1. NAME OF THE MEDICINAL PRODUCT

Sominex

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Promethazine hydrochloride EP 20 mg/tab

Excipient with known effect
Each tablet contains 276.00 mg lactose monohydrate.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

White, flat bevelled-edge tablet with S' engraved on one side and a score line on the other.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

As a night-time sleep aid, for the correction of temporary disturbances of sleep pattern where there is difficulty in going to sleep or staying asleep, caused for example by specific dislocation of normal routine.

4.2 Posology and method of administration

Posology
For bedtime use only.

Adults
One tablet at bedtime. May be taken up to one hour after going to bed when sleep is difficult to achieve.

Paediatric population
Not to be given to children under the age of 16 years except on medical advice.

Elderly
The normal adult dose may be taken.

Method of administration
For oral administration.

4.3 Contraindications

- Hypersensitivity to promethazine, other phenothiazines or to any of the excipients listed in section 6.1.
- Sominex should not be used in patients in coma or suffering from CNS depression of any cause.
- Sominex should be avoided in patients taking monoamine oxidase inhibitors up to 14 days previously.

4.4 Special warnings and precautions for use

This product should be used with caution in patients with seizure disorders or in patients receiving medication which may affect the seizure threshold because of risk of convulsions.

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

Sominex should be avoided in patients with liver or renal dysfunction, Parkinson's disease, hypothyroidism, cardiac failure, pheochromocytoma, myasthenia gravis, or 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 Sominex due to the risk of sedation. Combined use with other sedative medicinal products is not recommended (see section 4.5).

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

Caution should be used in patients with:

- Asthma, bronchitis or bronchiectasis. Sominex may thicken or dry lung secretions and impair expectoration.
- Severe coronary artery disease.
- Epilepsy.
- Bladder neck or pyloro-duodenal obstruction.

<u>Ototoxicity</u>
Promethazine may mask the warning signs of ototoxicity caused by ototoxic drugs e.g. salicylates. It may also delay the early diagnosis of intestinal obstruction or raised intracranial pressure through the suppression of vomiting.

<u>Neuroleptic malignant syndrome</u>
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 with concomitant use with drugs known to cause NMS such as antipsychotics (see section 4.5). As this syndrome is potentially fatal, promethazine must be discontinued immediately and intensive clinical monitoring and symptomatic treatment should be initiated.

QT prolongation
Phenothiazine derivatives may potentiate QT interval prolongation which increases the risk of onset of serious ventricular arrhythmias of the torsade 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. drug 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).

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.

Photosensitivity reactions
Due to the risk of photosensitivity, exposure to strong sunlight or ultraviolet light should be avoided during or shortly after treatment (see section 4.8).

Paediatric population
Promethazine must not be used in children less than six years of age due to the potential for fatal respiratory depression, psychiatric and CNS events (see section 4.3 and section 4.8).
The use of promethazine should be avoided in children and adolescents with signs and symptoms suggestive of Reye's Syndrome.

Excipient(s) with known effect
Lactose
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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

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 anesthetics, or alcohol.

The occurrence of unexplained infections or fever may be evidence of blood dyscrasia (see section 4.8) and requires immediate hematological investigation.

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

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use with antipsychotics may increase possibility of neuroleptic malignant syndrome (NMS).

Sominex will enhance the action of any anticholinergic agent, tricyclic antidepressant, sedative or hypnotic.

Alcohol should be avoided during treatment. Combination with alcohol enhances the sedative effects of H_1 antihistamines.

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

Sominex should be discontinued at least 72 hours before the start of skin tests as it may inhibit the cutaneous histamine response thus producing false-negative results.

Special caution is required when promethazine is used concurrently with drugs known to cause QT prolongation (such as antiarrhythmics, antimicrobials, antidepressants, antipsychotics) to avoid exacerbation of risk of QT prolongation.

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.

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.

Sominex should be avoided in patients taking monamine oxidase inhibitors within the previous 14 days, and monamine oxidase inhibitors should be avoided while using Sominex.

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

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

Drugs with anticholinergic properties: Concomitant use of Sominex with drugs with anticholinergic properties enhances the anticholinergic effect.

4.6 Fertility, pregnancy and lactation

Pregnancy
The use of Sominex is not recommended during pregnancy and in women of childbearing potential not using contraception, unless the potential benefits outweigh the potential risks. When promethazine has been given in high doses during late pregnancy, promethazine has caused prolonged neurological disturbances in the infant.

Advise patients to inform their healthcare provider of a known or suspected pregnancy. Advise patients to avoid becoming pregnant while receiving this medicine. Advise female patients of reproductive potential to use effective contraception.

There are no available animal studies regarding reproductive toxicity.

Breast-feeding
Sominex is excreted in breast milk (see section 5.2). There are risks of neonatal irritability and excitement. Sominex is not recommended for use in breast-feeding.

Fertility
There are no relevant fertility data in animals.

4.7 Effects on ability to drive and use machines

Because the duration of action may be up to 12 hours, patients should be advised that if they feel drowsy, dizzy and have blurred vision, they should not drive or operate heavy machinery.

4.8 Undesirable effects

The following CIOMS frequency rating is used: Very common (≥ 1/10); common (≥ 1/100 to <1/10); uncommon (≥1/1000 to <1/100); rare (≥ 1/10 00 to <1/1000); very rare (<1/10,000), not known (cannot be estimated from the available data).

Blood and lymphatic system disorders
Frequency not known: Blood dyscrasias including haemolytic anaemia, agranulocytosis, leukopenia, eosinophilia, thrombocytopenia (including thrombocytopenic purpura).

Immune system disorders
Frequency not known: Allergic reactions, including anaphylactic reaction, urticaria, angioedema.

Metabolism and nutrition disorders
Frequency not known: Decreased appetite.

Psychiatric disorders
Frequency not known: Agitation, confusional state, anxiety.
Frequency not known: Hallucinations, aggression.
Frequency not known: Infants, newborns and premature are susceptible to the anticholinergic effects of promethazine, while other children may display paradoxical hyperexcitability, restlessness, nightmares, disorientation.
Frequency not known: Children less than 6 years of age also experienced aggression and hallucination.

Nervous system disorders
Very common: Sedation or somnolence.
Frequency not known: Dizziness, headaches, extrapyramidal effects including restless legs syndrome, muscle spasms and tic-like movements of the head and face.
Frequency not known: 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.
Frequency not known: 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 promethazine.
Frequency not known: Neuroleptic malignant syndrome, psychomotor hyperactivity.
Frequency not known: children less than 6 years of age also experienced psychomotor hyperactivity.

Eye disorders
Frequency not known: Blurred vision.

Cardiac disorders
Frequency not known: Palpitations, arrhythmias, QT prolongation, torsade de pointes.

Vascular disorders
Frequency not known: Hypotension.

Respiratory, thoracic and mediastinal disorders
Frequency not known: Respiratory depression (see Section 4.4), nasal congestion.

Gastrointestinal disorders
Frequency not known: Epigastric irritation/discomfort, dry mouth.

Hepatobiliary disorders
Frequency not known: Jaundice cholestatic.

Skin and subcutaneous tissue disorders
Frequency not known: Rash, photosensitivity reaction.

Renal and urinary disorders
Frequency not known: Urinary retention.

General disorders and administration site conditions
Frequency not known: Tiredness.

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 Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms
Symptoms of severe overdosage are variable. They are characterised in children by various combinations of excitation, ataxia, incoordination, athetosis and hallucinations, intellectual disability and cognition deficit in children less than 6 years of age 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 (supratherapeutic doses) can cause ventricular arrhythmias including QT prolongation and torsade de pointes (see section 4.8).
Prolonged QT interval and cases of severe arrhythmias with fatal outcome have been described in overdose of phenothiazines.

Management
If the patient is seen soon enough after ingestion, it should be possible to induce vomiting with ipecacuanha despite the antiemetic effect of promethazine; alternatively, gastric lavage may be used.

Treatment is otherwise supportive with attention to maintenance of adequate respiratory and circulatory status. Convulsions should be treated with diazepam or another suitable anticonvulsant.

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antihistamines for systemic use; Phenothiazine derivatives, ATC code: R06AD02
Potent, long acting, antihistamine with additional anti-emetic central sedative and anti-cholinergic properties.

5.2 Pharmacokinetic properties

Promethazine is distributed widely in the body. It enters the brain and crosses the placenta. Promethazine is slowly excreted via urine and bile. Phenothiazines pass into the milk at low concentrations.

Promethazine hydrochloride is readily absorbed from the gastrointestinal tract, but undergoes extensive first pass metabolism in the liver. With only 25% of the oral dose reaching the systemic circulation unchanged. After oral therapy therapeutic effects are identifiable at 15-30 minutes and peak plasma concentrations at 2 to 3 hours. Estimates of terminal half-life in blood plasma have been quoted as 4-6 hours. It is extensively plasma protein bound. It is eliminated mainly as metabolites, predominantly by the faecal (via biliary) route, with <1% of the parent compound and CA 10% as the sulfoxide metabolite being excreted in the urine over a 72 hour period.

5.3 Preclinical safety data

No additional preclinical data of relevance to the prescriber.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose, maize starch, croscarmellose sodium, magnesium stearate.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

No special precautions.

6.5 Nature and contents of container

Sominex 20 mg tablets are packed in opaque PVC/PVDC blister strip backed with aluminium foil. Each blister strip contains 8 tablets. The blister strips are packaged in cartons of 8 or 16 tablets.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Dexcel®-Pharma Ltd.,
2nd Floor, Bourn, 1 Manor House Drive, Coventry, CV1 2FX, UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 14017/0312

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 06 September 2002

10 DATE OF REVISION OF THE TEXT

05/03/2026