

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

ZIZ

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 10 mg of the active substance Promethazine hydrochloride

Excipient(s) with known effects:

Also contains 23.68 mg of lactose and 33.70 mg of sucrose.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Sugar-coated tablet

Blue sugar-coated tablet

4 CLINICAL PARTICULARS

4.1 Therapeutic 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 antiemetic.

For short term use:

- Treatment of insomnia in adults.
- As a paediatric sedative.

4.2 Posology and method of administration

Route of administration: Oral

Posology

Paediatric population:

Not for use in children under the age of 2 years (see section 4.3)

The use of Promethazine liquid is recommended for this age group.

As an antihistamine in allergy:

Children 5-10 years	Either 10 or 20 mg as a single dose*. Or 10 mg twice a day(bd). Maximum daily dose 20 mg.
Children over 10 years and adults (including elderly)	Initially 10 mg twice a day (bd). Increasing to a maximum of 20 mg three times a day (tds) as required.

*Single doses are best taken at night.

As an antiemetic:

Children 5-10 years	10 mg to be taken the night before the journey. To be repeated after 6–8 hours as required.
Children over 10 years and adults (including elderly)	20 mg to be taken the night before the journey. To be repeated after 6–8 hours as required.

As a paediatric sedative for short term use and for short term treatment of insomnia in adults:

Children 5-10 years	20 mg as a single dose at bedtime
Children over 10 years and adults (including elderly)	20 mg to be taken at bedtime, which may be increased up to 50 mg if necessary.

4.3 Contraindications

Ziz should not be given to patient with known hypersensitivity to the active substance, or to any of the excipients listed in section 6.1.

Ziz should not be used in patients:

- in coma or;
- suffering from CNS depression of any cause or,

Ziz is contraindicated for use in children less than two years old because of the potential for fatal respiratory depression. (This includes neonates and premature infants.)

Ziz should be avoided in patients taking monoamine oxidase inhibitors up to 14 days previously.

4.4 Special warnings and precautions for use

Promethazine should not be used for more than 7 days without seeking medical advice.

Caution should be used in patients with:

- asthma, bronchitis or bronchiectasis. Promethazine may thicken or dry lung secretions and impair expectoration.
- severe coronary artery disease
- narrow angle glaucoma,
- epilepsy
- hepatic and renal insufficiency
- bladder neck or pyloro-duodenal obstruction

Ototoxicity

Promethazine may mask the warning signs of ototoxicity caused by ototoxic drugs e.g. salicylates. It may also delay the early diagnosis of intestinal obstruction or raised intracranial pressure through the suppression of vomiting.

QT interval

As phenothiazines can prolong the QT interval, caution is advised in treated patients with pronounced bradycardia, cardiovascular disease, with a hereditary form of prolongation of the QT interval and concomitant use with other products leading to QT prolongation.

QT prolongation

Phenothiazine derivatives may potentiate QT interval prolongation which increases the risk of onset of serious ventricular arrhythmias of the torsade de pointes type, which is potentially fatal (sudden death). QT prolongation is exacerbated, in particular, in the presence of bradycardia, hypokalaemia, and acquired (i.e. drug induced) QT prolongation. If the clinical situation permits, medical and laboratory evaluations should be performed to rule out possible risk factors before initiating treatment with a phenothiazine derivative and as deemed necessary during treatment (see section 4.8).

Photosensitivity reactions

Due to the risk of photosensitivity, exposure to strong sunlight or ultraviolet light should be avoided during or shortly after treatment.

Paediatric population

The use of promethazine should be avoided in children and adolescents with signs and symptoms suggestive of Reye's Syndrome.

Excipient(s) with known effect

This medicine contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

This medicine contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Promethazine will enhance the action of any anti-cholinergic agent, tricyclic anti-depressant, sedative, hypnotic.

Alcohol should be avoided during treatment. Combination with alcohol enhances the sedative effects of H1 antihistamines.

Promethazine may interfere with immunological urine pregnancy tests to produce false- positive or false-negative results.

ZIZ should be discontinued at least 72 hours before the start of skin tests as it may inhibit the cutaneous histamine response and thus produce false-negative results.

Special caution is required when promethazine is used concurrently with other products leading to QT prolongation, including medicinal products such as antipsychotics, i.e., some phenothiazines (chlorpromazine, levomepromazine), benzamides (sulpiride, amisulpride, tiapride), pimozide, haloperidol, droperidol, citalopram, halofantrin, methadone, pentamidine, and moxifloxacin.

Special caution is required when promethazine is used concurrently with drugs known to cause QT prolongation (such as antiarrhythmics, antimicrobials, antidepressants), to avoid exacerbation of risk of QT prolongation.

4.6 Fertility, pregnancy and lactation

Pregnancy

ZIZ should not be used in pregnancy unless the physician considers it essential. The use of ZIZ is not recommended in the 2 weeks prior to delivery in view of the risk of irritability and excitement in the neonate.

Breast-feeding

Available evidence suggests that the amount of Promethazine excreted in breast milk is insignificant. However, there are risks of neonate irritability and excitement.

ZIZ is not recommended for use in breast-feeding.

4.7 Effects on ability to drive and use machines

Because the duration of action may be up to 12 hours, patients should be advised that if they feel drowsy they should not drive or operate heavy machinery.

4.8 Undesirable effects

The following CIOMS frequency rating is used: Very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1000$ to $< 1/100$); rare ($\geq 1/10000$ to $< 1/1000$); very rare ($< 1/10000$), not known (cannot be estimated from the available data).

Immune system disorders

Allergic reactions, including urticaria, rashes, pruritus pruritus and anaphylactic reactions have been reported.

Skin and subcutaneous tissue disorders

Photosensitive skin reactions have been reported, strong sunlight should be avoided during treatment.

Nervous system disorders

Somnolence, drowsiness, dizziness, headaches, extrapyramidal effects including restless legs syndrome, muscle spasms and tic-like movements of the head and face.

The elderly are particularly susceptible to the anticholinergic effects and confusion due to promethazine.

Not known: neuroleptic malignant syndrome, psychomotor hyperactivity

Psychiatric disorders

Restlessness, nightmares, and disorientation.

Infants are susceptible to the anticholinergic effects of promethazine, while other children may display paradoxical hyperexcitability.

Not known: hallucinations, aggression

Eye disorders

Blurred vision

Gastrointestinal disorders

Epigastric irritation /discomfort, dry mouth

Renal and urinary disorder

Urinary retention

Metabolism and nutrition disorders

anorexia

Cardiac disorders

Palpitations, arrhythmias

Not known: QT prolongation, Torsade de pointes

Vascular disorders

Hypotension

Hepatobiliary disorders

Jaundice

Blood and lymphatic system disorders

Blood dyscrasias including haemolytic anaemia rarely occur. Agranulocytosis.

Not known: thrombocytopenia

General and administration site conditions

Tiredness

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms

The symptoms of severe overdose are variable. They are characterised in children by various combinations of excitation, ataxia, incoordination, athetosis and hallucinations, while adults may become drowsy and lapse into coma. Convulsions may occur in both adults and children; coma or excitement may precede their occurrence. Tachycardia may develop. Cardio-respiratory depression is uncommon.

High doses (suprathapeutic doses) can cause ventricular arrhythmias including QT prolongation and torsade de pointes (see section 4.8).

Prolonged QT interval and cases of severe arrhythmias with fatal outcome have been described in overdose of phenothiazines.

Management

If the patient is seen soon enough after ingestion, it should be possible to induce vomiting with ipecacuanha despite the anti-emetic effect of Promethazine; alternatively, gastric lavage may be used.

Treatment is otherwise supportive with attention to maintenance of adequate respiratory and circulatory status. Convulsions should be treated with Diazepam or other suitable anticonvulsant.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antihistamines for systemic use; Phenothiazine derivatives, ATC code: R06AD02

Potent, long acting, antihistamine with additional anti-emetic central sedative and anti-cholinergic properties.

5.2 Pharmacokinetic properties

ZIZ is distributed widely in the body. It enters the brain and crosses the placenta. ZIZ is slowly excreted via urine and bile. Phenothiazines pass into the milk at low concentrations.

5.3 Preclinical safety data

No relevant information additional to that contained elsewhere in the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose
Maize Starch
Pregelatinised Maize Starch
Magnesium Stearate
Bleached Shellac
Talc, purified
Titanium Dioxide (E171)
Polyvinylpyrrolidone K25
Opalux AS-80924-Blue (with E132, E133, E171)
Sucrose
Beeswax
Carnauba Wax

6.2 Incompatibilities

Promethazine hydrochloride is incompatible with alkaline substances, which precipitate Promethazine Base.

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Do not store above 25°C. Store in the original packaging. Keep the blister pack in the outer carton.

6.5 Nature and contents of container

Strips of 250 micron PVC and 20 micron aluminium foil, with 5/6 gsm heat-seal lacquer on the dull side and printed on the bright side.

Pack size: 16 tablets.

6.6 Special precautions for disposal

No special precautions.

7 MARKETING AUTHORISATION HOLDER

Chelonia Healthcare Limited
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3rd Floor, 1060 Nicosia
Cyprus

8 MARKETING AUTHORISATION NUMBER(S)

PL 33414/0146

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

28/11/2006

10 DATE OF REVISION OF THE TEXT

05/06/2025