Professional Information for PHENERGAN 10 and 25

SCHEDULING STATUS:

S2

1. NAME OF THE MEDICINE

PHENERGAN 10 coated tablets

PHENERGAN 25 coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

PHENERGAN 10: Each tablet contains 10 mg promethazine hydrochloride.

PHENERGAN 25: Each tablet contains 25 mg promethazine hydrochloride.

Excipients with known effect:

Contains sugar.

PHENERGAN 10: Each tablet contains 11,7 mg lactose monohydrate and 13,7 mg sucrose.

PHENERGAN 25: Each tablet contains 29,3 mg lactose monohydrate and 29,6 mg sucrose.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Coated tablets.

PHENERGAN 10: Round, blue sugar-coated tablet, approximately 2,7 mm thick and approximately 4,5 mm in diameter.

PHENERGAN 25: Round, blue sugar-coated tablet, approximately 3,6 mm thick and approximately 6,1 mm in diameter.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

PHENERGAN has been shown to be of value in many allergic disorders and anaphylactic reactions including hay fever, vasomotor rhinorrhoea, urticaria, angioneurotic oedema and sensitisation reactions to various medicines and other substances. PHENERGAN may be of symptomatic value in relieving pruritus.

4.2 Posology and method of administration

Posology

The effect of a single dose of PHENERGAN is maintained for an average of 16 – 18 hours. If gastric upset or other side effects occur, it is recommended that PHENERGAN be taken with food or with a well-sweetened drink. The initial PHENERGAN dose should be small and the subsequent doses adjusted to the needs of the patient.

Adults:

The initial daily dose should be one 25 mg tablet given late in the evening. This dose may be increased, if necessary, to 50 mg to 100 mg (two to four 25 mg tablets) on the following evenings. When daytime dosage is indicated, 10 mg three times daily is suggested initially.

As an antihistaminic:

For children 5 – 10 years: 10 mg – 25 mg

The smaller amount stated is generally sufficient if the dose is to be given twice in 24 hours.

PHENERGAN 10 and PHENERGAN 25 is not suitable for children younger than 5 years.

Method of administration

PHENERGAN is given orally.

4.3 Contraindications

- Hypersensitivity to promethazine hydrochloride, other phenothiazines or to any of the other ingredients in the formulation of PHENERGAN (see section 6.1).
- PHENERGAN is contraindicated for use in children less than 2 years of age because of the potential for fatal respiratory depression (see section 4.4).
- Children and adolescents with signs and symptoms suggestive of Reye's syndrome.
- PHENERGAN should be used with care in children, especially those who are acutely ill or dehydrated as these patients have an increased incidence of dystonias.
- Acute asthma attacks.
- PHENERGAN should not be used in patients in a coma or suffering from central nervous system (CNS) depression of any cause.
- Patients taking monoamine oxidase inhibitors up to 14 days previously.

4.4 Special warnings and precautions for use

Hypersensitivity reactions including anaphylaxis, urticaria and angioedema have been reported with PHENERGAN use. In case of allergic reaction, treatment with PHENERGAN must be discontinued and appropriate symptomatic treatment initiated (see section 4.8).

PHENERGAN should be avoided in patients with liver or renal dysfunction, Parkinson's disease, hypothyroidism, cardiac failure, pheochromocytoma, myasthenia gravis, prostate hypertrophy or in patients with a history of narrow angle glaucoma or agranulocytosis.

Caution must be exercised when using H_1-antihistamines such as PHENERGAN due to the risk of sedation. Combined use with other sedative medicines is not recommended (see section 4.5).

Due to the risk of photosensitivity, exposure to the sun or ultraviolet light should be avoided during or shortly after treatment.

PHENERGAN must not be used in children below two years of age due to the potential for fatal respiratory depression (see section 4.3).

The use of promethazine should be avoided in children and adolescents with signs and symptoms suggestive of Reye's syndrome.

Phenothiazine derivatives, as contained in PHENERGAN, may potentiate QT interval prolongation which increases the risk of onset of serious ventricular dysrhythmias of the torsades de pointes type, which is potentially fatal (sudden death). QT prolongation is exacerbated, in particular, in the presence of bradycardia, hypokalaemia and acquired (i.e. medicine induced) QT prolongation. If the clinical situation permits, medical and laboratory evaluations should be performed to rule out possible risk factors before initiating treatment with a phenothiazine derivative and as deemed necessary during treatment (see section 4.8).

Prolonged administration of any phenothiazine may result in tardive dyskinesia, particularly in the elderly and children.

Alcohol and alcohol-containing medicines should be avoided while on this medicine (see section 4.5).

Phenothiazines may be additive with, or may potentiate the action of other CNS depressants, such as opiates or other analgesics, barbiturates or other sedatives, general anaesthetics, or alcohol.

As agranulocytosis has been reported, regular monitoring of the complete blood count is recommended. The occurrence of unexplained infections or fever may be evidence of blood dyscrasia (see section 4.8) and requires immediate haematological investigation.

All patients should be advised that, if they experience fever, sore throat or any other infection, they should inform their medical practitioner immediately and undergo a complete blood count. Treatment should be discontinued if any marked changes (hyperleukocytosis or granulocytopenia) are observed in the blood count.

There have been case reports of medicine abuse with promethazine. The risk of abuse is greater in patients with a history of drug abuse.
As with neuroleptics, neuroleptic malignant syndrome (NMS) characterised 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.

PHENERGAN should be used with caution in patients with severe coronary artery disease.
Caution should be exercised in patients with bladder neck or pyloro-duodenal obstruction.
PHENERGAN should be used with caution in patients with epilepsy. PHENERGAN may precipitate epileptiform seizures in patients with focal lesions of the cerebral cortex.

PHENERGAN may delay the early diagnosis of intestinal obstruction or increased intracranial pressure through the suppression of vomiting.

PHENERGAN may mask the warning signs of ototoxicity caused by ototoxic medicines, such as aminoglycoside antibiotics and salicylates.
PHENERGAN may thicken or dry lung secretions and impair expectoration. It should be used with caution in patients with asthma, bronchitis or bronchiectasis.

PHENERGAN should not be used for longer than 7 days without seeking medical advice.

Contains sugar

PHENERGAN contains lactose monohydrate and sucrose. Patients with rare hereditary problems of fructose intolerance, galactose intolerance, total lactase deficiency, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take PHENERGAN.

4.5 Interaction with other medicines and other forms of interaction

PHENERGAN should be discontinued at least three days before the skin test as it may inhibit the cutaneous histamine response thus producing false-negative results.

Medicines known to cause QT prolongation: Special caution is required when promethazine, as in PHENERGAN, is used concurrently with medicines known to cause QT prolongation (such as antidysrhythmics, antimicrobials, antidepressants or antipsychotics) to avoid exacerbation of the risk of QT prolongation.

PHENERGAN will enhance the action of any anticholinergic medicine, tricyclic antidepressant, sedative or hypnotic.

Cytochrome P450 2D6 metabolism: Some phenothiazines are moderate inhibitors of CYP2D6. There is a possible pharmacokinetic interaction between inhibitors of CYP2D6, such as phenothiazines and CYP2D6 substrates. Co-administration of promethazine with amitriptyline/amitriptylinoxide, a CYP2D6 substrate, may lead to an increase in the plasma levels of amitriptyline/amitriptylinoxide. Monitor patients for dose-dependent adverse reactions associated with amitriptyline/amitriptylinoxide.

PHENERGAN is contraindicated in patients taking monoamine oxidase inhibitors within the previous 14 days, and monoamine oxidase inhibitors should be avoided while using PHENERGAN (see section 4.3).

Seizure threshold-lowering medicines: Concomitant use of seizure-inducing medicines or seizure threshold-lowering medicines should be carefully considered due to the severity of the risk for the patient (see section 4.4).

Gastrointestinal medicines that are not absorbed (magnesium, aluminium and calcium salts, oxides and hydroxides): Reduced gastrointestinal absorption of phenothiazines may occur. Such gastrointestinal medicines should not be taken at the same time as phenothiazines (at least 2 hours apart, if possible).

Medicines with anticholinergic properties: Concomitant use of PHENERGAN with medicines with anticholinergic properties enhances the anticholinergic effect.

PHENERGAN may potentiate the hypotensive effect of some antihypertensive medicines. Some combinations of PHENERGAN and tricyclic antidepressants have resulted in increased plasma concentrations of both medicines.

PHENERGAN may interfere with immunological urine pregnancy tests to produce false-positive or false-negative results.

Alcohol should be avoided during treatment. Combination with alcohol enhances the sedative effects of H1 antihistamines.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety in pregnancy and lactation has not been established.

The use of PHENERGAN is not recommended during pregnancy.

The use of PHENERGAN is not recommended in the 2 weeks prior to delivery in view of the risk of irritability and excitement in the neonate.

Breastfeeding

PHENERGAN crosses the placenta and is distributed in breast milk. There are risks of neonatal irritability and excitement. PHENERGAN is not recommended for use in breastfeeding.

Fertility

There are no relevant fertility data in animals.

4.7 Effects on the ability to drive and use machines

PHENERGAN may cause drowsiness, dizziness and blurred vision and can considerably affect the ability to drive a vehicle and use machines (see section 4.8). Caution is advised before driving a vehicle or operating machinery until the effects of PHENERGAN are known.

4.8 Undesirable effects

The following side effects have been reported and the frequencies may be unknown.
PHENERGAN is generally well tolerated at normal dosage levels, but side effects occur in some patients.

Immune system disorders

Frequency unknown: Allergic reactions, including anaphylactic reaction, urticaria, angioedema.

Blood and lymphatic system disorders

Frequency unknown: Blood dyscrasias including haemolytic anaemia, agranulocytosis, leukopenia, eosinophilia, thrombocytopenia (including thrombocytopenic purpura).

Metabolism and [~~nutritious~~]nutrition disorders

Frequency unknown: Decreased appetite.

Psychiatric disorders

Frequency unknown: Agitation, confusional state, anxiety.

Infants, newborns and prematures are susceptible to the anticholinergic effects of PHENERGAN, while other children may display paradoxical hyperexcitability, disorientation.

Nervous system disorders

Frequent: Sedation or somnolence is the most frequent and generally occurs when the medicine is given during the daytime. Other side effects include dizziness, slight disorientation, headache, twitching and jerking of limbs at night and ataxia.

Less frequent: Drowsiness, restlessness, nightmares.

Frequency unknown: Paradoxical central nervous system stimulation may occur especially in children, with insomnia, nervousness, tachycardia, tremors and convulsions, euphoria.

Neuroleptic malignant syndrome, dystonia, including oculogyric crisis, usually transitory are commoner in children and young adults, and usually occur within the first 4 days of treatment or after dosage increases.

Extrapyramidal effects may occur, including muscle spasm, tic-like movements of the head and face. Anticholinergic effects such as ileus paralytic, risk of urinary retention, dry mouth, constipation, accommodation disorder.

The elderly are particularly susceptible to the anticholinergic effects and

confusion due to PHENERGAN.

Eye disorders

Frequency unknown: Blurred vision.

Ear and labyrinth disorders

Frequency unknown: Tinnitus.

Cardiac disorders

Frequency unknown: Palpitations, arrhythmias, QT prolongation, torsades de pointes.

Vascular disorders

Frequency unknown: Hypotension.

Respiratory, thoracic and mediastinal disorders

Frequency unknown: Respiratory depression, nasal congestion.

Gastrointestinal disorders

Frequency unknown: Nausea, diarrhoea or constipation, vomiting, increased appetite, epigastric pain, epigastric discomfort, dry mouth.

Hepatobiliary disorders

Frequency unknown: Jaundice cholestatic.

Skin and subcutaneous tissue disorders

Less frequent: Cases of allergic reactions, including urticaria, rash, pruritus and anaphylaxis have been reported.

Frequency unknown: Photosensitive skin reactions have been reported; strong sunlight should be avoided during treatment.

Musculoskeletal and connective tissue disorders

Frequency unknown: Muscular weakness, restless legs syndrome.

Renal and urinary disorders

Frequency unknown: Urinary retention.

General disorders and administration site conditions

Frequency unknown: Tiredness.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of PHENERGAN is important. It allows continued monitoring of the benefit/risk balance of PHENERGAN. Health care providers are asked to report any suspected adverse reactions to:

- The Pharmacovigilance Unit at Sanofi: za.drugsafety@sanofi.com (email) or 011 256-3700 (tel), or
- SAHPRA via the “6.04 Adverse Drug Reaction Reporting Form”, found online under SAHPRA’s publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

The chief symptom is unconsciousness, commonly delayed. Convulsions have occurred with unconsciousness in the intervening periods.

Symptoms of severe overdosage are variable. They are characterised in children by various combinations of excitation, ataxia, incoordination, athetosis and hallucinations, while adults may become drowsy and lapse into coma. Convulsions may occur in both adults and children: coma or

excitement may precede their occurrence. Tachycardia may develop. Cardiorespiratory depression is uncommon.

High doses can cause ventricular dysrhythmias including QT prolongation and torsades de pointes (see section 4.8).

In the event of overdose of PHENERGAN, take all appropriate measures immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 5.7.1 Antihistaminics

Pharmacotherapeutic group: Phenothiazine derivatives

ATC code: R06AD02

Mechanism of action

Promethazine hydrochloride is a potent histamine antagonist and has a prolonged action.
It has a local analgesic action and some anti-epinephrine (anti-adrenaline) and atropine-like effects.

5.2 Pharmacokinetic properties

Promethazine is well absorbed after oral administration. Peak plasma concentrations have been observed 2 to 3 hours after administration by this route although there is lower systemic bioavailability after oral administration due to high first pass metabolism in the liver. Values from 76 to 93 % have been reported for plasma protein binding. Elimination half-lives of 5 to 14 hours have been reported. Promethazine crosses the blood-brain barrier and the placenta, and is distributed in breast milk.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Acacia powder

Brilliant Blue FCF (colourant) (E133)

Carnauba wax

Dextrin white (technical)

Kaolin light

Lactose monohydrate

Magnesium stearate

Sucrose

Talcum powder

Vinnapas B60 (Vinac B7).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store at or below 25 °C.

Protect from light.

6.5 Nature and contents of container

PHENERGAN 10 and 25 tablets are packed in securitainers of 100 and 500.

6.6 Special precautions for disposal and other handling

Not applicable.

7. HOLDER OF CERTIFICATE OF REGISTRATION

sanofi-aventis south africa (pty) ltd

Hertford Office Park, Building I, 5th Floor

90 Bekker Road, Vorna Valley

Midrand 2196

South Africa

8. REGISTRATION NUMBERS

PHENERGAN 10: C855 (Act 101/1965)

PHENERGAN 25: C858 (Act 101/1965)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of registration: Old Medicine (Act 101/1965)

10. DATE OF REVISION OF THE TEXT

Date of revision: 06 November 2023