SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

PHENERGAN 0.1 PERCENT, syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Promethazine hydrochloride ..... 0.113 g
Corresponding quantity of promethazine base ..... 0.100 g
Per 100 ml of syrup.
One 5 ml (1 tsp) measuring cup graduation contains 5 mg of promethazine base.
One 10 ml (2 tsp) measuring cup graduation contains 10 mg of promethazine base.

Excipients with known effects : alcohol, sucrose.
One 5 ml (1 tsp) measuring cup graduation contains 37 mg of alcohol and 4.2 g of sucrose.
A 10 ml (2 tsp) measuring cup graduation contains 73 mg of alcohol and 8.3 g of sucrose.
Alcohol content : 0.9% (V/V).

For the full list of excipients, see section 6.1 .

3. PHARMACEUTICAL FORM

Syrup.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Symptomatic treatment of allergic reactions miscellaneous:

• rhinitis (seasonal or perennial),

Conjunctivitis

· Hives.

4.2. Posology and method of administration

RESERVED FOR ADULTS AND CHILDREN OVER 2 YEARS OLD.

Posology
Use the measuring cup graduated at 5 and 10 ml or a teaspoon :
For children aged 2 to 6 years: it is imperative to consult a doctor and follow their prescription.
For children aged 6 to 12 years : 1 to 2 graduations of 5 ml from the measuring cup per dose, 2 to 3 times a day, without exceeding 5 graduations of 5 ml per day.
For children over 12 years : 1 to 2 graduations of 10 ml from the measuring cup per dose, 4 times a day, without exceeding 5 graduations of 10 ml per day.
For adults : 2 graduations of 10 ml from the measuring cup per dose, 4 to 5 times a day.
Given the pronounced sedative effect of promethazine, the strongest dose should be reserved for the evening.

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 in the following cases:

- Child under 2 years old

• Hypersensitivity to antihistamines,

• history of agranulocytosis,

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

• risk of angle-closure glaucoma.

This medication is GENERALLY NOT RECOMMENDED:

· in combination with sultopride (see section 4.5),

· in case of breastfeeding

4.4. Special warnings and precautions for use

Special warnings

If 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.

WARNING: THIS MEDICINE CONTAINS ALCOHOL.
The alcohol content of the solution is 0.9%, which is:

· 37 mg of alcohol per 5 ml graduation of the measuring cup,

· 73 mg of alcohol per 10 ml graduation of the measuring cup.

This medicine contains 0.9% v/v ethanol (alcohol), i.e., up to 73 mg of alcohol per 10 ml dose. Use of this medicine is dangerous for individuals with alcoholism and should be carefully considered in pregnant or breastfeeding women, children, and high-risk groups such as those with liver failure or epilepsy.
This medicine contains sucrose. Its use is not recommended in patients with sucrose intolerance.

Precautions for use

Since phenothiazines such as promethazine have been considered as hypothetical risk factors in the occurrence of sudden infant death syndrome, this drug is contraindicated in children under 2 years of age .
Clinical and possibly electrical monitoring should be reinforced in epileptics due to the possibility of lowering the epileptogenic threshold.
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 or other 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.
This medicine contains 4.2 g of sucrose per graduation of 5 ml measuring cup and 8.3 g of sucrose per graduation of 10 ml measuring cup, which should be taken into account in the daily intake in the case of a low-sugar diet or diabetes.

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

Associations not recommended

+ Alcohol
Alcohol increases the sedative effect of H1 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, 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

• **Malformative aspect** (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, digestive signs related to the atropinic properties of phenothiazines (abdominal distension, meconium ileus, delayed passage of meconium, difficulty initiating feeding, tachycardia, neurological disorders...) have been rarely described.

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

It is not known whether 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

Attention is drawn, particularly among machine operators, to the risks of drowsiness associated with the use of this medication, especially at the start of treatment .
This phenomenon is exacerbated by the consumption of alcoholic beverages or other medications containing alcohol.
It is best to start the treatment 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,

shock ,

o photosensitivity;

• **Hematological effects :**

o leukopenia, neutropenia, exceptional agranulocytosis ;

thrombocytopenia ,

o hemolytic anemia.

4.9. Overdose

Signs of a **promethazine overdose :**

o Convulsions (especially in infants and children),

o Disturbances of 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 (**D: Dermatology**) (**R: Respiratory system**)

Promethazine
H_1 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 , by competitive antagonism more or less reversible, the effects of histamine, particularly on blood vessels, skin and conjunctival, bronchial and intestinal mucous membranes.

5.2. Pharmacokinetic properties

Promethazine
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 applicable.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Citric acid monohydrate, sodium gentisate , alcohol, deterpenated sweet orange essential oil, orange blossom essential oil, caramel (E150), purified water, sucrose solution.

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

150 ml type III amber glass bottle, closed with an aluminium cap fitted with a polyethylene seal (+ polypropylene measuring cup graduated at 5 ml and 10 ml)

6.6. Special precautions for disposal and handling

No special requirements.
Any unused medicinal product or waste material should be disposed of in accordance with local regulations.

7. OPERATOR AND MANUFACTURERS

Operator of the export marketing authorization
FRILAB SA
17, rue des Pierres du Niton
1207 Geneva SWITZERLAND

Manufacturer
TERIAK, Industrial Zone, Djebel Ouest, Zaghouan, Tunisia

ITC Farma Srl , Via Pontina , 5, 00071 Pomezia (Rome), Italy

8. DATE OF TEXT UPDATE

29 July 2022.

9. DOSIMETRY

Not applicable.

CONDITIONS FOR PRESCRIPTION AND DISPENSING

This medication is not subject to medical prescription.