

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Prometazin Actavis 25 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 25 mg of promethazine hydrochloride.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet

White coloured, oval shaped, 9.8 x 6.2 mm biconvex, film-coated tablets debossed with "C25" on one side and plain on other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- Short-term treatment of sleep disorders
- Symptomatic short-term treatment of anxiety
- Premedication in surgical and dental practice
- Motion sickness
- Allergic reactions of different origins
- Pruritus
- Nausea and vertigo (morning sickness, Ménière's disease, nausea after radium treatment and anesthetics)

4.2 Posology and method of administration

Promethazine should be used at the lowest effective dose and for the shortest possible treatment period. The recommended dose should not be exceeded (see also section 4.4).

Symptomatic short-term treatment of anxiety:

Adults: 25-50 mg, 1-3 times a day.

Short-term treatment of sleep disorders:

Adults: 25-50 mg 1-2 hours before bedtime.

Sometimes this dose can lead to residual morning drowsiness, which disappears after a few days' continuous medication, in many cases, a lower dose will give adequate effect. In more severe cases, the dose is increased.

Children 6-17 years-of-age: 20-25 mg 1-2 hours before bedtime.

Usually, the hypnotic effect decreases with continuous use. In more severe cases of sleep disorder, intermittent medication may be necessary (a break every third or fourth night).

Elderly people can usually take promethazine continuously as a hypnotic.

Patients with some form of lesion will rarely tolerate high doses.

Motion sickness:

Adults: 25 mg, 1-2 hours before the trip or alternatively the evening before the trip. If needed, two extra doses can be taken within a 24-hour period.

Adolescents 13-17 years: 20-25 mg 1-2 hours before the trip or alternatively the evening before the trip. If needed, two extra doses can be taken within a 24-hour period (maximum daily dose 60 mg)

Allergic conditions:

Adults: 25-50 mg at night

Premedication:

Adults: 25-50 mg one hour before treatment; if necessary, the same dose the evening before treatment.

Children 6-12 years-of-age and adolescents 13-17 years: 25 mg one hour before treatment; if necessary, the same dose the evening before treatment.

For dosages, which cannot be achieved with Prometazin Actavis other strengths of promethazine medicinal products are available.

Method of Administration

Oral use.

4.3 Contraindications

Prometazin Actavis should not be used:

- in patients with hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- in children less than six years of age
- in patients taking monoamine oxidase inhibitors up to 14 days previously.

4.4 Special warnings and precautions for use

Patients are strongly advised to abstain from consumption of alcoholic beverages and/or substance use during treatment. Deaths have been reported with concomitant alcohol consumption and/or substance use (see sections 4.5 and 4.9).

Do not use in patients who suffer from any kind of CNS depression.

Promethazine should not be administered as a daily sedative for depressions where inhibition and aversion are the dominant symptoms.

Caution is advised when treating patients with prostatic hypertrophy, bladder neck obstruction, pyloro-duodenal obstruction, myasthenia gravis and hepatitis.

During long-term treatment, a dry mouth can result in dental and oral mucosal damage. Teeth should be thoroughly cleaned with fluoride toothpaste twice daily.

Reduced lacrimation can result in problems for contact lens wearers

An almost 3-fold increased risk of cerebrovascular events has been observed in randomised, placebo-controlled clinical trials of some atypical neuroleptics in patients with dementia. The underlying mechanistic explanation to this increased risk is unknown. An increased risk for other neuroleptics and among other patient populations cannot be ruled out. Consequently, Promethazine should be used with caution for patients with risk factors for stroke.

Neuroleptic malignant syndrome

As with neuroleptics, neuroleptic malignant syndrome (NMS) characterized by hyperthermia, extrapyramidal disorders, muscle rigidity, altered mental status, autonomic nervous instability and

elevated CPK may occur. As this syndrome is potentially fatal, promethazine must be discontinued immediately and intensive clinical monitoring and symptomatic treatment should be initiated.

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 (see sections 4.5, 4.8, 4.9).

Excipient(s)

Sodium

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Caution is advised when using concomitantly with certain other medicinal products as serious adverse reactions and deaths have been reported (see sections 4.4 and 4.9). The sedative effect of phenothiazines and phenothiazine derivatives may be increased by alcohol, anxiolytics, hypnotics, barbiturates, opiates and other sedative agents.

The anticholinergic effect of phenothiazines and phenothiazine derivatives may be enhanced by other medicinal products with anticholinergic activity.

Promethazine may interfere with immunological urine pregnancy tests to produce false-positive or 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, halofantrine, methadone, pentamidine, and moxifloxacin, class IA and III antiarrhythmics, erythromycin, mefloquine, tricyclic antidepressants, lithium or cisapride. Concomitant medication with medicinal products that can give rise to electrolyte disturbances such as thiazide diuretics (hypokalemia) should be considered as this will increase the risk of malignant arrhythmias (also see Section 4.4.).

Effect of other medicinal products on the pharmacokinetics of promethazine

Based on in vitro data promethazine is a substrate of CYP2D6. The clinical relevance is not known, but the exposure of promethazine may be increased upon co-administration of strong CYP2D6-inhibitors (e.g. paroxetine, quinidine, terbinafine and fluoxetine).

Effect of promethazine on the pharmacokinetics of other medicinal products

In vitro and in vivo studies have shown that promethazine inhibits the CYP2D6-mediated metabolism. This finding may be of clinical relevance for compounds predominantly metabolised by CYP2D6, e.g. certain members of the following drug classes, tricyclic antidepressants (TCAs), beta-blockers, selective serotonin reuptake inhibitors (SSRIs), antiarrhythmics (including class 1A, 1B and 1C) and monoamine oxidase inhibitors (MAOIs) Type B, especially if they also have a narrow therapeutic window.

Haloperidol:

Co-administration of promethazine 150 mg/day and the CYP2D6 substrate haloperidol 60 mg/day for one week resulted in a 2-fold increase in plasma concentrations of haloperidol.

4.6 Fertility, pregnancy and lactation

Pregnancy

A large amount of data from pregnant women (more than 1000 pregnancies) does not indicate a

teratogen risk, nor fetal/neonatal toxicity of promethazine in the first trimester. Promethazine can be used during the first trimester of pregnancy if it is clinically necessary.

The use of promethazine could be considered during the second and third trimesters of pregnancy if clinically necessary.

Treatment with promethazine must stop two weeks before the planned delivery, because there may be a risk of respiratory depression in the newborn child.

Breast-feeding

There is insufficient information on the excretion of promethazine and its metabolites in breast milk. A risk to the newborn child/infant cannot be excluded. When using promethazine during breastfeeding, the advantages should be carefully weighed against the disadvantages.

Fertility

No data on the effect of promethazine on fertility are available.

4.7 Effects on ability to drive and use machines

Reactions may be impaired during treatment with promethazine. This should be taken into consideration when alertness is required, for example when driving.

Because the duration of action may be up to 12 hours, impaired reactions and sedation may still occur the following morning. Patients should be sure that they are not affected before driving or operating machinery.

4.8 Undesirable effects

The most common adverse effect is drowsiness, which occurs in 5-10% of patients. The adverse effects are pharmacologically induced and are thus, to a great extent, dose dependent.

Adverse effects are listed below according to organ system and frequency. Frequencies are defined as:

Very common ($\geq 1/10$)

Common ($\geq 1/100$ to $< 1/10$)

Uncommon ($\geq 1/1,000$ to $< 1/100$)

Rare ($\geq 1/10,000$ to $< 1/1,000$)

Not known (cannot be estimated from the available data)

System Organ Class	Common	Uncommon	Rare	Not known
Blood and lymphatic system disorders				Thrombocytopenia
Psychiatric disorders				Hallucinations, aggression
Nervous system disorders				Extrapyramidal effects, neuroleptic malignant syndrome, psychomotor hyperactivity
Eye disorders		Reduced lacrimation, accommodation disturbances		

Cardiac disorders			Cardiac arrest, ventricular arrhythmias (ventricular fibrillation, ventricular tachycardia)	QT prolongation, torsade de pointes
Gastrointestinal disorders	Dry mouth	Constipation		
Hepatobiliary disorders			Hepatitis with stasis-type jaundice	
Renal and urinary disorders		Urinary retention		
General disorders and administration site conditions	Drowsiness			

Prolonged use can cause dry mouth resulting in a risk of dental and oral mucosal damage.

Treatment with phenothiazines can result in a prolongation of the QT interval and cardiac arrhythmias. Cases of sudden death that may be due to a cardiac event (see Section 4.4) have been reported during treatment with such medicinal products.

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 the national reporting system listed in [Appendix V*](#).

4.9 Overdose

Toxicity

200 mg to a 2-year-old produced lethal intoxication. 50 mg to a 2½ year-old resulted in mild intoxication after a gastric lavage. 100 mg to a 3-year-old resulted in moderate intoxication and 200 mg to a 3-year-old produced severe intoxication. 200 mg to a 6-year-old who had been given a gastric lavage produced moderate intoxication, while 200 mg to a 12-year-old produced severe intoxication. 250 mg to an adult produced moderate intoxication, 500 mg produced moderate to severe intoxication, 2.25 g produced severe intoxication. 50 mg intramuscularly to a 2-month-old child produced severe intoxication.

Overdosage of promethazine carries mortality risk. Overdosage in combination with alcohol, substance use or other medicinal products is associated with additional mortality risk (see 4.4 and 4.5).

Symptoms

Somnolence, unconsciousness and/or excitation (primarily in children). Ataxia, tremor, headache, hallucinations, cramps. Dry mouth, flush, hyperthermia, mydriasis. Urine retention. Tachycardia; possible drop in blood pressure and arrhythmias for massive doses. Nausea and vomiting.

Extrapyramidal symptoms are also conceivable with phenothiazine derivatives. The symptoms are dominated by central anticholinergic symptoms and CNS depression and cramps.

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

Treatment

With regard to gastric lavage (induction of vomiting is only worthwhile at an early stage when Promethazine has an antiemetic effect, thus normally a gastric lavage), charcoal. Diazepam for cramps and acute dystonia. For pronounced central anticholinergic symptoms (excitation, hallucinations) possibly physostigmine 1-2 (up to 3) mg slowly intravenously (2 minutes); children 0.02-0.04 mg/kg for central anticholinergic symptoms. Titrated to an effective dose (atropine available for reversing any overdose symptoms). The effective dose can be repeated after 30-60 minutes. Alternatively, physostigmine can be administered as a continuous infusion of 1-3 mg/hour. If there is any cardiac effect other than sinus tachycardia, the advisability of administering physostigmine should be discussed on a case-by-case basis. In the event of a drop in blood pressure, fluids should be administered intravenously and, where necessary, dobutamine and/or noradrenaline (initially 0.05 µg/kg/min, increase as necessary by 0.05 µg/kg/min every 10 minutes). Ensure adequate diuresis. Other symptomatic therapy as needed.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antihistamines for systemic use; Phenothiazine derivatives

ATC code: R06AD02

Promethazine, a phenothiazine, is a potent, long-acting antihistamine with a predominantly H₁-receptor blocking action and a strong anticholinergic, sedative and anti-emetic effect. Blockade of the histamine H₁ receptor in the central nervous system takes part in the sleeping effect of antihistamines, thus decreasing arousal.

Profound acute effects on sleep have been reported for promethazine in both healthy volunteers and poor sleepers. Compared with placebo, promethazine has been shown to be an effective hypnotic by subjective and objective criteria.

Promethazine also potentiates the effect of hypnotics, analgesics and anaesthesia.

5.2 Pharmacokinetic properties

Absorption

Promethazine hydrochloride is readily absorbed from the gastrointestinal tract. Maximum plasma concentrations are reached after 2-3 hours.

Distribution

The volume of distribution is approximately 13 l/kg body weight and protein binding is 80-90%.

Metabolism

The systemic bioavailability is low after oral administration due to the high first pass metabolism in the liver.

Elimination

Slowly via urine and bile, mainly as metabolites. The half-life is approximately 13 hours.

5.3 Preclinical safety data

No additional preclinical data of relevance to the prescriber.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Microcrystalline cellulose
Calcium hydrogen phosphate dihydrate
Sodium starch glycolate
Stearic acid
Magnesium stearate

Tablet Coating:

Hypromellose (E464)
Macrogol (E1521)
Titanium dioxide (E171)
Talc

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions

6.5 Nature and contents of container

Blister packs (White opaque PVC/PCTFE foil with lidding plain push through aluminium foil, PVC/PCTFE/PVC foil lidding aluminum foil or PVC/PVDC/PVC with lidding aluminum foil) of 2, 4, 8, 12, 16, 30, 50, 100 film-coated tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<Date of first authorisation: {DD month YYYY}>

<Date of latest renewal: {DD month YYYY}>

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

2025-07-04