CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40191

DRAFT FINAL PRINTED LABELING

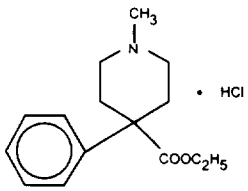
MEPERIDINE HYDROCHLORIDE, USP
TABLETS

Ⓒ II

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.

Meperdine Hydrochloride has the following structural formula



$C_{15}H_{21}NO_2 \cdot HCl$ MW=283.8

Each tablet, for oral administration, contains 50 mg or 100 mg meperidine hydrochloride. In addition, each tablet contains the following inactive ingredients: microcrystalline cellulose, pregelatinized starch, sodium starch glycolate and stearic acid.

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.

INDICATIONS AND USAGE

Meperidine hydrochloride tablets USP are indicated for the relief of moderate to severe pain.

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.)

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.

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 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.

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

PRECAUTIONS

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.

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.

Gastrointestinal. Dry mouth, constipation, biliary tract spasm.

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

Genitourinary. Urinary retention.

Allergic. Pruritus, urticaria, other skin rashes.

Other. 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.

In cases of overdosage with meperidine hydrochloride tablets, the stomach should be evacuated by emesis or gastric lavage.

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

Dosage should be adjusted according to the severity of the pain and the response of the patient. Meperidine is less effective orally than on parenteral administration. The dose of meperidine hydrochloride 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 hydrochloride tablets.

Adults. The usual dosage is 50 mg to 150 mg orally every 3 to 4 hours as necessary.

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

HOW SUPPLIED

Meperidine HCl Tablets of 50 mg, white, round, bisected tablets debossed "4171" and a "V" are available in bottles of 100 (NDC# 0254-4171-28). Meperidine HCl Tablets of 100 mg, white, unscored, round tablets debossed "4172" and a "V" are available in bottles of 100 (NDC# 0254-4172-28).

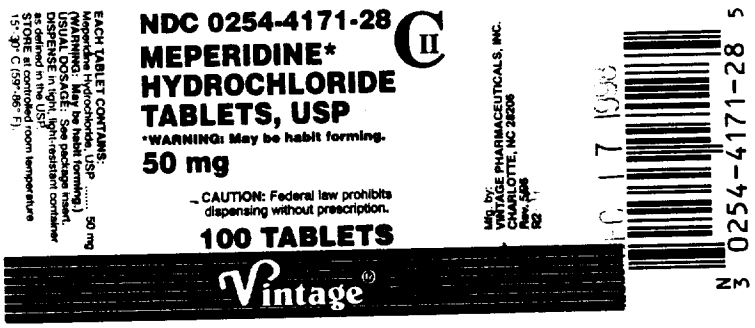
Dispense in a tight, light resistent container as defined in the USP.

Store at controlled room temperature 15°–30°C (59°–86°F)

CAUTION: Federal law prohibits dispensing without a prescription.

Manufactured by
VINTAGE PHARMACEUTICALS, INC.
CHARLOTTE, NC 28206

IN-79
Rev. 10/97
R5


NDC 0254-4171-28
MEPERIDINE*
HYDROCHLORIDE
TABLETS, USP
*WARNING: May be habit forming.
50 mg
CII
CAUTION: Federal law prohibits dispensing without prescription.
100 TABLETS
Vintage
EACH TABLET CONTAINS:
Meperidine Hydrochloride, USP ..... 50 mg
(WARNING: May be habit forming.)
USUAL DOSAGE: See package insert.
DISPENSE in tight, light-resistant container as defined in USP.
STORE at controlled room temperature 15°-30° C (59°-86° F).
Mfg. by:
VINTAGE PHARMACEUTICALS, INC.
CHARLOTTE, NC 28206
Rev. 5/95
82
N 3 0254-4171-28 5

NDC 0254-4172-28
MEPERIDINE*
HYDROCHLORIDE
TABLETS, USP
*WARNING: May be habit forming.
100 mg
CAUTION: Federal law prohibits dispensing without prescription.
100 TABLETS
Vintage
EACH TABLET CONTAINS: Meperidine Hydrochloride, USP ..... 100 mg
(Warning - May be habit forming.)
USUAL DOSAGE: See package insert.
DISPENSE in light, light-resistant container as defined in the USP.
STORE at controlled room temperature 15°-30° C (59°-86° F).
Mfg. by:
VINTAGE PHARMACEUTICALS, INC.
CHARLOTTE, NC 28206
Rev. 5/98
R2
DEC 17 1998
N3 0254-4172-28 2