# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE MEDICINAL PRODUCT

Farghess 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 (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
- Nausea and vertigo (morning sickness, Ménière's disease, nausea after radium treatment and anaesthetics)

### 4.2 Posology and method of administration

Farghess should be used at the lowest effective dose and for the shortest possible duration necessary to relieve symptoms. The recommended dose should not be exceeded (see also section 4.4).

**Short-term treatment of sleep disorders:**
*Adults:* 25-50 mg 1-2 hours before bedtime.
In many cases, a lower dose will give adequate effect.

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.

**Symptomatic short-term treatment of anxiety:**
Adults: 25-50 mg, 1-3 times a day.

**Premedication:**
*Adults:* 25-50 mg one hour before treatment; if necessary, the same dose the evening before treatment.
*Children 6-17 years-of-age:* 25 mg one hour before treatment; if necessary, the same dose the evening before treatment.

**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.

**Allergic conditions:** *Adults:* 25-50 mg at night.

**Nausea and vertigo:**
*Adults:* 25 mg 1-4 times daily

Method of Administration
Oral use.

## 4.3 Contraindications

Farghess 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 five 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 section 4.5 and 4.9).

Do not use in patients who have 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, pyloroduodenal 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.

*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 section 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 section 4.4 and 4.9). The sedative effect of phenothiazines and phenothiazines derivates may be increased by alcohol, anxiolytics, hypnotics, barbiturates, opiates and other sedative agents.
The anticholinergic effect of phenothiazines and phenothiazines derivates 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, halofantrin, methadone, pentamidine, and moxifloxacine. Concomitant medication with medicinal products that can give rise to electrolyte disturbances such as Thiazide diuretics (hypokalaemia) should be considered as this will increase the risk of malign 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*
Considerable data on pregnant women (over 1000 pregnancies) does not indicate a teratogen risk, nor fetal/neonatal toxicity of promethazine in the first trimester of pregnancy. Promethazine can be used in the first trimester of pregnancy if it is clinically necessary.

The use of promethazine can be considered in the second and third trimesters of pregnancy if it is clinically necessary.

The use of promethazine must be discontinued two weeks in advance of the expected date of birth to avoid risk of respiratory depression in the neonate.

*Breast-feeding*
There is insufficient data on excretion of promethazine or metabolites in breast milk. A risk to the newborn baby can not be excluded. If use of promethazine is considered during breast-feeding, the benefits must be weighed against the risks.

*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 (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥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 | | | | 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 and phenothiazine derivatives 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 reaction via the national reporting system listed in Appendix V.

By reporting side effects, you can help provide more information on the safety of this medicine.

### 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 section 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 phenothiazines derivative. 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 distonias. 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, Dobutimine 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 $H_1$-receptor blocking action and a strong anticholinergic, sedative and anti-emetic effect. Blockade of the histamine $H_1$ 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 (E460)
Calcium hydrogen phosphate dihydrate (E341)
Sodium starch glycolate
Stearic acid
Magnesium stearate (E470B)

*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

Farghess is available in blister packs (PVC/PCTFE/PVC foil or PVC/PVDC/PVC foil and lidding aluminium foil) of 20, 30, 56 and 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

<[To be completed nationally]>

## 10. DATE OF REVISION OF THE TEXT

2025-09-04