Promethazine hydrochloride occurs as a white to faint yellow, practically odorless, crystalline powder and is chemically designated as 10H-Phenothiazine-10-ethanamine, N,N-
trimethyl-monohydrochloride. Promethazine hydrochloride occurs as a white to faint yellow, practically odorless, crystalline powder which is odorless and tasteless in solution when used with alcohol in solution. It has a molecular weight of 370.33, a molecular formula of C_{18}H_{21}N_{2}OClH, and the following structural formula:

![Structural formula of Promethazine hydrochloride](image)

Promethazine may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks, such as driving a vehicle or operating machinery. Ambulatory patients should be told to avoid engaging in such activities until it is known that they do not become drowsy or dizzy from promethazine and dextromethorphan therapy. Children should be supervised to avoid potential harm in bike riding or in other hazardous activities.

Promethazine should be used cautiously in patients with cardiovascular disease or with impairment of liver function.

Information For Patients: Promethazine and dextromethorphan may cause marked dryness of the mouth and may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks, such as driving a vehicle or operating machinery. Ambulatory patients should be told to avoid engaging in such activities until it is known that they do not become drowsy or dizzy from promethazine and dextromethorphan therapy. Children should be supervised to avoid potential harm in bike riding or in other hazardous activities.

The concomitant use of alcohol or other central nervous system depressants, including narcotic analgesics, sedatives, hypnotics, and tranquilizers, may have an additive effect and should be avoided or their dosage reduced.

Patients should be advised to report any involuntary muscle movements.

Avoid prolonged exposure to the sun.

Drug Interactions: Dextromethorphan: Hypersensitivity, hypotension, and death have been reported in patients with undiagnosed primary disease, e.g., encephalopathy or encephalopathy of known etiology. The extrapyramidal symptoms which can occur secondary to promethazine hydrochloride administration may be confused with the CNS signs of undiagnosed primary disease, e.g., encephalopathy or Rey’s syndrome. The use of promethazine products should be avoided in pediatric patients whose signs and symptoms may suggest Rey’s syndrome or other hepatic diseases.

Promethazine and dextromethorphan should be given to a pregnant woman only if clearly needed.

Dextromethorphan should be given to a pregnant woman only if clearly needed.

PRECAUTIONS

Promethazine hydrochloride and dextromethorphan hydrobromide syrup is indicated for the temporary relief of cough associated with colds and other upper respiratory symptoms associated with allergy or the common cold.

CONTRAINDICATIONS

Dextromethorphan should not be used in patients receiving a monoamine oxidase inhibitor (MAO) (see PRECAUTIONS, Drug Interactions).

Dextromethorphan is contraindicated in comatosia states, and in individuals known to be hypersensitive to promethazine or to other phenothiazines.

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

WARNINGS

WARNING

PROMETHAZINE HYDROCHLORIDE SHOULD NOT BE USED IN PEDIATRIC PATIENTS LESS THAN 2 YEARS OF AGE BECAUSE OF THE POTENTIAL FOR FATAL RESPIRATORY DEPRESSION AND OVERDOSE.

POSTMARKETING CASES OF RESPIRATORY DEPRESSION, INCLUDING FATALITIES, HAVE BEEN REPORTED WITH USE OF PROMETHAZINE HYDROCHLORIDE IN PEDIATRIC PATIENTS LESS THAN 2 YEARS OF AGE. IN PEDIATRIC PATIENTS, WITH THE POSSIBILITIES OF CONVULSIONS, USE OF CONVENTIONAL DOSES OF PROMETHAZINE HYDROCHLORIDE HAVE RESULTED IN RESPIRATORY DEPRESSION IN THESE PATIENTS. CAUTION SHOULD BE EXERCISED WHEN ADMINISTERING PROMETHAZINE HYDROCHLORIDE TO PEDIATRIC PATIENTS 2 YEARS OF AGE AND OLDER. IT IS RECOMMENDED THAT THE LOWEST EFFECTIVE DOSE OF PROMETHAZINE HYDROCHLORIDE BE USED IN PEDIATRIC PATIENTS 2 YEARS OF AGE AND OLDER AND MANAGED ADMINISTRATION OF OTHER DRUGS WITH RESPIRATORY DEPRESSANT EFFECTS BE AVOIDED.

Promethazine: CNS Depressants - Promethazine may increase, prolong, or intensify the sedative or central nervous system depressant effects of alcohol, sedatives/hypnotics (including barbiturates), narcotics, narcotic analgesics, general anesthetics, tricyclic antidepressants, and tranquilizers; therefore, such agents should be avoided or administered with caution to patients receiving promethazine HCl. When given concomitantly with promethazine, the dose of barbiturates should be reduced by at least one-half, and the dose of narcotics should be reduced by at least one-third. All doses of promethazine HCl should be titrated; dosage should be individualized. Excessive amounts of promethazine HCl relative to a narcotic may lead to restlessness and motor hyperactivity in the patient with pain; these symptoms usually disappear with adequate control of the pain.

Pregnancy - Because of the potential for promethazine to reverse epinephrine’s vasopressor effect, epinephrine should not be used to treat hypertension associated with promethazine overdose.

Anticholinergic - Concomitant use of other agents with anticholinergic properties should be undertaken with caution.

Monoamine Oxidase Inhibitors (MAO) - Drug interactions, including an increased incidence of extrapyramidal effects, have been reported when some MAO and phenothiazines are used concomitantly.

Drug/Laboratory Test Interactions: The following laboratory tests may be affected in patients who are receiving therapy with promethazine hydrochloride.

Carboxyhemoglobin, Metabolism, Impairment Of Fertility: Long-term animal studies have not been performed to assess the carcinogenic potential of promethazine or of dextromethorphan. There are no animal or human data concerning the carcinogenicity, mutagenicity, or impairment of fertility with these drugs.

Carcinogenesis, Mutagenesis, Impairment Of Fertility:

Glucose Tolerance Test: An increase in blood glucose has been reported in patients receiving promethazine. anti-HCG may result in false-negative or false-positive interpretations.

Pregnancy Tests: Diagnostic pregnancy tests based on immunological reactions between HCG and antibodies to HCG are not affected by promethazine or dextromethorphan.

Neutralization of Major Nonsteroidal Antinflammatory Drugs: Promethazine and dextromethorphan may be neutralized in the body.
Labor And Delivery: Limited data suggest that use of promethazine HCl during labor and delivery does not have a appreciable effect on the duration of labor or delivery and does not increase the risk of need for intervention in the newborn. The effect on later growth and development of the newborn is unknown. See also “Nonteratogenic Effects.”

Nursing Mothers: It is not known whether promethazine or dextromethorphan is excreted in human milk.

Caution should be exercised when promethazine and dextromethorphan is administered to a nursing woman.

Pediatric Use: PROMETHAZINE HYDROCHLORIDE AND DEXTROMETHORPHAN HYDROBROMIDE SYRUP IS CONTRAINDICATED FOR USE IN PEDIATRIC PATIENTS LESS THAN TWO YEARS OF AGE (see WARNINGS – Black Box Warning and Use In Pediatric Patients).

Promethazine hydrochloride and dextromethorphan hydrobromide syrup should be used with caution in pediatric patients 2 years of age and older (see WARNINGS – Use In Pediatric Patients).

Geriatric Use: Clinical studies of promethazine hydrochloride and dextromethorphan hydrobromide syrup 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 responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, 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.

Sedating drugs may cause confusion and over-sedation in the elderly; elderly patients generally should be started on low doses of promethazine hydrochloride and dextromethorphan hydrobromide syrup and observed closely.

ADVERSE REACTIONS

Dextromethorphan: Dextromethorphan hydrobromide occasionally causes slight drowsiness, dizziness, and gastrointestinal disturbances.

Promethazine: Central Nervous System - Drowsiness is the most prominent CNS effect of this drug. Sedation, somnolence, blurred vision, dizziness, confusion, disorientation, and extrapyramidal symptoms such as incoordination, diarrhea, and tongue protrusion; lassitude, tinnitus, hyperreflexia, hypertonia, ataxia, athetosis, and extensor-plantar reflexes (Babinski reflex).

Cardiovascular - Increased or decreased blood pressure, tachycardia, bradycardia, faintness.

Dermatologic - Dermal rash, photosensitivity, urticaria.

Hematologic - Leukopenia, thrombocytopenia, thrombocytopenic purpura, agranulocytosis.

Gastrointestinal - Dry mouth, nausea, vomiting, diarrhea.

Respiratory - Asthma, nasal stuffiness, respiratory depression (potentially fatal) and apnea (potentially fatal). (See WARNINGS - Promethazine; Respiratory Depression.)

Other - Agranulocytosis, aplastic anemia, Leukopenia, thrombocytopenia, thrombocytopenic purpura, agranulocytosis.

Paradoxical Reactions - Hyperexcitability and abnormal movements have been reported in patients following a single administration of promethazine HCl. Consideration should be given to the discontinuation of promethazine HCl and to the use of other drugs if these reactions occur. Respiratory depression, nightmares, delirium, and agitated behavior have also been reported in some of these patients.

DRUG ABUSE AND DEPENDENCE

According to the WHO Expert Committee on Drug Dependence, dextromethorphan could produce very slight psychic dependence but no physical dependence.

OVERDOSAGE

Dextromethorphan: Dextromethorphan may produce central excitement and mental confusion. Very high doses may produce respiratory depression. One case of toxic psychosis (hyperactivity, marked visual and auditory hallucinations) after ingestion of a single dose of 20 tablets (300 mg) of dextromethorphan has been reported.

Promethazine: Signs and symptoms of overdose with promethazine HCl range from mild depression of the central nervous system and cardiovascular system to profound hypotension, respiratory depression, unconsciousness, and sudden death. Other reported reactions include hyperpyrexia, hyperesthesia, alliaxia, ataxia, and extensor-planter reflexes (Babinski reflex).

Stimulation may be evident, especially in children and geriatric patients. Convulsions may rarely occur. A paradoxical reaction has been reported in children receiving single doses of 75 mg to 125 mg orally, characterized by hyperexcitability and nightmares.

Atropine-like signs and symptoms - dry mouth, fixed dilated pupils, flushing, as well as gastrointestinal symptoms, may occur.

Treatment: The treatment of overdose with promethazine and dextromethorphan is essentially symptomatic and supportive. Only in cases of extreme overdose or individual sensitiveness do vital signs including respiration, pulse, blood pressure, temperature, and EKG need to be monitored. Activated charcoal or by lavage may be given; or sodium or magnesium sulfate orally as a cathartic. 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. Diaphoresis may be used to control convulsions. Acidosis and electrolyte losses should be corrected. The antidiuretic efficacy of narcotic analgesics to dextromethorphan has not been established; note that any of the depressant effects of promethazine are not reversed by naloxone. Avoid analeptics, which may cause convulsions.

Severe hypoxia usually responds to the administration of norepinephrine or phenylephrine. EPINEPHRINE SHOULD NOT BE USED, since its use in a patient with partial adrenergic blockage may further lower the blood pressure.

Limited experience with dialysis indicates that it is not helpful.

DOSAGE AND ADMINISTRATION

Promethazine hydrochloride and dextromethorphan hydrobromide syrup is contraindicated for children under 2 years of age (see WARNINGS – Black Box Warning and Use In Pediatric Patients).

The average effective dose is given in the following table:

- Adults: 1 teaspoonful (5 mL) every 4 to 6 hours, not to exceed 30 mL in 24 hours.
- Children 2 Years To Under 6 Years: ½ to 1 teaspoonful (2.5 to 5 mL) every 4 to 6 hours, not to exceed 10 mL in 24 hours.
- Children 6 Years To Under 12 Years: ½ to 1 teaspoonful (1.25 to 2.5 mL) every 4 to 6 hours, not to exceed 10 mL in 24 hours.

HOW SUPPLIED

This preparation is a clear syrup with yellow color and pineapple menthol odor, containing promethazine hydrochloride 2.5 mg/mL, dextromethorphan hydrobromide 15 mg/5 mL, and alcohol 7 percent, and is available in 4 fluid ounce (118 mL) and 8 fluid ounce (237 mL) and one pint (473 mL).

Keep tightly closed. Protect from light.

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

Dispense in a tight, light-resistant container with a child-resistant closure as defined in the USP.

Manufactured for:

QUALITEST PHARMACEUTICALS
Huntsville, AL 35811