SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

PHENERGAN 2.5%, solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Promethazine hydrochloride ..... 2.820 g
Corresponding quantity of promethazine base ..... 2.500 g
For 100 ml of injectable solution.

Excipients with known effect: potassium disulfite (E224), anhydrous sodium sulfite (E221).
For the full list of excipients, see section 6.1 .

3. PHARMACEUTICAL FORM

Injectable solution.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Symptomatic treatment of acute urticaria.

4.2. Posology and method of administration

RESERVED FOR ADULTS AND CHILDREN OVER 15 YEARS OLD.

Posology
1 ampoule to be replaced once if necessary.

Method of administration
Deep intramuscular injection or intravenous infusion.

4.3. Contraindications

This medication is CONTRAINDICATED in the following cases:

• Hypersensitivity to any of the ingredients,

· child under 15 years of age,

• due to the presence of promethazine :

o history of agranulocytosis with other phenothiazines,

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

o 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

The use of this medication should not delay the administration of adrenaline if needed.
This medicine contains "sulfite" and may cause severe allergic reactions and bronchospasm.

Precautions for use

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 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 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, 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

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

Particular attention is drawn, especially among vehicle drivers and 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 medications containing alcohol.

4.8. Undesirable 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.

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;

A **treatment** **symptomatic** treatment will be administered in a specialized setting.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic class: ANTIHISTAMINE FOR SYSTEMIC USE, ATC code: R06AD02 (**D: Dermatology**)

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, 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

Promethazine
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

Potassium disulfite (E 224), anhydrous sodium sulfite (E 221), sodium gentisate , water for injections.

6.2. Incompatibilities

In the absence of compatibility studies, this medicine should not be mixed with other medicines.

6.3. Shelf life

5 years.
After opening/ dilution: the product must be used immediately.

6.4. Special precautions for storage

This medicine does not require any special temperature storage conditions. Store away from light.

6.5. Nature and contents of container

2 ml colorless glass ampoule (type I). Box of 5

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. OPERATORS AND MANUFACTURERS

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

Manufacturer :
Haupt Pharma Livron SAS – 1, Rue Comte de Sinard, 26250 Livron-sur-Drôme, FRANCE

8. DATE OF REVISION OF THE TEXT

29 July 2022.

9. DOSIMETRY

Not applicable.

CONDITIONS FOR PRESCRIPTION AND DISPENSING

List I