

DEMEROL - meperidine hydrochloride injection, solution
Physicians Total Care, Inc.

Demerol™

meperidine hydrochloride injection, USP

CII

Rx only

DESCRIPTION

Meperidine hydrochloride is ethyl 1-methyl-4-phenylisonipecotate hydrochloride, a white crystalline substance with a melting point of 186°C 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.

DEMEROL injectable is supplied in Carpuject™ with luer lock of 2.5% (25 mg/1 mL), 5% (50 mg/1 mL), 7.5% (75 mg/1 mL), and 10% (100 mg/1 mL). Uni-Amp™ unit dose pak-ampuls of 5% solution (25 mg/0.5 mL), (50 mg/1 mL), (75 mg/1.5 mL), (100 mg/2 mL), and 10% solution (100 mg/1 mL). Multiple-dose vials of 5% and 10% solutions contain metacresol 0.1% as preservative.

The pH of DEMEROL solutions is adjusted between 3.5 and 6 with sodium hydroxide or hydrochloric acid.

DEMEROL, brand of meperidine hydrochloride, 5 percent solution has a specific gravity of 1.0086 at 20°C and 10 percent solution, a specific gravity of 1.0165 at 20°C.

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.

In clinical studies reported in the literature, 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. The free fraction of meperidine in plasma may be higher in patients over 45 years of age than in younger patients.

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 DEMEROL 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, and 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**), SEDATIVE-HYPNOTICS (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 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 psychophysiologic functions in the newborn. Resuscitation may be required (see **OVERDOSAGE**).

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

PRECAUTIONS

As with all intramuscular preparations, DEMEROL 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 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 DEMEROL 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. (See **DOSAGE AND ADMINISTRATION**.)

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

This drug is known to be 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:

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.

OVERDOSAGE

Symptoms. Serious overdosage 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 overdosage, 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 overdosage or unusual sensitivity to narcotics, including meperidine. Therefore, an appropriate dose of this antagonist 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. The dose of DEMEROL 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 DEMEROL.

Adults. The usual dosage is 50 mg to 150 mg intramuscularly or subcutaneously every 3 or 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 mg/lb to 0.8 mg/lb intramuscularly or subcutaneously up to the adult dose, every 3 or 4 hours as necessary.

For Preoperative Medication

Adults. The usual dosage is 50 mg to 100 mg intramuscularly or subcutaneously, 30 to 90 minutes before the beginning of anesthesia. 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 mg/lb 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 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 mg 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 and discoloration prior to administration whenever solution and container permit.

HOW SUPPLIED

For Parenteral Use

Solutions of DEMEROL for parenteral use are clear and colorless and are available as follows:

NDC Number	Container	Concentration	Fill (mL)	Quantity
54868-5808-0	Carpject with luer lock	5% (50 mg/mL)	1	10
54868-3230-1	Uni-Amp unit dose pak	5% (50 mg)	1	25
54868-4751-0	Uni-Amp unit dose pak	10% (100 mg)	1	25
54868-4751-1	Uni-Amp unit dose pak	10% (100 mg)	1	1

Carpject™ are packaged in a Slim-Pak™ tamper detection package. To prevent needle-stick injuries, needles should not be recapped, purposely bent, or broken by hand. Blunt cannulas should not be recapped, purposely bent or broken by hand.

NOTE: The pH of DEMEROL solutions is adjusted between 3.5 and 6 with sodium hydroxide or hydrochloric acid. Multiple-dose vials contain metacresol 0.1 percent as preservative. No preservatives are added to the ampuls or Carpuject™ sterile cartridge units.

Store at 20 to 25°C (68 to 77°F). [See USP Controlled Room Temperature.]

Demerol is not a trademark of Hospira.

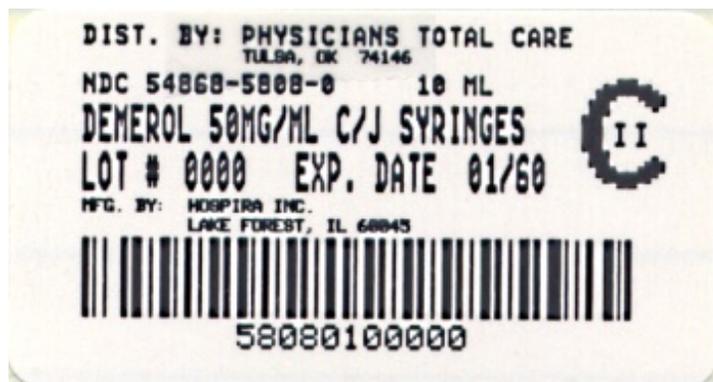
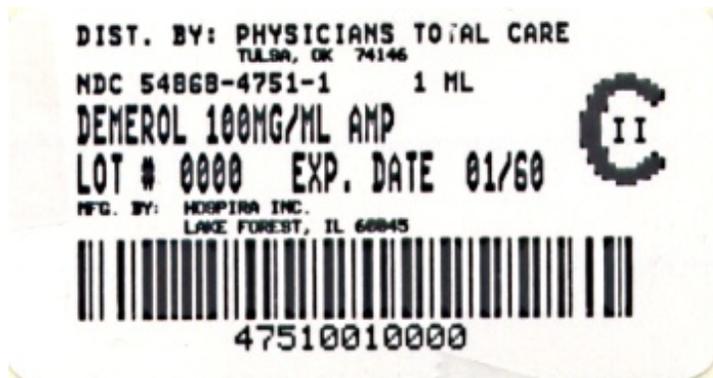
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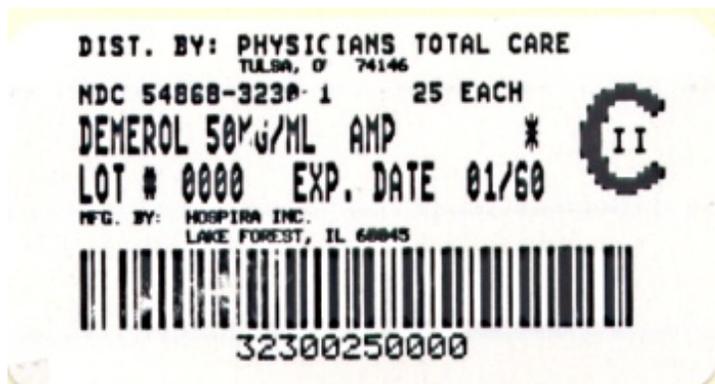
Printed in USA EN-2526

Hospira, Inc., Lake Forest, IL 60045

Additional bar code label applied by:
Physicians Total Care, Inc.
Tulsa, Oklahoma 74146

PRINCIPAL DISPLAY PANEL - PACKAGE LABEL





DEMEROL

meperidine hydrochloride injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:54868-5808(NDC:0409-1178)
Route of Administration	INTRAMUSCULAR, INTRAVENOUS, SUBCUTANEOUS	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
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:54868-5808-0	10 in 1 BOX		
1		1 mL in 1 CARTRIDGE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021171	08/21/2007	

DEMEROL

meperidine hydrochloride injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:54868-3230 (NDC:0409-1253)
Route of Administration	INTRAMUSCULAR, INTRAVENOUS, SUBCUTANEOUS	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
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:54868-3230-0	25 in 1 BOX		
1		1 mL in 1 AMPULE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021171	04/11/1994	

DEMEROL

meperidine hydrochloride injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:54868-4751(NDC:0409-1256)
Route of Administration	INTRAMUSCULAR, INTRAVENOUS, SUBCUTANEOUS	DEA Schedule	CII

Active Ingredient/Active Moiety

Ingredient Name		Basis of Strength	Strength	
MEPERIDINE HYDROCHLORIDE (UNII: N8E7F7Q170) (MEPERIDINE - UNII:9E338QE28F)		MEPERIDINE HYDROCHLORIDE	100 mg in 1 mL	
Inactive Ingredients				
Ingredient Name		Strength		
SODIUM HYDROXIDE (UNII: 55X04QC32I)				
HYDROCHLORIC ACID (UNII: QTT17582CB)				
Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:54868-4751-0	25 in 1 BOX		
1		1 mL in 1 AMPULE		
2	NDC:54868-4751-1	1 in 1 BOTTLE, DISPENSING		
2		1 mL in 1 AMPULE		
Marketing Information				
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date	
NDA	NDA021171	03/11/2003		

DEMEROL			
meperidine hydrochloride injection, solution			
Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:54868-0616 (NDC:0409-1181)
Route of Administration	INTRAMUSCULAR, INTRAVENOUS, SUBCUTANEOUS	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	
SODIUM HYDROXIDE (UNII: 55X04QC32I)			
HYDROCHLORIC ACID (UNII: QTT17582CB)			
METACRESOL (UNII: GGO4Y809LO)			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:54868-0616-0	1 in 1 BOX		
1		30 mL in 1 VIAL, MULTI-DOSE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021171	07/13/2000	06/30/2011

DEMEROL

meperidine hydrochloride injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:54868-3610(NDC:0409-1201)
Route of Administration	INTRAMUSCULAR, INTRAVENOUS, SUBCUTANEOUS	DEA Schedule	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
MEPERIDINE HYDROCHLORIDE (UNII: N8E7F7Q170) (MEPERIDINE - UNII:9E338QE28F)	MEPERIDINE HYDROCHLORIDE	100 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	
METACRESOL (UNII: GGO4Y809LO)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:54868-3610-0	1 in 1 BOX		
1		20 mL in 1 VIAL, MULTI-DOSE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021171	07/05/1995	06/30/2011

Labeler - Physicians Total Care, Inc. (194123980)

Establishment

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

Revised: 12/2011

Physicians Total Care, Inc.