MEPERIDINE
Hydrochloride
Injection, USP

300 mg (10 mg/mL)

ONLY FOR USE WITH A COMPATIBLE HOSPIRA PCA PUMP SET WITH INJECTOR
AND A COMPATIBLE HOSPIRA INFUSION DEVICE.

Rx only

WARNING: ADDICTION, ABUSE, AND MISUSE; LIFE-THREATENING RESPIRATORY
DEPRESSION; NEONATAL OPIOID WITHDRAWAL SYNDROME; and RISKS FROM
CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS

Addiction, Abuse, and Misuse
Meperidine hydrochloride injection exposes patients and other users to the risks of opioid
addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient’s risk prior
to prescribing meperidine hydrochloride injection, and monitor all patients regularly for the
development of these behaviors or conditions [see WARNINGS].

Life-Threatening Respiratory Depression
Serious, life-threatening, or fatal respiratory depression may occur with use of meperidine
hydrochloride injection. Monitor for respiratory depression, especially during initiation of
meperidine hydrochloride injection or following a dose increase [see WARNINGS].

Neonatal Opioid Withdrawal Syndrome
Prolonged use of meperidine hydrochloride injection during pregnancy can result in neonatal
opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and
requires management according to protocols developed by neonatology experts. If opioid use is
required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal
opioid withdrawal syndrome and ensure that appropriate treatment will be available [see
WARNINGS].

Risks From Concomitant Use With Benzodiazepines Or Other CNS Depressants
Concomitant use of opioids with benzodiazepines or other central nervous system (CNS)
depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and
death [see WARNINGS, PRECAUTIONS; Drug Interactions].

- Reserve concomitant prescribing of meperidine hydrochloride and benzodiazepines or other
  CNS depressants for use in patients for whom alternative treatment options are inadequate.
- Limit dosages and durations to the minimum required.
- Follow patients for signs and symptoms of respiratory depression and sedation.
DESCRIPTION
Meperidine Hydrochloride Injection, USP 10 mg/mL is a sterile, nonpyrogenic, hypotonic solution of meperidine hydrochloride, USP, in an acetate buffer. This product is to be administered by the intravenous route via a compatible Hospira infusion device.

Each mL contains meperidine hydrochloride 10 mg. Sodium acetate, anhydrous 1.5 mg and glacial acetic acid, 0.0012 mL are added as buffers. pH 4.5 (3.5 to 6.0).

The solution contains no bacteriostat or antimicrobial agent and is intended only for use as a single-dose unit to provide analgesia via the intravenous route using a compatible Hospira infusion device.

Meperidine is classified pharmacologically as a synthetic narcotic analgesic.

Meperidine Hydrochloride is ethyl-1-methyl-4-phenylisonipecotate hydrochloride, a white, crystalline substance with a melting point of 186° to 189°C. It is readily soluble in water and has a neutral reaction and a slightly bitter taste. The solution is not decomposed by a short period of boiling.

It has the following structural formula:

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C\textsubscript{15}H\textsubscript{21}NO\textsubscript{2} • HCl M.W. 283.80

CLINICAL PHARMACOLOGY
Meperidine hydrochloride is a narcotic analgesic with multiple actions qualitatively similar to those of morphine; the most prominent of these involve the central nervous system and organs composed of smooth muscle. The principal actions of therapeutic value are analgesia and sedation.

There is some evidence which suggests that meperidine may produce less smooth muscle spasm, constipation, and depression of the cough reflex than equianalgesic doses of morphine. Meperidine, in 60 mg to 80 mg parenteral doses, is approximately equivalent in analgesic effect to 10 mg of morphine. The onset of action is slightly more rapid than with morphine, and the duration of action is slightly shorter. Meperidine is significantly less effective by the oral than by the parenteral route, but the exact ratio of oral to parenteral effectiveness is unknown.

Meperidine is metabolized through biotransformation. The elimination half-life is 3 to 8 hours in healthy volunteers and is 1.3 to 2 times greater in post-operative or cirrhotic patients. The only bioactive metabolite is normeperidine which has an average elimination half-life of 20.6 hours. Elevated serum levels have been reported to cause central nervous system excitatory effects.

INDICATIONS AND USAGE
Meperidine hydrochloride is indicated for the management of moderate to pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.
Limitations of Use

Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses [see WARNINGS], reserve meperidine hydrochloride for use in patients for whom alternative treatment options [e.g., non-opioid analgesics or opioid combination products]

- Have not been tolerated, or are not expected to be tolerated,
- Have not provided adequate analgesia, or are not expected to provide adequate analgesia

CONTRAINDICATIONS

Meperidine Hydrochloride Injection is contraindicated in patients with:

- Significant respiratory depression [see WARNINGS]
- Acute of severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment [see WARNINGS]
- Hypersensitivity to meperidine.
- Meperidine is contraindicated in patients who are receiving monoamine oxidase (MAO) inhibitors or those who have recently received such agents. Therapeutic doses of meperidine have occasionally precipitated unpredictable, severe, and occasionally fatal reactions in patients who have received such agents within 14 days. The mechanism of these reactions is unclear, but may be related to a pre-existing hyperphenylalaninemia. Some have been characterized by coma, severe respiratory depression, cyanosis, and hypotension, and have resembled the syndrome of acute narcotic overdose. In other reactions the predominant manifestations have been hyperexcitability, convulsions, tachycardia, hyperpyrexia, and hypertension. Although it is not known that other narcotics are free of the risk of such reactions, virtually all of the reported reactions have occurred with meperidine. If a narcotic is needed in such patients, a sensitivity test should be performed in which repeated, small, incremental doses of morphine are administered over the course of several hours while the patient’s condition and vital signs are under careful observation. (Intravenous hydrocortisone or prednisolone have been used to treat severe reactions, with the addition of intravenous chlorpromazine in those cases exhibiting hypertension and hyperpyrexia. The usefulness and safety of narcotic antagonists in the treatment of these reactions is unknown).

WARNINGS

Addiction, Abuse, and Misuse

Meperidine Hydrochloride Injection is a Schedule II controlled substance. As an opioid, meperidine hydrochloride exposes users to the risks of addiction, abuse, and misuse [see DRUG ABUSE AND DEPENDENCE].

Although the risk of addiction in any individual is unknown, it can occur in patients appropriately prescribed meperidine hydrochloride. Addiction can occur at recommended dosages and if the drug is misused or abused

Assess each patient’s risk for opioid addiction, abuse, or misuse prior to prescribing meperidine hydrochloride injection, and monitor all patients receiving meperidine for the development of these behaviors or conditions. Risks are increased in patients with a personal or family history of substance abuse (including drug or alcohol abuse or addiction) or mental illness (e.g., major depression). The potential for these risks should not, however, prevent the proper management of pain in any given patient. Patients at increased risk may be prescribed opioids such as meperidine, but use in such patients necessitates intensive counseling about the risks and proper use of meperidine hydrochloride along with intensive monitoring for signs of addiction, abuse, and misuse.
Opioids are sought by drug abusers and people with addiction disorders and are subject to criminal diversion. Consider these risks when prescribing or dispensing meperidine hydrochloride. Strategies to reduce these risks include prescribing the drug in the smallest appropriate quantity.

Contact local state professional licensing board or state controlled substances authority for information on how to prevent and detect abuse or diversion of this product.

**Life-Threatening Respiratory Depression**

Serious, life-threatening, or fatal respiratory depression has been reported with the use of opioids, even when used as recommended. Respiratory depression, if not immediately recognized and treated, may lead to respiratory arrest and death. Management of respiratory depression may include close observation, supportive measures, and use of opioid antagonists, depending on the patient’s clinical status [see OVERDOSAGE]. Carbon dioxide (CO$_2$) retention from opioid-induced respiratory depression can exacerbate the sedating effects of opioids.

While serious, life-threatening, or fatal respiratory depression can occur at any time during the use of meperidine hydrochloride, the risk is greatest during the initiation of therapy or following a dosage increase. Monitor patients closely for respiratory depression, especially within the first 24 to 72 hours of initiating therapy with and following dosage increases of meperidine hydrochloride.

To reduce the risk of respiratory depression, proper dosing and titration of meperidine hydrochloride are essential [see DOSAGE AND ADMINISTRATION]. Overestimating the meperidine hydrochloride dosage when converting patients from another opioid product can result in a fatal overdose with the first dose.

**Neonatal Opioid Withdrawal Syndrome**

Prolonged use of meperidine hydrochloride during pregnancy can result in withdrawal in the neonate. Neonatal opioid withdrawal syndrome, unlike opioid withdrawal syndrome in adults, may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available [see PRECAUTIONS; Information for Patients, Pregnancy].

**Head Injury and Increased Intracranial Pressure.** The respiratory depressant effects of meperidine and its capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions, or a preexisting increase in intracranial pressure. Furthermore, narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries. In such patients, meperidine must be used with extreme caution and only if its use is deemed essential.

**Intravenous Use:** See DOSAGE AND ADMINISTRATION.

**Hypotensive Effect.** The administration of meperidine may result in severe hypotension in the postoperative patient or any individual whose ability to maintain blood pressure has been compromised by a depleted blood volume or the administration of drugs such as the phenothiazines or certain anesthetics.

**Usage in Ambulatory Patients.** Meperidine may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery. The patient should be cautioned accordingly.

Meperidine, like other narcotics, may produce orthostatic hypotension in ambulatory patients.
Usage in Pregnancy and Lactation. Meperidine should not be used in pregnant women prior to the labor period, unless in the judgment of the physician the potential benefits outweigh the possible hazards, because safe use in pregnancy prior to labor has not been established relative to possible adverse effects on fetal development.

When used as an obstetrical analgesic, meperidine crosses the placental barrier and can produce depression of respiration and psychophysioologic functions in the newborn. Resuscitation may be required (see section on OVERDOSAGE).

Meperidine appears in the milk of nursing mothers receiving the drug.

Risks from Concomitant Use with Benzodiazepines or Other CNS Depressants

Profound sedation, respiratory depression, coma, and death may result from the concomitant use of meperidine hydrochloride with benzodiazepines or other CNS depressants (e.g., non-benzodiazepine sedatives/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, other opioids, alcohol). Because of these risks, reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate.

Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of drug-related mortality compared to use of opioid analgesics alone. Because of similar pharmacological properties, it is reasonable to expect similar risk with the concomitant use of other CNS depressant drugs with opioid analgesics [see PRECAUTIONS; Drug Interactions].

If the decision is made to prescribe a benzodiazepine or other CNS depressant concomitantly with an opioid analgesic, prescribe the lowest effective dosages and minimum durations of concomitant use. In patients already receiving an opioid analgesic, prescribe a lower initial dose of the benzodiazepine or other CNS depressant than indicated in the absence of an opioid, and titrate based on clinical response. If an opioid analgesic is initiated in a patient already taking a benzodiazepine or other CNS depressant, prescribe a lower initial dose of the opioid analgesic, and titrate based on clinical response. Follow patients closely for signs and symptoms of respiratory depression and sedation.

Advise both patients and caregivers about the risks of respiratory depression and sedation when meperidine hydrochloride is used with benzodiazepines or other CNS depressants (including alcohol and illicit drugs). Advise patients not to drive or operate heavy machinery until the effects of concomitant use of the benzodiazepine or other CNS depressant have been determined. Screen patients for risk of substance use disorders, including opioid abuse and misuse, and warn them of the risk for overdose and death associated with the use of additional CNS depressants including alcohol and illicit drugs [see PRECAUTIONS; Drug Interactions and PRECAUTIONS; Information for Patients].

Life-Threatening Respiratory Depression in Patients with Chronic Pulmonary Disease or in Elderly, Cachectic, or Debilitated Patients

The use of meperidine hydrochloride in patients with acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment is contraindicated.

Patients with Chronic Pulmonary Disease: Meperidine hydrochloride - treated patients with significant chronic obstructive pulmonary disease or cor pulmonale, and those with a substantially decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression are at increased risk of decreased respiratory drive including apnea, even at recommended dosages of meperidine hydrochloride [see WARNINGS].
**Elderly, Cachetic, or Debilitated Patients:** Life-threatening respiratory depression is more likely to occur in elderly, cachectic, or debilitated patients because they may have altered pharmacokinetics or altered clearance compared to younger, healthier patients [see WARNINGS].

Monitor such patients closely, particularly when initiating and titrating meperidine hydrochloride and when meperidine hydrochloride is given concomitantly with other drugs that depress respiration [see WARNINGS]. Alternatively, consider the use of non-opioid analgesics in these patients.

**Adrenal Insufficiency**

Cases of adrenal insufficiency have been reported with opioid use, more often following greater than 1 month of use. Presentation of adrenal insufficiency may include non-specific symptoms and signs including nausea, vomiting, anorexia, fatigue, weakness, dizziness, and low blood pressure. If adrenal insufficiency is suspected, confirm the diagnosis with diagnostic testing as soon as possible. If adrenal insufficiency is diagnosed, treat with physiologic replacement doses of corticosteroids. Wean the patient off of the opioid to allow adrenal function to recover and continue corticosteroid treatment until adrenal function recovers. Other opioids may be tried as some cases reported use of a different opioid without recurrence of adrenal insufficiency. The information available does not identify any particular opioids as being more likely to be associated with adrenal insufficiency.

**PRECAUTIONS**

Do not use unless solution is clear and package is undamaged (see DOSAGE AND ADMINISTRATION).

**General:**

*Supraventricular Tachycardias.* Meperidine should be used with caution in patients with atrial flutter and other supraventricular tachycardias because of a possible vagolytic action which may produce a significant increase in the ventricular response rate.

*Convulsions.* Meperidine may aggravate pre-existing convulsions in patients with convulsive disorders. If dosage is escalated substantially above recommended levels because of tolerance development, convulsions may occur in individuals without a history of convulsive disorders. The convulsive potential of meperidine may be further increased if prolonged infusions or repeated doses are administered due to high serum levels of normeperidine.

*Acute Abdominal Conditions.* The administration of meperidine or other narcotics may obscure the diagnosis or clinical course in patients with acute abdominal conditions.

*Special Risk Patients.* Meperidine should be given with caution and the initial dose should be reduced in certain patients such as the elderly or debilitated, and those with severe impairment of hepatic or renal function, hypothyroidism, Addison’s disease, and prostatic hypertrophy or urethral stricture.

**Information for Patients**

**Addiction, Abuse, and Misuse**

Inform patients that the use of meperidine hydrochloride, even when taken as recommended, can result in addiction, abuse, and misuse, which can lead to overdose and death [see WARNINGS].

Instruct patients not to share meperidine hydrochloride with others and to take steps to protect meperidine hydrochloride from theft or misuse.
Life-Threatening Respiratory Depression

Inform patients of the risk of life-threatening respiratory depression, including information that the risk is greatest when starting meperidine hydrochloride or when the dosage is increased, and that it can occur even at recommended dosages [see WARNINGS]. Advise patients how to recognize respiratory depression and to seek medical attention if breathing difficulties develop.

Interactions with Benzodiazepines and Other CNS Depressants

Inform patients and caregivers that potentially fatal additive effects may occur if meperidine hydrochloride is used with benzodiazepines or other CNS depressants, including alcohol, and not to use these concomitantly unless supervised by a health care provider [see WARNINGS, PRECAUTIONS; Drug Interactions].

Serotonin Syndrome

Inform patients that meperidine hydrochloride could cause a rare but potentially life-threatening condition resulting from concomitant administration of serotonergic drugs. Warn patients of the symptoms of serotonin syndrome and to seek medical attention right away if symptoms develop. Instruct patients to inform their physicians if they are taking, or plan to take serotonergic medications [see WARNINGS, PRECAUTIONS; Drug Interactions].

Pregnancy

Neonatal Opioid Withdrawal Syndrome

Inform patients that prolonged use of meperidine hydrochloride during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated [see WARNINGS, PRECAUTIONS; Pregnancy]

Embryo-Fetal Toxicity

Inform female patients of reproductive potential that meperidine hydrochloride can cause fetal harm and to inform the prescriber of a known or suspected pregnancy [see PRECAUTIONS; Pregnancy].

Lactation

Advise nursing mothers to monitor infants for increased sleepiness (more than usual), breathing difficulties, or limpness. Instruct nursing mothers to seek immediate medical care if they notice these signs [see PRECAUTIONS; Nursing Mothers].

Drug Interactions

Benzodiazepines and Other Central Nervous System (CNS) Depressants

Due to additive pharmacologic effect, the concomitant use of benzodiazepines or other CNS depressants such as alcohol, other sedatives/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, and other opioids, can increase the risk of respiratory depression, profound sedation, coma, and death.

Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate. Limit dosages and durations to the minimum required. Follow patients closely for signs of respiratory depression and sedation [see WARNINGS].

Serotonergic Drugs

The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system, such as selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors
(SNRIs), tricyclic antidepressants (TCAs), triptans, 5-HT3 receptor antagonists, drugs that effect the serotonin neurotransmitter system (e.g., mirtazapine, trazodone, tramadol), and monoamine oxidase (MAO) inhibitors (those intended to treat psychiatric disorders and also others, such as linezolid and intravenous methylene blue), has resulted in serotonin syndrome. [see WARNINGS, PRECAUTIONS; Information for Patients].

If concomitant use is warranted, carefully observe the patient, particularly during treatment initiation and dose adjustment. Discontinue meperidine hydrochloride if serotonin syndrome is suspected.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Infertility
Chronic use of opioids may cause reduced fertility in females and males of reproductive potential. It is not known whether these effects on fertility are reversible [see ADVERSE REACTIONS].

Pregnancy
Fetal/Neonatal Adverse Reactions
Prolonged use of opioid analgesics during pregnancy for medical or nonmedical purposes can result in physical dependence in the neonate and neonatal opioid withdrawal syndrome shortly after birth. Neonatal opioid withdrawal syndrome presents as irritability, hyperactivity and abnormal sleep pattern, high pitched cry, tremor, vomiting, diarrhea and failure to gain weight. The onset, duration, and severity of neonatal opioid withdrawal syndrome vary based on the specific opioid used, duration of use, timing and amount of last maternal use, and rate of elimination of the drug by the newborn. Observe newborns for symptoms of neonatal opioid withdrawal syndrome and manage accordingly [see WARNINGS].

Labor or Delivery
Opioids cross the placenta and may produce respiratory depression and psycho-physiologic effects in neonates. An opioid antagonist, such as naloxone, must be available for reversal of opioid-induced respiratory depression in the neonate. Meperidine hydrochloride is not recommended for use in pregnant women during or immediately prior to labor, when other analgesic techniques are more appropriate. Opioid analgesics, including meperidine hydrochloride, can prolong labor through actions which temporarily reduce the strength, duration, and frequency of uterine contractions. However, this effect is not consistent and may be offset by an increased rate of cervical dilation, which tends to shorten labor. Monitor neonates exposed to opioid analgesics during labor for signs of excess sedation and respiratory depression.

Nursing Mothers
The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for meperidine hydrochloride and any potential adverse effects on the breastfed infant from meperidine hydrochloride or from the underlying maternal condition.

Infants exposed to meperidine hydrochloride through breast milk should be monitored for excess sedation and respiratory depression. Withdrawal symptoms can occur in breastfed infants when maternal administration of an opioid analgesic is stopped, or when breast-feeding is stopped.

Geriatric Use
Elderly patients (aged 65 years or older) may have increased sensitivity to meperidine hydrochloride. In general, use caution when selecting a dosage for an elderly patient, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other drug therapy.
Respiratory depression is the chief risk for elderly patients treated with opioids, and has occurred after large initial doses were administered to patients who were not opioid-tolerant or when opioids were co-administered with other agents that depress respiration. Titrate the dosage of meperidine hydrochloride slowly in geriatric patients [see WARNINGS].

Physicians should assure the patient, or their caregiver, has received adequate instructions for use prior to commencing therapy via PCA.

Pediatric Use. Meperidine Hydrochloride administered by the intravenous route via a compatible infusion device is not recommended for use in individuals younger than 19 years of age.

ADVERSE REACTIONS

The major hazards of meperidine, as with other narcotic analgesics, are respiratory depression and, to a lesser degree, circulatory depression; respiratory arrest, shock, and cardiac arrest have occurred.

The most frequently observed adverse reactions include light-headedness, dizziness, sedation, nausea, vomiting, and sweating. These effects seem to be more prominent in ambulatory patients and in those who are not experiencing severe pain. In such individuals, lower doses are advisable. Some adverse reactions in ambulatory patients may be alleviated if the patient lies down. Other adverse reactions include:

Nervous System. Euphoria, dysphoria, weakness, headache, agitation, tremor, uncoordinated muscle movements, severe convulsions, transient hallucinations and disorientation, visual disturbances. Inadvertent injection about a nerve trunk may result in sensory-motor paralysis which is usually, though not always, transitory.

Gastrointestinal. Dry mouth, constipation, biliary tract spasm.

Cardiovascular. Flushing of the face, tachycardia, bradycardia, palpitation, hypotension (see WARNINGS), syncope, phlebitis following intravenous injection.

Genitourinary. Urinary retention.

Allergic. Pruritus, urticaria, other skin rashes, wheal and flare over the vein with intravenous injection.

Other. Pain at injection site; local tissue irritation and induration following subcutaneous injection, particularly when repeated; antidiuretic effect.

Postmarketing Experience

- serotonin syndrome
- adrenal insufficiency

Androgen deficiency

Chronic use of opioids may influence the hypothalamic-pituitary-gonadal axis, leading to androgen deficiency that may manifest as symptoms of hypogonadism, such as impotence, erectile dysfunction, or amenorrhea. The causal role of opioids in the syndrome of hypogonadism is unknown because the various medical, physical, lifestyle, and psychological stressors that may influence gonadal hormone levels have not been adequately controlled for in studies conducted to date. Patients presenting with symptoms of androgen deficiency should undergo laboratory evaluation.

DRUG ABUSE AND DEPENDENCE

Meperidine hydrochloride is a Schedule II controlled substance.
Abuse
Meperidine hydrochloride is a substance with a high potential for abuse similar to other opioids including. Meperidine hydrochloride can be abused and is subject to misuse, addiction, and criminal diversion [see WARNINGS].

All patients treated with opioids require careful monitoring for signs of abuse and addiction, since use of opioid analgesic products carries the risk of addiction even under appropriate medical use.

Prescription drug abuse is the intentional non-therapeutic use of a prescription drug, even once, for its rewarding psychological or physiological effects.

Drug addiction is a cluster of behavioral, cognitive, and physiological phenomena that develop after repeated substance use and includes: a strong desire to take the drug, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, increased tolerance, and sometimes a physical withdrawal.

“Drug-seeking” behavior is very common in persons with substance use disorders. Drug-seeking tactics include emergency calls or visits near the end of office hours, refusal to undergo appropriate examination, testing, or referral, repeated “loss” of prescriptions, tampering with prescriptions and reluctance to provide prior medical records or contact information for other treating health care provider(s). “Doctor shopping” (visiting multiple prescribers) to obtain additional prescriptions is common among drug abusers and people suffering from untreated addiction. Preoccupation with achieving adequate pain relief can be appropriate behavior in a patient with poor pain control.

Abuse and addiction are separate and distinct from physical dependence and tolerance. Health care providers should be aware that addiction may not be accompanied by concurrent tolerance and symptoms of physical dependence in all addicts. In addition, abuse of opioids can occur in the absence of true addiction.

Meperidine hydrochloride, like other opioids, can be diverted for non-medical use into illicit channels of distribution. Careful record-keeping of prescribing information, including quantity, frequency, and renewal requests, as required by state and federal law, is strongly advised.

Proper assessment of the patient, proper prescribing practices, periodic re-evaluation of therapy, and proper dispensing and storage are appropriate measures that help to limit abuse of opioid drugs.

Dependence
Both tolerance and physical dependence can develop during chronic opioid therapy. Tolerance is the need for increasing doses of opioids to maintain a defined effect such as analgesia (in the absence of disease progression or other external factors). Tolerance may occur to both the desired and undesired effects of drugs, and may develop at different degrees for different effects.

Physical dependence results in withdrawal symptoms after abrupt discontinuation or a significant dosage reduction of a drug. Withdrawal also may be precipitated through the administration of drugs with opioid antagonist activity (e.g., naloxone, nalmefene), mixed agonist/antagonist analgesics (pentazocine, butorphanol, nalbuphine), or partial agonists (buprenorphine). Physical dependence may not occur to a clinically significant degree until after several days to weeks of continued opioid usage.

Meperidine hydrochloride should not be abruptly discontinued [see DOSAGE AND ADMINISTRATION]. If meperidine hydrochloride is abruptly discontinued in a physically dependent patient, a withdrawal syndrome may occur. Some or all of the following can characterize this syndrome: restlessness, lacrimation, rhinorrhea, yawning, perspiration, chills, myalgia, and mydriasis. Other signs and symptoms also may develop, including: irritability, anxiety, backache, joint pain, weakness,
abdominal cramps, insomnia, nausea, anorexia, vomiting, diarrhea, or increased blood pressure, respiratory rate, and heart rate.

Infants born to mothers physically dependent on opioids will also be physically dependent and may exhibit respiratory difficulties and withdrawal signs [see PRECAUTIONS; Pregnancy].

OVERDOSAGE

Clinical Presentation

Acute overdose with meperidine can be manifested by respiratory depression, somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, constricted pupils, and, in some cases, pulmonary edema, bradycardia, hypotension, partial or complete airway obstruction, atypical snoring, and death. Marked mydriasis rather than miosis may be seen with hypoxia in overdose situations.

Treatment of Overdose

In case of overdose, priorities are the reestablishment of a patent and protected airway and institution of assisted or controlled ventilation, if needed.

Employ other supportive measures (including oxygen and vasopressors) in the management of circulatory shock and pulmonary edema as indicated. Cardiac arrest or arrhythmias will require advanced life-support techniques.

The opioid antagonists, naloxone or nalmefene, are specific antidotes to respiratory depression resulting from opioid overdose. For clinically significant respiratory or circulatory depression secondary to meperidine hydrochloride overdose, administer an opioid antagonist. Opioid antagonists should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to meperidine hydrochloride overdose.

Because the duration of opioid reversal is expected to be less than the duration of action of meperidine in meperidine hydrochloride injection, carefully monitor the patient until spontaneous respiration is reliably re-established. If the response to an opioid antagonist is suboptimal or only brief in nature, administer additional antagonist as directed by the product’s prescribing information.

In an individual physically dependent on opioids, administration of the recommended usual dosage of the antagonist will precipitate an acute withdrawal syndrome. The severity of the withdrawal symptoms experienced will depend on the degree of physical dependence and the dose of the antagonist administered. If a decision is made to treat serious respiratory depression in the physically dependent patient, administration of the antagonist should be begun with care and by titration with smaller than usual doses of the antagonist.

DOSAGE AND ADMINISTRATION

Important Dosage and Administration Instructions

For use as a single-dose unit to provide analgesia via the intravenous route using a compatible Hospira infusion device. Each vial is intended for SINGLE DOSE ONLY. When the dosing requirement is complete, the unused portion should be discarded in an appropriate manner.

DO NOT AUTOCLAVE.

PHYSICIANS SHOULD COMPLETELY FAMILIARIZE THEMSELVES WITH A COMPATIBLE HOSPIRA INFUSION DEVICE BEFORE DECIDING TO ADMINISTER MEPERIDINE HYDROCHLORIDE INJECTION VIA THE INFUSER.
Initiate the dosing regimen for each patient individually, taking into account the patient’s severity of pain, patient response, prior analgesic treatment experience, and risk factors for addiction, abuse, and misuse [see WARNINGS].

Monitor patients closely for respiratory depression, especially within the first 24 to 72 hours of initiating therapy and following dosage increases with meperidine hydrochloride and adjust the dosage accordingly [see WARNINGS].

Parenteral drug products should be inspected visually for particulate matter and discoloration whenever solution and container permit prior to administration.

**Initial Dosage**

When administered intravenously, meperidine hydrochloride should be given very slowly. Rapid intravenous injection increases the incidence of adverse reactions; severe respiratory depression, apnea, hypotension, peripheral circulatory collapse and cardiac arrest have occurred. This drug should be administered intravenously only if a narcotic antagonist (i.e., naloxone) and the facilities for assisted or controlled respiration are immediately available. When meperidine hydrochloride is given parenterally, especially intravenously, the patient should be lying down.

**Adults:** The usual initial dose for adult administration via a compatible Hospira infusion device is 10 mg, with a range of 1 to 5 mg per incremental dose. The recommended Lockout Interval is 6 to 10 minutes. The minimum recommended Lockout Interval is 5 minutes.

The physician may adjust the dosage either upward or downward; or, increase or decrease the Lockout Interval, depending on patient response. For continuous infusion the usual adult dose is 15 to 35 mg per hour administered intravenously as required.

**Incompatibility:** Meperidine hydrochloride is incompatible with soluble barbiturates, aminophylline, heparin, morphine sulfate, methicillin, phenytoin, sodium bicarbonate, iodide, sulfadiazine and sulfisoxazole.

**Dosage Modifications in Patients**

Reduced dosage is indicated in poor-risk patients, in the very young or very old, in patients with impaired renal or hepatic function and in patients receiving other central nervous system depressants. For surgical patients, dosage should be based on response of the patient, other premedication and concomitant medications, the anesthetic being used and the nature and duration of the operation.

**Titration and Maintenance of Therapy**

Individually titrate meperidine hydrochloride to a dose that provides adequate analgesia and minimizes adverse reactions. Continually reevaluate patients receiving meperidine hydrochloride to assess the maintenance of pain control and the relative incidence of adverse reactions, as well as monitoring for the development of addiction, abuse, or misuse [see WARNINGS]. Frequent communication is important among the prescriber, other members of the healthcare team, the patient, and the caregiver/family during periods of changing analgesic requirements, including initial titration.

If the level of pain increases after dosage stabilization, attempt to identify the source of increased pain before increasing the meperidine hydrochloride dosage. If unacceptable opioid-related adverse reactions are observed, consider reducing the dosage. Adjust the dosage to obtain an appropriate balance between management of pain and opioid-related adverse reactions.
Discontinuation of meperidine hydrochloride

When a patient who has been taking meperidine hydrochloride regularly and may be physically dependent no longer requires therapy with meperidine hydrochloride, use a gradual downward titration of the dosage to prevent signs and symptoms of withdrawal. Do not stop meperidine hydrochloride abruptly [see WARNINGS, DRUG ABUSE AND DEPENDENCE].

HOW SUPPLIED

Meperidine Hydrochloride Injection, USP 10 mg/mL is supplied in a 30 mL single-dose container, NDC 0409-6030-04.

This vial is only for use with a compatible Hospira PCA pump set with injector and a compatible Hospira infusion device (see directions for use supplied with the set or infuser). Store at 20 to 25°C (68 to 77°F). [See USP Controlled Room Temperature.]

Revised: 9/2016

LAB-0833-1.0

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