Promethazine hydrochloride suppositories, USP

Rx Only

DESCRIPTION

Promethazine hydrochloride suppositories contain 12.5 mg or 25 mg promethazine HCl with an absorbent polysaccharide, calcium silicate, white wax, hard, and soft stabilizers. Promethazine HCl suppositories are for rectal administration only.

Promethazine HCl is a racemic compound; the empirical formula is C₂₁H₂₃ClN₂OS•HCl and its molecular weight is 320.88.

Promethazine HCl, a phenothiazine derivative, is designated chemically as 10H-Pyrido[4,3-b]carbazole, 10-[(1R,2S,4R,5S)-4,5-dimethyl-2,4-dihydroxytetrahydro-furan-3-yl]methyl]-, (S)- with the following structural formula:

\[
\text{CH}_2\text{CH(CH}_3\text{)N(CH}_3\text{)}_2\text{CH}_{10\text{H}}\text{ClN}_2\text{OS}\cdot\text{HCl}
\]

Promethazine HCl occurs as a white to yellowish, practically odorless, crystals powder, which slowly solution and form creme on prolonged exposure to air. It is soluble in water and freely soluble in alcohol.

GLOBAL PHARMACOKINETICS

Promethazine is a phenothiazine derivative, which differs structurally from the antiparkinsonian phenothiazines by the presence of the pyrido[4,3-b]carbazole moiety. This substitution is responsible for several properties that distinguish promethazine from other phenothiazines.

Promethazine is an H₁ receptor blocker. In addition to its antiatherogenic action, it provides clinically useful sedative and anxiolytic effects.

Promethazine is predominantly biotransformed by the liver and is excreted in the urine. The bioavailability is 93%. The drug is extensively bound to plasma proteins (96%).

Rapid absorption occurs following rectal administration. Peak plasma concentrations are usually reached within 30 minutes. The peak plasma concentrations are usually reached within 30 minutes. The drug is extensively bound to plasma proteins (96%).

Antiemetic therapy in postoperative patients.

Therapy adjunctive to meperidine or other analgesics for control of postoperative pain.

Anaphylactic reactions, as adjunctive therapy to epinephrine and other standard measures, after the acute manifestations have been controlled.

Prevention and control of nausea and vomiting associated with certain types of anesthesia and surgery.

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Antacids and laxatives may be used to minimize any constipation which may occur with prolonged use of promethazine HCl suppositories.

Promethazine HCl suppositories may lead to potentially fatal respiratory depression.

Respiratory Depression

Promethazine HCl suppositories may be used with caution in patients with chronic respiratory disease, as driving or performing hazardous tasks such as driving or operating machinery may be impaired.

DOSAGE AND ADMINISTRATION

Promethazine HCl suppositories may induce drowsiness and dizziness, especially during the first few days of therapy. Their use is therefore recommended for patients not required to perform tasks demanding mental alertness and physical coordination (e.g., driving a vehicle or operating machinery). The impairment may be amplified by concomitant use of other central-nervous-system depressants (e.g., narcotics, sedatives/hypnotics, alcohol).

Promethazine HCl suppository is contraindicated for use in the treatment of lower respiratory tract symptoms including asthma.

Antihistamines are contraindicated for use in the treatment of lower respiratory tract symptoms including asthma.

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Promethazine HCl suppositories are contraindicated in comatose states, and in individuals known to be hypersensitive or to have had an anaphylactic reaction to promethazine HCl or to other phenothiazines.

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Promethazine HCl suppositories are contraindicated in persons with cardiovascular disease or with impairment of liver function.

Drugs having anticholinergic properties should be used with caution in patients with narrow-angle glaucoma, prostatic hypertrophy, stenosing peptic ulcers, and uterine hypertension.

Hallucinations and convulsions have occurred with therapeutic doses and overdoses of promethazine HCl in pediatric patients. In pediatric patients, use of promethazine HCl suppositories for the treatment of motion sickness and for sedation and pain control should be limited to situations in which the benefit-risk ratio is favorable.

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The use of promethazine HCl suppositories must be individualized. Excessive amounts of promethazine HCl relative to a narcotic analgesic may increase the risk of respiratory depression.

Promethazine HCl suppositories may increase, prolong, or intensify the sedative action of other central-nervous-system depressants, such as alcohol, sedative/hypnotics (including barbiturates), narcotics, sedatives/hypnotics, general anesthetics, inhaled anesthetics, and other phenothiazines.

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Drug Interactions
The following laboratory tests may be affected in patients who are receiving therapy with promethazine HCl:
- Hematologic: Leukopenia, thrombocytopenia, thrombocytopenic purpura, agranulocytosis.
- Hepatic: The biochemical effects have not been determined in the clinical studies. Laboratory data, such as blood urea nitrogen, blood glucose, uric acid, and conjugated bilirubin concentrations, have been unchanged in clinical trials. However, concomitant use of drugs which are known to be hepatic enzyme inhibitors, such as cimetidine, may increase the serum level of promethazine HCl.
- ECG: No significant electrocardiographic changes were observed in the clinical use of promethazine HCl at normal therapeutic levels. ECG changes occurred only when it was used in combination with other drugs, or in toxic manifestations.

Premedication
Promethazine HCl Suppositories are contraindicated in patients with a history of hypersensitivity to promethazine, piperazine or related compounds. Patients with a history of asthma, nasal stuffiness, respiratory depression (potentially fatal) and apnea (potentially fatal). (See PRECAUTIONS — Respiratory System). Patients with a history of severe adrenergic or cholinergic overactivity should be treated with caution.

OVERDOSAGE
The effects of promethazine HCl overdose may be treated with activated charcoal orally or by lavage, or both. Generally, no specific therapy should be given, as overdosage is characterized by depression of the central nervous system and respiratory depression. There is no known specific antidote for promethazine HCl poisoning. Life support measures, including cardiopulmonary resuscitation, dialysis, and mechanical ventilation should be considered if necessary.

Pregnancy
Promethazine HCl may be used alone or as an adjunct to narcotic analgesics during labor and delivery. (See “DOSAGE AND ADMINISTRATION”). Use in Pregnancy (see USP). There is no evidence of increased risk of congenital malformations, and of concomitant disease or other drug therapy. The use of promethazine HCl in the labor and delivery period is based on observations during the use of promethazine HCl for many years.

Teratogenic effects have not been demonstrated in rat-feeding studies at doses of 6.25 and 12.5 mg/kg of promethazine. These doses are from approximately 1/2 to 1.5 times the maximum recommended single dose of promethazine for a 70-kg patient, depending upon the indication for which the drug is used (See “DOSAGE AND ADMINISTRATION”). Only single doses of 25 mg or less have been found to have appreciable teratogenic activity in the rat. The precise teratogenic risk associated with use of any drug in pregnancy is unknown. However, since many drugs are excreted in human milk, it is not known whether promethazine HCl is so excreted.

Drip Therapy
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