-3 hours.
Oral: 3 hours.
Subcutaneous: 2-3 hours.

Elimination:
Renal, 5-23% as unchanged pentazocine, and biliary.

Precautions¾
Drug interactions and/or related problems:
May antagonize the effects of mu-receptor agonists.

Medical considerations/contraindications:
Must be used with caution in patients physically dependent on opioid agonists and in patients with acute myocardial infarction.

Side/adverse effects¾
Although occurs rarely, more likely than butorphanol or nalbuphine to cause subjective and psychotomimetic effects characteristic of sigma receptor agonists.
Respiratory depression subject to a "ceiling effect,"" after which the depth of respiratory depression does not increase with dose.
Has lower dependence liability than opioid agonists.
Withdrawal symptoms less severe than those produced by opioid agonist analgesics.

Additional Dosing Information

See also General Dosing Information.

The naloxone present in the pentazocine and naloxone dosage formulation has no pharmacologic activity when administered orally. If the product is misused by injection, the naloxone antagonizes the effects of pentazocine. Also, injection of the medication will precipitate withdrawal symptoms if the patient is physically dependent on an opioid agonist.
For long-term administration, the oral form of the medication is preferred. If the parenteral form is used instead, dosage should be reduced gradually when the medication is to be discontinued to reduce the risk of withdrawal symptoms.

The extent to which pentazocine may produce withdrawal symptoms in patients who are physically dependent on opioid analgesics depends upon the dose of pentazocine, the specific opioid drug involved, and the degree to which physical dependence has developed.
For parenteral dosage forms only

Intravenous or intramuscular administration is recommended, especially when repeated doses are required. Subcutaneous administration may lead to severe tissue damage at the injection site. When the intramuscular route is used, rotation of injection sites is essential to prevent tissue damage.

Oral Dosage Forms

PENTAZOCINE HYDROCHLORIDE TABLETS USP

Usual adult dose

Analgesic¾
Oral, 50 mg of pentazocine (base) every three to four hours as needed. The dose may be increased to 100 mg (base) if necessary, but total daily dosage should not exceed 600 mg (base).

Usual adult prescribing limits

Analgesic¾
Up to 600 mg of pentazocine (base) per day.

Usual pediatric dose

Dosage has not been established.

Strength(s) usually available

U.S.¾Not commercially available.
Canada¾50 mg (base) (Rx)[Talwin 74 (scored) (sulfites)]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight, light-resistant container.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in Canada.

PENTAZOCINE AND NALOXONE HYDROCHLORIDES TABLETS USP

Usual adult dose

Analgesic¾
Oral, 50 mg of pentazocine (base) every three to four hours as needed. The dose may be increased to 100 mg (base) if necessary, but total daily dosage should not exceed 600 mg (base).

Usual adult prescribing limits

Analgesic¾
Up to 600 mg of pentazocine (base) per day.

Usual pediatric dose

Dosage has not been established.

Strength(s) usually available

U.S.¾50 mg (base), with 500 mcg (0.5 mg) of naloxone hydrochloride (Rx)[Talwin-Nx 75 (scored)]

Canada¾Not commercially available.

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight, light-resistant container.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in the U.S.

Parenteral Dosage Forms

PENTAZOCINE LACTATE INJECTION USP

Usual adult dose

Analgesic¾
Intramuscular, intravenous, or subcutaneous, 30 mg (base) every three to four hours as needed.
Obstetrical analgesia¾
Intramuscular, 30 mg (base) as a single dose; or
Intravenous, 20 mg (base) administered when contractions become regular and repeated two or three times at two- to three-hour intervals as needed.

Usual adult prescribing limits

Up to 360 mg (base) daily.
As a single dose, up to 30 mg (base) intravenously or 60 mg (base) intramuscularly.

Usual pediatric dose

Dosage has not been established.

Strength(s) usually available

U.S.¾With preservative

30 mg (base) per mL (Rx)[Talwin 76 (acetone sodium bisulfite) (methylparaben)]

Without preservative

30 mg (base) per mL (Rx)[Talwin 76 (may contain acetone sodium bisulfite)]

Canada¾Without preservative

30 mg (base) per mL (Rx)[Talwin 77]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from freezing.

Incompatibilities:

Precipitation will occur if a soluble barbiturate is mixed in the same syringe as pentazocine.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in both the U.S. and Canada.

PROPOXYPHENE

Summary of Differences

Pharmacology/pharmacokinetics¾
Mechanism of action/effect:

An opioid agonist analgesic; has agonist activity at the mu receptor.

Equivalence:
Dose therapeutically equivalent to 10 mg of intramuscular morphine too toxic to administer.

Protein binding:
High.

Biotransformation:
Metabolite norpropoxyphene is toxic.

Half-life:
Propoxyphene: 6-12 hours.
Norpropoxyphene: 30-36 hours.

Onset of action:
Oral: 15-60 minutes.

Time to peak concentration:
Oral: 2-2.5 hours.

Peak plasma concentration:
0.05-0.1 mcg per mL.

Time to peak effect:
Oral: 2 hours.

Duration of action (nontolerant patients only; decreases as tolerance develops during chronic therapy):
Oral: 4-6 hours.

Elimination:
Renal, < 10% as unchanged propoxyphene; biliary.

Precautions¾
Drug interactions and/or related problems:
Risk of convulsions if overdose of propoxyphene administered to amphetamine-treated patients.
May increase effects of coumarin- or indandione-derivative anticoagulants.
Concurrent use with carbamazepine not recommended because may decrease carbamazepine metabolism, leading to increased risk of toxicity.
Effects may be decreased in patients who smoke because tobacco smoking increases propoxyphene metabolism.

Laboratory value alterations:
May elevate levels of enzymes in liver function tests.

Side/adverse effects¾
May be more likely than most opioid analgesics to cause convulsions.

Hepatotoxicity has been reported.
Has lower dependence liability than other opioid agonists.
Withdrawal symptoms less severe than those produced by stronger opioid agonist analgesics.

Additional Dosing Information

See also General Dosing Information.

100 mg of propoxyphene napsylate are equivalent to 65 mg of propoxyphene hydrochloride.

Oral Dosage Forms

PROPOXYPHENE HYDROCHLORIDE CAPSULES USP

Usual adult dose

Analgesic¾
Oral, 65 mg every four hours as needed.

Usual adult prescribing limits

Up to 390 mg daily.

Usual pediatric dose

Dosage has not been established.

Strength(s) usually available

U.S.¾65 mg (Rx)[Cotanal-65 20] [Darvon 78] [PP-Cap 79] [Generic] 20

Canada¾Not commercially available.

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F). Store in a tight container.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in both the U.S. and Canada.

PROPOXYPHENE HYDROCHLORIDE TABLETS

Usual adult dose

Analgesic¾
Oral, 65 mg every four hours as needed.

Usual adult prescribing limits

Analgesic¾
Oral, up to 390 mg daily.

Usual pediatric dose

Dosage has not been established.

Strength(s) usually available

U.S.¾Not commercially available.
Canada¾65 mg (Rx)[642 80 (scored)]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a well-closed container, unless otherwise specified by manufacturer.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in Canada.

PROPOXYPHENE NAPSYLATE CAPSULES

Usual adult dose

Analgesic¾
Oral, 100 mg every four hours as needed.

Usual adult prescribing limits

Analgesic¾
Up to 600 mg daily.

Usual pediatric dose

Dosage has not been established.

Strength(s) usually available

U.S.¾Not commercially available.
Canada¾100 mg (Rx)[Darvon-N 81]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight container.

Auxiliary labeling:

· May cause drowsiness.
· Avoid alcoholic beverages.
· May be habit-forming.

Note: Controlled substance in Canada.

PROPOXYPHENE NAPSYLATE ORAL SUSPENSION USP

Usual adult dose

Analgesic¾
Oral, 100 mg every four hours as needed.

Usual adult prescribing limits

Analgesic¾
Up to 600 mg daily.

Usual pediatric dose

Dosage has not been established.

Strength(s) usually available

U.S.¾50 mg per 5 mL (Rx)[Darvon-N 82 (butylparaben) (methylparaben) (propylparaben) (saccharin) (sucrose)]

Canada¾Not commercially available.

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight container. Protect from light. Protect from freezing.

Auxiliary labeling:

- Shake well.
- May cause drowsiness.
- Avoid alcoholic beverages.
- May be habit-forming.

Note: Controlled substance in the U.S.

PROPOXYPHENE NAPSYLATE TABLETS USP

Usual adult dose

Analgesic¾
Oral, 100 mg every four hours as needed.

Usual adult prescribing limits

Analgesic¾
Up to 600 mg daily.

Usual pediatric dose

Dosage has not been established.

Strength(s) usually available

U.S.¾100 mg (Rx)[Darvon-N 82] [Generic] 20

Canada¾Not commercially available.

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight container.

Auxiliary labeling:

- May cause drowsiness.
- Avoid alcoholic beverages.
- May be habit-forming.

Note: Controlled substance in the U.S.