NITE CAP

1.Name of the medicinal product

NITE CAP 50 mg capsules, hard

2.Qualitative and quantitative composition

NITE CAP

Each capsule contains 50 mg of Diphenhydramine Hydrochloride

For the full list of excipients, see section 6.1.

3.Pharmaceutical form

Capsule, hard

White capsule no.2 filled with white to yellowish white powder.

4.Clinical Particulars

4.1 Therapeutic indications

- Diphenhydramine shares the actions and uses of other antihistamines. Treatment of allergic conditions e.g. hay fever, vasomotor rhinitis, stings, urticaria, angioneurotic edema, drug sensitivity, contact dermatitis and photosensitivity.

- Diphenhydramine is effective for the prevention and treatment of nausea, vomiting, and/or vertigo associated with motion sickness.

- Diphenhydramine also is used as a nighttime sleep aid for the short-term management of insomnia.

- Diphenhydramine, alone or in conjunction with other antiparkinsonian agents, may be useful as alternative therapy in the management of tremor early in the course of parkinsonian syndrome.

4.2 Posology and method of administration

Posology

Allergic Rhinitis, the Common Cold, and Cough: In adults is 50 mg every 4-6 hours, not to exceed 300 mg in 24 hours.

Motion, Sickness: For the prevention and treatment of nausea, vomiting, and/or vertigo associated with motion sickness, the usual oral dosage of diphenhydramine 50 mg every 4-6 hours, not to exceed 300 mg in 24 hours. For the prevention of motion sickness, a dose should be given 30 minutes before exposure to motion: subsequent doses may be given before meals and at bedtime for the duration of the exposure.

Insomnia: As a nighttime sleep aid, the usual oral dosage of diphenhydramine hydrochloride in adults is 50 mg at bedtime as needed, or as directed by a clinician.

Parkinsonian Syndrome: For the symptomatic treatment of parkinsonian syndrome, an initial oral dosage of 25 mg of diphenhydramine hydrochloride 3 times daily; if necessary, dosage is then gradually increased to 50 mg 4 times daily.

Method of administration

Oral use

4.3 Contraindication

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1. Contraindicated for use in patients with the following conditions: stenosing peptic ulcer, pyloroduodenal obstruction.

4.4 Special warning and precautions for use

Diphenhydramine should be used with caution in patients with myasthenia gravis, epilepsy or seizure disorders, prostatic hypertrophy, urinary retention, narrow-angle glaucoma, 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 a serious underlying medical illness.

This medicinal product should not be used continuously for longer 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 side-effects.

Avoid use in elderly patients with confusion.

4.5 Interactions with other medicinal products and other forms of interactions

Diphenhydramine may potentiate the sedative effects of alcohol and other CNS depressants (e.g. tranquillizers, hypnotics and anxiolytics).

Monoamine oxidase inhibitors (MAOIs) 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 metabolized 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

Diphenhydramine crosses the placenta. 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

Diphenhydramine has been detected in breast milk, but the effect of this on breastfed infants is unknown. Diphenhydramine is not recommended for use during lactation. Consult a doctor before use.

Fertility

There are no available data on the effect of diphenhydramine on fertility.

4.7 Effects on 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.

4.8 Undesirable effects

Specific estimation of the frequency of adverse events for 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 <1/1000).

System Organ Class	Very Common (≥1/10)	Common ≥1/100, <1/10	Uncommon ≥1/1,000, <1/100	Rare ≥1/10,000, <1/1000	Very Rare <1/10,000	Not known (cannot be estimated from available data)
Blood and lymphatic system disorders						Agranulocytosis
Cardiac Disorders						tachycardia, palpitations, arrhythmias
Eye Disorders						blurred vision
General disorders and administration site conditions:		fatigue				
Gastrointestinal Disorders		dry mouth				gastrointestinal disturbance including nausea, vomiting
Immune System Disorders						hypersensitivity reactions including rash, urticaria, dyspnea and angioedema
Musculoskeletal and connective tissue Disorders						muscle twitching
Nervous System Disorders		sedation, drowsiness, disturbance in attention, unsteadiness, dizziness				convulsions, headache, paresthesia, dyskinesias
Psychiatric Disorders						confusion, paradoxical excitation (e.g. increased energy, restlessness, nervousness), depression, sleep disturbances * The elderly are more prone to confusion and paradoxical excitation.
Renal and urinary disorders						urinary difficulty, urinary retention
Respiratory, thoracic and mediastinal disorders						thickening of bronchial secretions

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

Pharmacotherapeutic group: Antihistamines for systemic use – diphenhydramine, ATC Code: R06AA02.

Diphenhydramine is an ethanolamine-derivative anti-histamine with anti-cholinergic (anti-spasmodic), anti-tussive and sedative activity. It acts by inhibiting the effects on H1-receptors.

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

Diphenhydramine is a histamine H1 receptor antagonist.

The main site of metabolism is the liver.

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

Diphenhydramine is rapidly distributed throughout the whole body. 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 metabolized. It is metabolized 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

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

Not applicable

6.Pharmaceutical particulars

6.1 List of excipients

NITE CAP

Lactose monohydrate, Lactose suppertab, Corn starch, Colloidal silicon dioxide.

6.2 Incompatibilities

Incompatible with barbiturates and iodo compounds in solution.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store below 30°C

6.5 Nature and contents of container

NITE CAP

Capsules packed in PVC-aluminium blister pack of 10 and 14 capsules packed in paper box of 1, 3, 5, 10, 50 blisters

6.6 Special precautions for disposal and other handling

None.

7. **Manufacturer**

Millimed BFS Co., Ltd.

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8. Marketing authorization number(s)

1A 15222/65

9. Date of first authorization/renewal of the authorization

18 July 2022

10.Date of revision of the text

18 July 2022