1. Name of the medicinal product
Avro Night Capsule

2. Qualitative and quantitative composition
Avro Night Capsule contains 25mg Diphenhydramine Hydrochloride per capsule.

3. Pharmaceutical form
Capsules to be taken orally.

4. Clinical particulars
4.1 Therapeutic indications
Temporary relief of symptoms of allergic conditions.
Temporary relief of symptoms of common cold which is causing difficulty getting to sleep

4.2 Posology and method of administration
Oral administration only.

Adults(including the elderly) and children over 12 years of age:
Two capsules (50 mg) twenty minutes before going to bed if needed, or as directed by a physician.

Children under 12 years of age:
Not recommended for use.

Do not exceed the stated dose or frequency of dosing.
Do not use in children under 12 years.
This medication should not be used continuously for more than 2 weeks without consulting a doctor.

4.3 Contraindications
Contra-indicated in patients who are hypersensitive to diphenhydramine or to any ingredients of the capsules listed in section 6.1, and in those with the following conditions: asthma, narrow angle glaucoma, prostatic hypertrophy, stenosing peptic ulcer, pyloroduodenal obstruction or bladder neck obstruction and porphyria.

4.4 Special warnings and precautions for use
Avro Night Capsule should be used with caution in patients with myasthenia gravis, epilepsy or seizure disorders, narrow-angle glaucoma, prostatic hypertrophy, urinary retention, asthma, bronchitis and chronic obstructive pulmonary disease (COPD), moderate to severe hepatic impairment and moderate to severe renal impairment.
Tolerance may develop with continuous use. Seek medical advice if sleeplessness persists, as insomnia may be a symptom of serious underlying medical illness.
This medication should not be used continuously for more than 2 weeks without consulting a doctor.
May increase the effects of alcohol, therefore alcohol should be avoided.
Avoid use of other antihistamine-containing preparations, including topical antihistamines and cough and cold medicines.
Use with caution in the elderly, who are more likely to experience adverse effects. Avoid use in elderly patients with confusion.
Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
Diphenhydramine may exacerbate tinnitus in existing tinnitus sufferers.
Keep out of the sight and reach of children.

4.5 Interaction with other medicinal products and other forms of interaction
Diphenhydramine may potentiate the sedative effects of alcohol and other CNS depressants (e.g. tranquillizers, hypnotics and anxiolytics).
Monoamine oxidase inhibitors (MAOI) prolong and intensify the anticholinergic effects of diphenhydramine. The product should be used with caution with MAOIs or within 2 weeks of stopping an MAOI.
As diphenhydramine has some antimuscarinic activity, the effects of some anticholinergic drugs (e.g. atropine, tricyclic antidepressants) may be potentiated therefore medical advice should be sought before taking diphenhydramine with such medicines.
Diphenhydramine is an inhibitor of the cytochrome p450 isoenzyme CYP2D6. Therefore, there may be a potential for interaction with drugs which are primarily metabolised by CYP2D6, such as metoprolol and venlafaxine.
Diphenhydramine should not be used in patients receiving any of the above drugs unless directed by a doctor.

4.6 Fertility, pregnancy and lactation
Pregnancy
Risk benefit must be considered before administration in pregnancy. Diphenhydramine crosses the placental barrier and has been reported to cause jaundice and extrapyramidal symptoms in infants whose mothers received the drug during pregnancy.
Because animal reproduction studies are not always predictive of human response and since there is inadequate experience with use of diphenhydramine in pregnant women, the potential risk for humans is unknown.
Use of sedating antihistamines during the third trimester may result in reactions in the newborn or premature neonates. This drug is not recommended during pregnancy. Consult a doctor before use.

Lactation
If administered during breast feeding there is an increased risk of adverse effects of antihistamine, such as unusual excitation or irritability in infants.
Diphenhydramine hydrochloride is not recommended for use during lactation in nursing mothers. Consult a doctor before use.

4.7 Effects on ability to drive and use machines
Diphenhydramine has a major influence on the ability to drive and use machines. Diphenhydramine is a hypnotic and will produce drowsiness or sedation soon after the dose has been taken. It may also cause dizziness, blurred vision, cognitive and psychomotor impairment. These can seriously affect the patient's ability to drive and use machines. If affected, do not drive or operate machinery.
The patient should be warned not to drive or operate machinery within 8 hours of ingestion.

4.8 Undesirable effects
Specific estimation of the frequency of adverse events for OTC products is inherently difficult (particularly numerator data). Adverse reactions which have been observed in clinical trials and which are considered to be common (occurring in > 1/100 to < 1/10) or very common (occurring in > 1/10) are listed below by MedDRA System Organ Class. The frequency of other adverse reactions identified during post-marketing use is unknown, but these reactions are likely to be uncommon (occurring in > 1/1,000 to <1/100) or rare (occurring in < 1/1,000).

Body System	**Undesirable effect**	**Frequency**
General disorders and administration site conditions	fatigue	Common
Immune system disorders	Hypersensitivity reactions including rash, urticaria, dyspnoea and	Unknown

	angioedema	
Psychiatric disorders*	confusion, paradoxical excitation (e.g. increased energy, restlessness, nervousness)	Unknown
Nervous system disorders	sedation, drowsiness, disturbance in attention, unsteadiness, dizziness, convulsions, headache, paraesthesia, dyskinesias	Common Unknown
Eye disorders	blurred vision	Unknown
Cardiac disorders	tachycardia, palpitations	Unknown
Respiratory, thoracic and mediastinal disorders	thickening of bronchial secretions	Unknown
Gastrointestinal disorders	dry mouth gastrointestinal disturbance including nausea, vomiting	Common Unknown
Musculoskeletal and connective tissue disorders	muscle twitching	Unknown
Renal and urinary disorders	urinary difficulty, urinary retention	Unknown

* The elderly are more prone to confusion and paradoxical excitation.

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.

4.9 Overdose
Overdose is likely to result in effects similar to those listed under adverse reactions. Additional symptoms may include mydriasis, fever, flushing, agitation, tremor, dystonic reactions, hallucinations and ECG changes. Large overdose may cause rhabdomyolysis, convulsions, delirium, toxic psychosis, arrhythmias, coma and cardiovascular collapse.
Treatment should be supportive and directed towards specific symptoms. Convulsions and marked CNS stimulation should be treated with parenteral diazepam.

5. Pharmacological properties
5.1 Pharmacodynamic properties
Diphenhydramine is an ethanolamine-derivative antihistamine. It is an antihistamine with anticholinergic and marked sedative effects. It acts by inhibiting the effects on H1-receptors by competing with histamine for H_1receptor sites on effector cells, preventing but not reversing responses mediated by histamine alone.
Diphenhydramine is effective in reducing sleep onset (i.e, time to fall asleep) and increasing the depth and quality of sleep.

5.2 Pharmacokinetic properties
Absorption
Diphenhydramine hydrochloride is rapidly absorbed following oral administration. Apparently it undergoes first-pass metabolism in the liver and only about 40-60% of an oral dose reaches systematic circulation as unchanged Diphenhydramine.
Distribution
It is rapidly distributed throughout the whole body. Onset of action is 20 minutes and duration of effect being 4–6 hours. Peak plasma concentrations are attained within 1-4 hours. The sedative effect also appears to be maximal within 1-3 hours after administration of a single dose.

It is positively correlated with the plasma drug concentration.
Biotransformation
Diphenhydramine is approximately 80-85% bound to plasma proteins. Diphenhydramine is rapidly and almost completely metabolised. The drug is metabolised principally to Diphenylmetoxyacetic acid and is also dealkylated.
The metabolites are conjugated with glycine and glutamine and excreted in urine. Only about 1% of a single dose is excreted unchanged in urine.
Elimination
It is eliminated by the kidneys slowly, mainly as inactive as metabolites.
The elimination half-life ranges from 2.4-9.3 hours in healthy adults. The terminal elimination half-life is prolonged in liver cirrhosis.

5.3 Preclinical safety data
None stated.

6. Pharmaceutical particulars
6.1 List of excipients
Lactose Monohydrate
Magnesium Stearate
Sodium Lauryl Sulphate
Methyl Hydroxybenzoate
Propyl Hydroxybenzoate

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
3 years.

6.4 Special precautions for storage
Store below 30^{o}C.

6.5 Nature and contents of container
Aluminium /PVC blister strips enclosed in a cardboard outer containing 10 capsules.

6.6 Special precautions for disposal and other handling
Not applicable.

7. Applicant/Manufacturer
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