

Proezine

Tablet 25mg Film Coated



DESCRIPTION

A 6.5mm, round convex core tablet, film coated blue, one side marked 'UP' and scored, the other side plain.

Each tablet contains Promethazine HCl 25mg

INDICATIONS

As symptomatic treatment for allergic conditions of the upper respiratory tract and skin including allergic rhinitis, urticaria and anaphylactic reactions to drugs and foreign proteins.

As an adjunct in preoperative sedation in surgery and obstetrics.

As an antiemetic.

For short term use:

Sedation and treatment of insomnia in adults.

As a paediatric sedative.

PHARMACODYNAMICS

Promethazine is a phenothiazine-derivative antihistamine which acts by blocking the action of histamine through competitive, reversible inhibition of H₁ receptor sites on tissues; it does not inactivate histamine or prevent its synthesis or release. It thereby prevents, but does not reverse responses mediated by histamine alone. Histamine H₁ receptors are responsible for vasodilation, increased capillary permeability, flare and itch reactions in the skin, and to some extent for contraction of smooth muscle in the bronchial and gastrointestinal tract. Thus, blockage of H₁ receptors may inhibit these reactions. In addition, its anticholinergic effects which mediates via muscarinic receptors provide a drying effect on the nasal and oral mucosa. The mechanism by which promethazine exerts its antiemetic, anti-motion sickness, and anti-vertigo effects is not precisely known but may be related to its centrally anticholinergic actions. It diminishes vestibular stimulation and depresses labyrinthine function. Activity on the medullary chemoreceptive trigger zone may also be involved in the antiemetic effect. Promethazine crosses the blood-brain-barrier and produces sedation due to the inhibition of histamine N-methyl transferase and blockage of central histaminergic receptors. Antagonism of other central nervous system receptor sites, such as those for serotonin, acetylcholine, and alpha-adrenergic stimulation, may also be involved. Promethazine are thought to cause indirect reduction of stimuli to the brain stem reticular system.

PHARMACOKINETICS

Promethazine is well absorbed after oral administration. Peak plasma concentrations have been observed 2 to 3 hours after administrations although, there is low systemic bioavailability after oral administration, due to high first pass metabolism in the liver. Onset of action after oral administration is within 15 to 60 minutes. Duration of action is 4 to 6 hours; may persist for up to 12 hours. Promethazine is widely distributed; it enters the brain and crosses the placenta. Values ranging from 76% to 93% have been reported for plasma-protein binding. Promethazine undergoes extensive metabolism, predominantly to promethazine sulfoxide, and also N-desmethylpromethazine. It is excreted slowly via the urine and bile, chiefly as metabolites. Elimination half-lives of 5 to 14 hours have been reported.

DOSAGE

Route of administration: Oral.

Not for use in children under the age of 2 years because of the potential for fatal respiratory depression.

As an antihistamine in allergy:

Children 2-5 years:	The use of Proezine Syrup 5mg/5ml or 10mg/5ml is recommended for this age group.
Children 5-10 years	25 mg as a single dose*. Maximum daily dose 25 mg.
Children over 10 years and adults (including elderly)	25 mg as a single dose*. Increasing to a maximum of 25 mg twice daily as required.

*Single doses are best taken at night.

As an antiemetic:

Children 2-5 years:	The use of Proezine Syrup 5mg/5ml or 10mg/5ml is recommended for this age group.
Children 5-10 years	The use of Proezine Syrup 5mg/5ml or 10mg/5ml is recommended.
Children over 10 years and adults (including elderly)	25 mg to be taken the night before the journey. To be repeated after 6-8 hours as required.

Short term sedation:

Children 2-5 years:	The use of Proezine Syrup 5mg/5ml or 10mg/5ml is recommended for this age group.
Children 5-10 years	25 mg as a single night time dose.
Children over 10 years and adults (including elderly)	25 or 50 mg as a single night time dose.

SIDE EFFECT

Incidence more frequent:- Drowsiness, thickening of mucus

Incidence less frequent or rare:- Blurred vision or any change in vision; confusion; dizziness; tightness of chest; urination difficulty & retention; dryness of mouth, nose, or throat; hypotension; increased sweating; loss of appetite; reduction in tone & motility of gastrointestinal tract resulting in constipation & increase in gastric reflux; paradoxical reaction (nightmares; unusual excitement, nervousness, restlessness, or irritability); photosensitivity (increased sensitivity of skin to sun); ringing or buzzing in ears; skin rash; tachycardia; blood dyscrasias (sore throat and fever, unusual bleeding or brushing, usual tiredness or

weakness) confusion; difficult or painful urination; dizziness; drowsiness; dryness of mouth, nose, or throat are more likely to occur in the elderly. Nightmares; unusual excitement, nervousness, restlessness, or irritability are more likely to occur in children and elderly patients.

CONTRAINDICATIONS

As antihistamine may enhance the sedative effects of central nervous depressants, it is contraindicated in patients taking alcohol, barbiturates, hypnotics, opioid analgesics, anxiolytic sedatives, and neuroleptic. It is also contraindicated in patients with close-angle glaucoma due to its mydriatic effect which may lead to an increase in intraocular pressure. Promethazine is contraindicated with patients suffering from CNS depression of any cause, and patients using MAO inhibitors for the past 14 days. Promethazine should not be given to premature infant or neonates.

PRECAUTIONS

Promethazine should not be given to premature infants or neonates; this group of patients has an increased susceptibility to antimuscarinic effects. It should also be avoided in young children age 1 to 2 years because of the potential risk of central and obstructive apnoea and reduced arousal.

Many antihistamines may cause drowsiness; patients so affected should not drive or operate machinery. Patients should avoid alcoholic drink. Because of their antimuscarinic properties antihistamines should be used with care in conditions such as urinary retention, prostatic hyperplasia, or pyloroduodenal obstruction. Other adverse effects of antihistamines suggest caution in patients with epilepsy, severe cardiovascular disorders, and with liver disorder.

Laboratory Value Alteration

Promethazine hydrochloride may affect certain diagnostic test results. An increase in glucose tolerance has been reported in patients receiving phenothiazine-derivative antihistamines. Patients on this medication may also experience a false-positive or false-negative results of immunologic urine pregnancy tests, depending on the test used. Antihistamines may inhibit the cutaneous histamine response, thus producing false-negative results; it is thus recommended that antihistamines be discontinued at least 12 hours before testing begins.

WARNING

When used for treatment of cough and cold

- Promethazine should not be used in pediatric patients less than 2 years of age because of the potential for fatal respiratory depression.

- To be used with caution and doctor's/pharmacist's advice in children 2 to 6 years of age.

DRUG INTERACTIONS

The sedative action of promethazine is additive to the sedative effects of other central nervous system depressants, including alcohol, narcotic analgesic, sedatives, hypnotics, MAOIs, tricyclic antidepressants and tranquilisers; therefore these agents should be avoided or administered in reduced dosage to patients receiving promethazine. Alcohol should be avoided during treatment. Promethazine being a phenothiazine derivative has alpha-adrenergic blocking action and hence the following drugs effects may be antagonised or decreased when taken concomitantly: dopamine, ephedrine, methoxamine, metaraminol, epinephrine. The following medications should be used with caution. extrapyramidal reaction-causing medications, hepatotoxic medications, hypotension-producing medications, beta-adrenergic blocking drugs, levodopa (antiparkinsonism effects), ototoxic medications (as promethazine may mask the symptoms of toxicity), quinidine (concurrent use with promethazine may result in additive cardiac effects) and riboflavin (requirements of riboflavin may be increased in patients receiving promethazine).

OVERDOSAGE

Overdosage may be fatal especially in infants and children. Overdosage with promethazine is associated with antimuscarinic, extrapyramidal, gastrointestinal, and CNS effects. In infants and children CNS stimulation predominates over CNS depression, causing ataxia, excitation, tremors, psychoses, hallucinations, and convulsions; hyperpyrexia may also occur. Deepening coma and cardiorespiratory collapse may follow. In adults, CNS depression is more common with drowsiness, coma and convulsion, progression to respiratory failure or possibly cardiovascular collapse.

Symptoms of overdose:- Clumsiness or unsteadiness; severe drowsiness; severe dryness of mouth, nose, or throat; flushing or redness of face; shortness of breath or troubled breathing; hallucinations; seizures, trouble in sleeping; muscle spasms, especially of neck and back; restlessness; shuffling walk; jerky movements of head and face; trembling and shaking of hands; hypotension, severe (feeling faint).

Notes; Anticholinergic and CNS stimulation effects are more likely to occur in children with overdose. Hypotension may also occur in the elderly at usual dose.

Treatment

In severe overdose with antihistamines the stomach should be emptied. Emetic (syrup of ipecac recommended) may be tried if the patient is alert and there is no symptoms of toxicity; however precaution against aspiration is necessary, especially in infants and children. Emetic may be ineffective due to the antiemetic activity of the antihistamine. Activated charcoal and saline (isotonic or 0.45% sodium chloride solution) has been given. Anticholinergic antiparkinson agents, diphenhydramine, or barbiturates, could be used to control extrapyramidal reactions. Central stimulants may increase the risk of convulsions, and their avoidance is advisable. Other treatment is supportive and symptomatic and may include artificial respiration, external cooling for hyperpyrexia, and oxygen and intravenous fluids. Vasopressors to treat hypotension; however, epinephrine must not be given as it can lower the blood pressure further.

Up-to-date information on treatment of overdose can be obtained from
The National Poison Centre,
Universiti Sains Malaysia Tel: 1-800-8099

TOXICOLOGY

Carcinogenicity/Tumorigenicity/Mutagenicity

Long-term animal studies to assess the carcinogenic, tumorigenic, or mutagenic potential of promethazine have not been performed.

PREGNANCY AND LACTATION

Pregnancy/Reproduction

Phenothiazines have been reported to cause jaundice and extrapyramidal symptoms in infant whose mother received these medications during pregnancy. For promethazine, adequate and well-controlled studies in human have not been done. However, promethazine taken within 2 weeks prior to delivery may inhibit platelet aggregation in the newborn. Studies in rats with doses 2.1 to 4.2 times the maximum recommended human daily dose have not shown that promethazine causes adverse effects on fetal development. (FDA Pregnancy Category C)

Breast feeding

Small amount of antihistamines may be distributed into breast milk; use is not recommended in nursing mother because of the risks of adverse effects, such as unusual excitement or irritability, in infants. Antihistamines may inhibit lactation because of their anticholinergic actions. Some studies have indicated that the use of promethazine in children up to 2 years of age may be associated with the sudden infant death syndrome (SIDS) and an increase in sleep apnoea. Therefore the use of phenothiazine-derivative antihistamines by nursing mothers should be discouraged until more studies have been performed to confirm the potential risk of nursing mother.

Pediatric

Use is not recommended in newborn or premature infants because this age group has increased susceptibility to anticholinergic side effects, such as central nervous systems (CNS) excitation, and an increased tendency toward convulsions. A paradoxical reaction characterised by hyperexcitability may occur in children taking antihistamines. The use of phenothiazine-derivative antihistamines is not recommended in infants of up to 3 months of age, because of the possible absence or deficiency of detoxifying enzymes and inefficient renal function usually noted in this age group. Also, increased susceptibility to dystonia has been reported in newborn or premature infants, acutely ill or dehydrated children, and children with acute infections who have received phenothiazine medication. Some studies have associated the use of promethazine with sudden infant death syndrome (SIDS) and with an increase in infant sleep apnoea. Until more studies have been performed to confirm this potential risk, phenothiazine derivatives should not be used in children up to 2 years of age. In children with signs and symptoms suggestive of Reye's syndrome, phenothiazine derivatives should not be used since the extrapyramidal symptoms that may occur, especially after parenteral administration of large doses, may be confused with CNS signs of this syndrome, thus making diagnosis difficult.

Adolescents

In adolescents with symptoms suggestive of Reye's syndrome, phenothiazine derivatives should also be avoided since the extrapyramidal symptoms that may occur may be confused with the CNS signs of this syndrome thus making diagnosis difficult.

Geriatrics

Dizziness, sedation, confusion, and hypotension may be more likely to occur in geriatric patients taking antihistamines. A paradoxical reaction characterized by hyperexcitability may occur in geriatric patients taking antihistamines.

Geriatric patients are especially susceptible to the anticholinergic side effects such as dryness of mouth and urinary retention (especially in males) of the antihistamines. If these side effects occur and continue or are severe, the medication should probably be discontinued.

Extrapyramidal signs, especially parkinsonism, akathisia and persistent dyskinesia, may also be more likely to occur in geriatric patients, especially at the higher doses or with parenteral administration.

Dental

Prolonged use of antihistamines may decrease or inhibit salivary flow, especially in middle-aged or elderly patients, thus contributing to the development of caries, periodontal disease, oral candidiasis, and discomfort. Involuntary orificial muscle movement may result from extrapyramidal effects. These involuntary movements may result in occlusal adjustments, bite registration, and treatment for bruxism less reliable.

PRESENTATION

Blister pack of 10 x 10's and 100 x 10's

All pack sizes may not be available locally

STORAGE CONDITIONS AND USER INSTRUCTIONS

Store in a dry place below 30°C.
Protect from light.
Not recommended for children under 2 years.
Keep out of reach of children.
<i>Jauhi daripada kanak-kanak.</i>
Shelf life: Please refer to outer package.

Product Registration Holder:

Duopharma Marketing Sdn. Bhd.

Lot No. 2, 4, 6, 8 & 10, Jalan P/7,

Section 13, Bangi Industrial Estate,

43650 Bandar Baru Bangi, Selangor, Malaysia.

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