

MEPERIDINE HYDROCHLORIDE - meperidine hydrochloride injection
Physicians Total Care, Inc.

CII

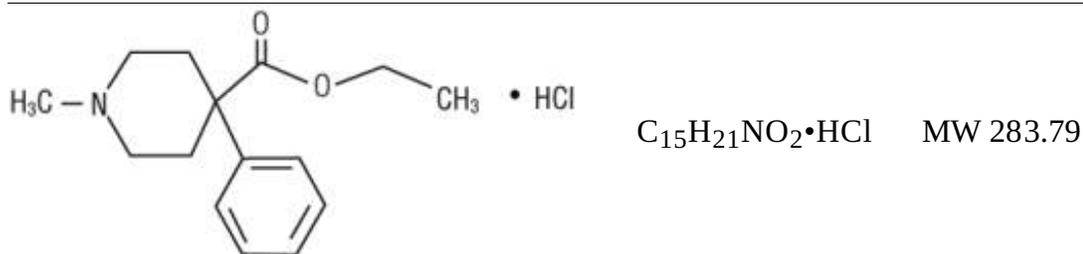
Rx only

DESCRIPTION

Meperidine Hydrochloride Injection, USP is a sterile solution for intramuscular, subcutaneous or slow intravenous use as a narcotic analgesic.

Each mL of the DOSETTE vial contains meperidine hydrochloride, either 25 mg, 50 mg, 75 mg or 100 mg in Water for Injection. Buffered with acetic acid-sodium acetate. pH 3.5-6.0.

Meperidine hydrochloride is ethyl 1-methyl-4-phenylisonipecotate hydrochloride, a white crystalline substance with a melting point of 186°-189°C. It is readily soluble in water and has a slightly bitter taste. Its structural formula is as follows:



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 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.

In clinical studies, changes in several pharmacokinetic parameters with increasing age have been observed. The initial volume of distribution and steady-state volume of distribution may be higher in elderly patients than in younger patients.¹ The free fraction of meperidine in plasma may be higher in patients over 45 years of age than in younger patients.²

INDICATIONS AND USAGE

For the relief of moderate to severe pain.

For preoperative medication.

For support of anesthesia.

For obstetrical analgesia.

CONTRAINDICATIONS

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 preexisting 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.)

Solutions of meperidine hydrochloride and barbiturates are chemically incompatible.

WARNINGS

Drug Dependence

Meperidine can produce drug dependence of the morphine type and therefore has the potential for being abused. Psychic dependence, physical dependence and tolerance may develop upon repeated administration of meperidine. It should be prescribed and administered with the same degree of caution appropriate to the use of morphine. Like other narcotics, meperidine is subject to the provisions of the Federal narcotic laws.

Interaction with Other Central Nervous System Depressants

MEPERIDINE SHOULD BE USED WITH GREAT CAUTION AND IN REDUCED DOSAGE IN PATIENTS WHO ARE CONCURRENTLY RECEIVING OTHER NARCOTIC ANALGESICS, GENERAL ANESTHETICS, PHENOTHIAZINES, OTHER TRANQUILIZERS (SEE DOSAGE AND ADMINISTRATION), SEDATIVEHYPNOTICS (INCLUDING BARBITURATES), TRICYCLIC ANTIDEPRESSANTS AND OTHER CNS DEPRESSANTS (INCLUDING ALCOHOL). RESPIRATORY DEPRESSION, HYPOTENSION AND PROFOUND SEDATION OR COMA MAY RESULT.

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

If necessary, meperidine may be given intravenously, but the injection should be given very slowly, preferably in the form of a diluted solution. Rapid intravenous injection of narcotic analgesics, including meperidine, increases the incidence of adverse reactions; severe respiratory depression, apnea, hypotension, peripheral circulatory collapse and cardiac arrest have occurred. Meperidine should not be administered intravenously unless a narcotic antagonist and the facilities for assisted or controlled respiration are immediately available. When meperidine is given parenterally, especially intravenously, the patient should be lying down.

Asthma and Other Respiratory Conditions

Meperidine should be used with extreme caution in patients having an acute asthmatic attack, patients with chronic obstructive pulmonary disease or cor pulmonale, patients having a substantially decreased respiratory reserve and patients with preexisting respiratory depression, hypoxia or hypercapnia. In such patients, even usual therapeutic doses of narcotics may decrease respiratory drive while simultaneously increasing airway resistance to the point of apnea.

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 already been compromised by a depleted blood volume or 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 psychophysiologic functions in the newborn. Resuscitation may be required (see section on OVERDOSAGE).

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

PRECAUTIONS

As with all intramuscular preparations, meperidine intramuscular injection should be injected well within the body of a large muscle.

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 preexisting 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.

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.

Geriatric Use

Clinical studies of meperidine did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in response between the elderly and younger patients. In general, dose selection for an elderly patient should be low, 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. Doses of meperidine should be reduced in elderly patients. (See DOSAGE AND ADMINISTRATION.)

Sedating drugs may cause confusion and oversedation in the elderly; elderly patients generally should be started on low doses of meperidine and observed closely.

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Clinical studies indicate that differences in various pharmacokinetic parameters may exist between elderly and younger patients. (See CLINICAL PHARMACOLOGY.)

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 lightheadedness, 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:

Central 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, palpitations, hypotension (see WARNINGS), syncope, phlebitis following intravenous injection.

Genitourinary-Urinary retention.

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

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

OVERDOSAGE

Symptoms

Serious overdose with meperidine is characterized by respiratory depression (a decrease in respiratory rate and/or tidal volume, Cheyne-Stokes respiration, cyanosis), extreme somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin and sometimes bradycardia and hypotension. In severe overdose, particularly by the intravenous route, apnea, circulatory collapse, cardiac arrest and death may occur.

Treatment

Primary attention should be given to the reestablishment of adequate respiratory exchange through provision of a patent airway and institution of assisted or controlled ventilation. The narcotic antagonist naloxone hydrochloride is a specific antidote against respiratory depression which may result from overdose or unusual sensitivity to narcotics, including meperidine. Therefore, an appropriate dose of naloxone hydrochloride should be administered, preferably by the intravenous route, simultaneously with efforts at respiratory resuscitation.

An antagonist should not be administered in the absence of clinically significant respiratory or cardiovascular depression. Oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated.

NOTE: In an individual physically dependent on narcotics, the administration of the usual dose of a narcotic antagonist will precipitate an acute withdrawal syndrome. The severity of this syndrome will depend on the degree of physical dependence and the dose of antagonist administered. The use of narcotic antagonists in such individuals should be avoided if possible. If a narcotic antagonist must be used to treat serious respiratory depression in the physically dependent patient, the antagonist should be administered with extreme care and only one-fifth to one-tenth the usual initial dose administered.

DOSAGE AND ADMINISTRATION

For Relief of Pain

Dosage should be adjusted according to the severity of the pain and the response of the patient. While subcutaneous administration is suitable for occasional use, intramuscular administration is preferred when repeated doses are required. If intravenous administration is required, dosage should be decreased and the injection made very slowly, preferably utilizing a diluted solution. Meperidine is less effective orally than by parenteral administration. The dose of meperidine should be proportionately reduced (usually by 25 to 50 percent) when administered concomitantly with phenothiazines and many other tranquilizers since they potentiate the action of meperidine.

Adults

The usual dosage is 50 to 150 mg intramuscularly or subcutaneously every 3 to 4 hours as necessary. Elderly patients should usually be given meperidine at the lower end of the dose range and observed closely.

Children

The usual dosage is 0.5 to 0.8 mg/lb intramuscularly or subcutaneously up to the adult dose, every 3 to 4 hours as necessary.

For Preoperative Medication

The usual dosage is 50 to 150 mg intramuscularly or subcutaneously every 3 to 4 hours as necessary. Elderly patients should usually be given meperidine at the lower end of the dose range and observed closely.

Children

The usual dosage is 0.5 to 1 mg/lb intramuscularly or subcutaneously up to the adult dose, 30 to 90 minutes before the beginning of anesthesia.

For Support of Anesthesia

Repeated slow intravenous injections of fractional doses (e.g., 10 mg/mL) or by a continuous intravenous infusion of a more dilute solution (e.g., 1 mg/mL) should be used. The dose should be titrated to the needs of the patient and will depend on the premedication and type of anesthesia being employed, the characteristics of the particular patient and the nature and duration of the operative procedure. Elderly patients should usually be given meperidine at the lower end of the dose range and observed closely.

For Obstetrical Analgesia

The usual dosage is 50 to 100 mg intramuscularly or subcutaneously when pain becomes regular and may be repeated at 1 to 3 hour intervals.

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

HOW SUPPLIED

Meperidine Hydrochloride Injection, USP is available in the following packages:

50 mg/mL

1 mL DOSETTE vials packaged in 25s (*NDC 54868-3559-1*)

Storage

Store at 20°-25°C (68°-77°F), excursions permitted to 15°-30°C (59°-86°F) [see USP Controlled Room Temperature].

REFERENCES

1. Mather, LE et al: Meperidine kinetics in man. Intravenous injection in surgical patients and volunteers. *Clin Pharmacol Ther* 17:21-30, 1975.

2. Herman, RJ et al: Effects of age on meperidine disposition. *Clin Pharmacol Ther* 37:19-24, 1985.

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Manufactured by

Baxter Healthcare Corporation

Deerfield, IL 60015 USA

For Product Inquiry 1 800 ANA DRUG (1-800-262-3784)

MLT-01168/3.0

Relabeling of "Additional Barcode" by:

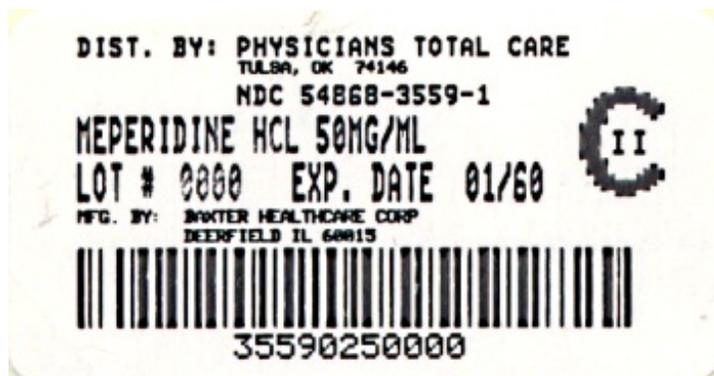
Physicians Total Care, Inc.

Tulsa, OK 74146

PRINCIPAL DISPLAY PANEL

Meperidine Hydrochloride Injection, USP

50 mg/mL



MEPERIDINE HYDROCHLORIDE

meperidine hydrochloride injection

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:54868- 3559(NDC:10019-160)
Route of Administration	INTRAMUSCULAR	DEA Schedule	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
MEPERIDINE HYDROCHLORIDE (UNII: N8E7F7Q170) (MEPERIDINE - UNII:9E338QE28F)	MEPERIDINE HYDROCHLORIDE	50 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
ACETIC ACID (UNII: Q40Q9N063P)	
SODIUM ACETATE (UNII: 4550K0SC9B)	
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:54868-3559-1	25 in 1 PACKAGE		
1		1 mL in 1 VIAL		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA080455	03/04/2010	

Labeler - Physicians Total Care, Inc. (194123980)

Establishment

Name	Address	ID/FEI	Business Operations
Physicians Total Care, Inc.		194123980	relabel

Revised: 5/2010

Physicians Total Care, Inc.