SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

PHENERGAN 25 mg, coated tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Promethazine hydrochloride .....28.21 mg
Corresponding quantity of promethazine base ..... 25.00 mg
For a coated tablet.
Excipients with known effects: wheat starch (gluten), lactose, sucrose.
For the full list of excipients, see section 6.1 .

3. PHARMACEUTICAL FORM

Coated tablet.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Symptomatic treatment of various allergic manifestations :

• rhinitis (seasonal or perennial),

Conjunctivitis

· Hives.

Occasional insomnia,
Transient insomnia.

4.2. Posology and method of administration

FOR ADULTS ONLY.

Posology
Allergic reactions : 1 to 2 tablets per dose, to be repeated if necessary after a minimum of 4 hours, without exceeding 6 tablets per day.
Evening doses are preferable due to promethazine's pronounced sedative effect. Treatment should be short-term.
Occasional insomnia, transient insomnia : 1 to 2 tablets in the evening, 15 to 30 minutes before bedtime.
The treatment should be as short as possible (2 to 5 days).
If insomnia persists beyond this period, the treatment should be reassessed.

Method of administration
Oral route.

4.3. Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.
This medication is CONTRAINDICATED due to the presence of promethazine in the following cases:

• Hypersensitivity to antihistamines,

· child under 15 years of age,

• history of agranulocytosis with other phenothiazines,

• risk of urinary retention related to urethro-prostatic disorders,

• risk of angle-closure glaucoma,

This medicine is contraindicated in patients with a wheat allergy (other than celiac disease).

This medication is GENERALLY NOT RECOMMENDED:

· in case of breastfeeding (see section 4.6),

· in combination with sultopride (see section 4.5).

4.4. Special warnings and precautions for use

Special warnings

For adults only.
If allergic symptoms persist or worsen (respiratory distress, edema, skin lesions, etc.) or if there are associated signs of viral infection, the course of action should be reassessed.
The cause of insomnia should be identified if possible, and any underlying factors treated. If insomnia persists after 5 days of this treatment, it may indicate an underlying condition, and the treatment should be reassessed.
This medication can be administered in cases of celiac disease. The wheat starch may contain gluten, but only in trace amounts, and is therefore considered safe for individuals with celiac disease.
This medicine contains lactose and sucrose. Its use is not recommended in patients with lactose and sucrose intolerance.

Precautions for use

Clinical and possibly electrical monitoring should be reinforced in epileptics due to the possibility of lowering the epileptogenic threshold with phenothiazines.
Promethazine should be used with caution:

• in elderly patients presenting with:

o increased sensitivity to orthostatic hypotension, dizziness, and sedation,

o chronic constipation (risk of paralytic ileus),

o a possible prostatic hypertrophy;

• in subjects with certain cardiovascular conditions, due to the tachycardic and hypotensive effects of phenothiazines,

· in cases of severe hepatic and/or renal insufficiency (due to the risk of accumulation).

The consumption of alcoholic beverages and medication containing alcohol (see section 4.5) is strongly discouraged during the course of treatment.
Given the photosensitizing effect of phenothiazines, it is best to avoid sun exposure during treatment.

4.5. Interactions with other medicinal products and other forms of interaction

Associations not recommended

+ Alcohol
Alcohol increases the sedative effect of antihistamines. Impaired alertness may make driving and operating machinery dangerous.
Avoid consuming alcoholic beverages and medications containing alcohol.
+ Sultopride
Increased risk of ventricular rhythm disturbances, particularly torsades de pointes, due to the additive electrophysiological effects.

Associations to consider

+ Other central nervous system depressants (sedative antidepressants, barbiturates, benzodiazepines, clonidine and related drugs, hypnotics, morphine derivatives (analgesics and antitussives), methadone, neuroleptics, anxiolytics)

Increased central nervous system depression. Impaired alertness may make driving and operating machinery dangerous.
+ Atropine and other atropinic substances (imipramine antidepressants, anticholinergic antiparkinsonian drugs, atropinic antispasmodics, disopyramide, phenothiazine neuroleptics)
Addition of atropine-like side effects such as urinary retention, constipation, dry mouth.

4.6. Pregnancy and breastfeeding

Pregnancy

• **Malformation** (1st trimester):

o there are no reliable animal teratogenicity data for promethazine.

o In clinical practice, the use of promethazine in a limited number of pregnancies has not revealed any particular malformative or fetotoxic effects to date. However, further studies are needed to assess the consequences of exposure during pregnancy

• **Fetal toxicity** (2nd and 3rd trimesters):

In newborns of mothers treated long-term with high doses of an anticholinergic antihistamine such as promethazine, digestive signs related to the atropinic properties of phenothiazines have been rarely described (abdominal distension, meconium ileus, delayed meconium passage, difficulty initiating feeding, tachycardia, neurological disorders...).
Given this data , the use of this medication should be avoided , as a precautionary measure, during the first trimester of pregnancy. It should only be prescribed thereafter if necessary, and in the third trimester, its use should be limited to occasional use .
If this medication was administered late in pregnancy, it seems justified to observe a period of monitoring of the newborn's neurological and digestive functions.

Breastfeeding

Promethazine passes into breast milk. Given the potential for sedation or paradoxical excitation in newborns, and especially the risk of sleep apnea associated with phenothiazines, this medication is not recommended during breastfeeding.

4.7. Effects on the ability to drive vehicles and use machinery

Particular attention should be paid, especially by drivers and machine operators, to the risk of drowsiness associated with the use of this medication, particularly at the start of treatment. This effect is exacerbated by the consumption of alcoholic beverages or medications containing alcohol.
It is best to start treatment for allergic reactions in the evening.

4.8. Undersirable effects

The pharmacological characteristics of **promethazine** are responsible for adverse effects of varying intensity, which may or may not be dose-related (see section 5.1):

• **Neurovegetative effects :**

o sedation or drowsiness, more pronounced at the beginning of treatment ;

o anticholinergic effects such as dry mucous membranes, constipation, accommodation disorders, mydriasis, heart palpitations, risk of urinary retention;

o orthostatic hypotension;

o balance problems, dizziness, decreased memory or concentration;

o motor incoordination, tremors (more frequent in the elderly);

o mental confusion, hallucinations;

or more rarely, excitation-type effects: agitation, nervousness, insomnia;

• **Awareness-raising reactions :**

or erythema, eczema, pruritus, purpura, possibly giant urticaria,

o edema, more rarely Quincke's edema,

Anaphylactic shock.

o photosensitization;

• **Hematological effects :**

o leukopenia, neutropenia, exceptional agranulocytosis ;

thrombocytopenia,

o hemolytic anemia.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions is important. It allows for continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals must report any suspected adverse reactions according to the procedures defined in the Therapeutic Use and Data Collection Protocol (PUT RD).

4.9. Overdose

Signs of **promethazine overdose** : convulsions (especially in infants and children), impaired consciousness, coma;

Symptomatic treatment will be initiated in a specialized setting.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic class: ANTIHISTAMINE FOR SYSTEMIC USE, ATC code: R06AD02 (**R: respiratory system; D: dermatological; N: nervous system**)

Mechanism of action
H1 antihistamine , a phenothiazine with an aliphatic side chain, characterized by:

• a marked sedative effect at usual doses, of central histaminergic and adrenolytic origin,

· an anticholinergic effect causing peripheral side effects .

• a peripheral adrenolytic effect, which may have hemodynamic consequences (risk of orthostatic hypotension).

Antihistamines have in common the property of opposing, through more or less reversible competitive antagonism, the effects of histamine, particularly on the skin, blood vessels and conjunctival, nasal, bronchial and intestinal mucous membranes.

5.2. Pharmacokinetic properties

The bioavailability of promethazine is between 13 and 40%.
The time to reach maximum plasma concentration is 1.5 to 3 hours.
The volume of distribution is high due to the liposolubility of the molecule, approximately 15 l/kg.

The fraction bound to plasma proteins is equal to 75-80%.
The half-life is between 10 and 15 hours.
The metabolism consists of sulfoxidation followed by demethylation.
Renal clearance accounts for less than 1% of total clearance, and approximately 1% of the administered promethazine is recovered unchanged in the urine. Metabolites found in the urine, particularly sulfoxide, represent approximately 20% of the dose.
Physiopathological variation : risk of accumulation of antihistamines in patients with renal or hepatic insufficiency.

5.3. Preclinical safety data

Not specified.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Core : Wheat starch, Lactose monohydrate, Talc, Icing sugar starch (sucrose containing 2 to 3% starch), Hydrated colloidal silica, Magnesium stearate.

Coating : polyvinyl acetate, carnauba wax, patent blue V (E 131), sucrose.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

5 years.

6.4. Special precautions for storage

This medicine does not require any special storage conditions with regard to temperature.

6.5. Nature and contents of container

20 coated tablets in thermoformed blisters (PVC/Aluminium).

6.6. Special precautions for disposal and handling

Any unused medicinal product or waste material should be disposed of in accordance with local regulations.

7. OPERATORS AND MANUFACTURERS

Operator of the export marketing authorization

FRILAB SA
17, rue des Pierres du Niton
1207 Geneva SWITZERLAND

Manufacturers

SYNERLAB - Sophartex , 21 rue du Pressoir, 28500 Vernouillet , France

ITC Farma Srl , Via Pontina, 5, 0071 Pomezia (Rome), Italy

8. DATE OF REVISION OF THE TEXT

29 July 2022.

9. DOSIMETRY

Not applicable.

CONDITIONS FOR PRESCRIPTION AND DISPENSING

This medication is not subject to medical prescription.