PRODUCT MONOGRAPH

[N]M. O. S. Suppositories
(Morphine Hydrochloride)

Opiod Analgesic

Valeant Canada limitée/Limited
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(Morphine Hydrochloride)

Opiod Analgesic

ACTIONS:

Morphine hydrochloride is a potent analgesic, with major effects on the central nervous system and the bowel. Opioids act as agonists, interacting with stereospecific and saturable binding sites on receptors in the brain and other tissues. Morphine hydrochloride given as a rectal suppository can produce analgesic effects and duration similar to that of oral administration at similar dose levels. Analgesic effects are commonly seen 20 to 60 minutes after administration.

INDICATIONS:

For the symptomatic relief of severe pain.

CONTRAINDICATIONS:

Hypersensitivity to morphine; respiratory insufficiency or depression; severe CNS depression; attack of bronchial asthma; heart failure secondary to chronic lung disease; cardiac arrhythmias; increased intracranial or cerebrospinal pressure; head injuries; brain tumor; acute alcoholism; delerium tremens; convulsive disorders; after biliary tract surgery; suspected surgical abdomen; surgical anastomosis; concomitantly with MAO inhibitors or within 14 days of such treatment.

WARNINGS:

Morphine can produce drug dependence and therefore has the potential for being abused. Psychic dependence, physical dependence, and tolerance may develop upon repeated administration of morphine.

Morphine should be used with caution and in reduced dosage in patients who are concurrently receiving other narcotic analgesics, general anesthetics, phenothiazines, other tranquilizers, sedative-hypnotics, tricyclic antidepressants, and other CNS depressants (including alcohol). Respiratory depressions, hypotension and profound sedation or coma may result.

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

Morphine 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 pre-existing respiratory depression, hypoxia, or hypercapnia. In such patients even low therapeutic doses of narcotics may decrease respiratory drive while simultaneously increasing airway resistance to the point of apnea.

Morphine should not be used in pregnant women prior to the labor period unless 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.

PRECAUTIONS:

Acute Abdominal Conditon: The administration of morphine or other narcotics may obscure the diagnosis or clinical course in patients with acute abdominal conditions.

Special Risk Patients: Morphine should be given with caution to 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. Morphine hydrochloride should be used with extreme caution in patients with disorders characterized by hypoxia, since even usual therapeutic doses of narcotics may decrease respiratory drive to the point of apnea while simultaneously increasing airway resistance.

Hypotensive Effect: The administration of morphine hydrochloride may result in severe hypotension in the post-operative patient or any individual whose ability to maintain blood pressure has been compromised by a depleted blood volume or the administration of such drugs as the phenothiazines of certain anesthetics.

Supraventricular Tachycardias: Because of possible vagolytic action that may produce a significant increase in the ventricular response rate, morphine hydrochloride should be used with caution in patients with atrial flutter and other supraventricular tachycardias.

Convulsions: Morphine hydrochloride 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.

Kidney or Liver Dysfunction: Morphine hydrochloride may have a prolonged duration and cumulative effect in patients with kidney or liver dysfunction.

Information for Patients: Morphine may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks, such as driving a car or operating machinery. Morphine in combination with other narcotic analgesics, phenothiazines, sedative/hypnotics, and alcohol has additive depressant effects. The patients should be cautioned accordingly.

Drug Interactions: Morphine in combination with other narcotic analgesics, general anesthetics, phenothiazines, tranquilizers, sedative/hypnatics, or other CNS depressants

(including alcohol) has additive depressant effects. When such combination therapy is contemplated, the dosage of one or both agents should be reduced.

Carcirnogenesis, Mutaqenesis Impairment of Fertility: Morphine has no known carcinogenic or mutagenic potential. However, no long term animal studies are available to support this observation.

Usage in Preqnancy: Animal reproduction studies have not been conducted with morphine hydrochloride. It is not known whether morphine hydrochloride can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. On the basis of the historical use of morphine hydrochloride during all stages of pregnancy, there is no known risk of fetal abnormality. Morphine hydrochloride should be given to a pregnant woman only if clearly needed.

Labor and Delivery: The use of morphine hydrochloride in obstetrics may prolong labor. It passes the placental barrier and may produce depression of respiration in the newborn. Resuscitation and in severe depression, the administration of a narcotic antagonist such as naloxone or nalorphine may be required.

Nursing Mothers: Morphine hydrochloride appears in the milk of nursing mothers. Cautions should be exercised when it is administered to a nursing mother.

ADVERSE REACTIONS:

The major hazards of morphine as of 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 suffering severe pain. In such individuals, lower doses are advisable. Some adverse reactions may be alleviated in the ambulatory patient if he lies down. Other adverse reactions include the following:

Central Nervous System: Euphoria, dysphoria, weakness, headache, insomnia, agitation, disorientation, and visual disturbances.

Gastrointestinal: Dry mouth, anorexia, constipation, and biliary tract spasm.

Cardiovascular: Flushing of the face, bradycardia, palpitation, faintness, and syncope.

Genitourinary: Urinary retention or hesitance, anti-diuretic effect and reduced libido and/or potency.

Allergic: Pruritus, urticaria, other skin rashes, edema, and rarely hemorrhagic urticaria.

OVERDOSE: (SYMPTOMS):

Serious overdosage with morphine 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, apnea, circulatory collapse, cardiac arrest, and death may occur.

TREATMENT: Primary attention should be given to the re-establishment of adequate respiratory exchange through provision of a patent airway and institution of assisted or controlled ventilation. The narcotic antagonists, naloxone and levalorphan tartrate, are specific antidotes against respiratory depression which may result from overdosage or unusual sensitivity to narcotics. Therefore, an appropriate dose of one of these antagonists should be administered preferably by the i.v. route, simultaneously with efforts at respiratory resuscitation.

An antagonist should not be administered in the absence of clinically significant respiratory or cardiovascular depression.

Oxygen, i.v. 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 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 about 10 to 20% 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.

Usual Adult Dosage: 10 to 30 mg every 4 hours or as directed by the physician.

Morphine Dosage Reduction: During the first two to three days of effective pain relief, the patient may sleep for many hours. This can be misinterpreted as the effect of excessive analgesic dosing rather than the first sign of relief in a pain exhausted patient. The dose, therefore, should be maintained for at least 3 days before reduction, if respiratory activity and other vital signs are adequate. Following successful relief of severe pain, periodic attempts to reduce the narcotic dose should be made. Smaller doses or complete discontinuation of the narcotic analgesic may become feasible due to a physiological change or the improved mental state of the patient.

The suppository should be placed against the rectal mucosa. The drug is not absorbed if pushed into a mass of stool or if it is placed in the anal canal.

Storage: Keep container well closed. Protect from light. Keep out of reach of children.

AVAILABILITY:

M:O.S. "10" Suppository - each suppository contains10 mg of morphine hydrochloride in a bland, white vegetable oil base.
M.O.S. "20" Suppository - each suppository contains 20 mg of morphine hydrochloride in a bland, yellow vegetable oil base.
M.O.S."30" Suppository - each suppository contains 30 mg of morphine hydrochloride in a bland, pink vegetable oil base.

Morphine is included in the Schedule to the Narcotic Control Act.