

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Nytol One-A-Night 50 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50 mg Diphenhydramine Hydrochloride (equivalent to 43.8 mg Diphenhydramine base)

Excipients with known effect: 168.75 mg lactose.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

A white to off white, 15 mm in length, oblong capsule-shaped tablet, embossed with “N50” logo on both sides.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Nytol One-A-Night 50 mg Tablets are indicated as a symptomatic aid to the relief of temporary sleep disturbance in adults.

4.2 Posology and method of administration

Posology

Adults

One tablet to be taken 20 minutes before going to bed, or as directed by a physician. Do not exceed the maximum dose of one tablet in 24 hours.

Elderly

The product should only be given to the elderly if the benefits for the patient outweigh the potential risks (see section 4.4).

Renal and Hepatic Impairment

In patients with moderate to severe renal or hepatic impairment, a lower dose might be required (see section 4.4).

Paediatric population

Nytol One-A-Night 50mg Tablets should not be used in children under 18 years.

Method of administration Oral administration only.

Do not exceed the stated dose or frequency of dosing. The product should not be taken for more than 7 days without consulting a doctor.

4.3 Contraindications

Nytol One-A-Night 50 mg Tablets are contraindicated in patients who are hypersensitive to the active substance (diphenhydramine hydrochloride) or to any of the excipients listed in section 6.1.

Nytol One-A-Night 50mg Tablets are also contraindicated in patients with the following conditions:

- Stenosing peptic ulcer
- Pyloroduodenal obstruction
- Pheochromocytoma
- Known acquired or congenital QT interval prolongation
- Known risk factors for QT interval prolongation including a known cardiovascular disease, significant electrolytes imbalance (hypokalaemia, hypomagnesaemia), family history of sudden cardiac death, significant bradycardia, concomitant use with drugs known to prolong the QT interval and/or induce Torsade de Pointes (see sections 4.4 and 4.5).

4.4 Special warnings and precautions for use

Nytol One-A-Night 50 mg Tablets 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).

Diphenhydramine has been associated with prolongation of the QT interval on the electrocardiogram. During post-marketing surveillance there have been cases of QT interval prolongation and torsade de pointes associated with overdose (see Section 4.9).

Treatment should be stopped if signs or symptoms occur that may be associated with cardiac arrhythmia, and patients should seek immediate medical attention. Patients should be advised to promptly report any cardiac symptoms.

Diphenhydramine should be used for the shortest possible duration. Tolerance and / or dependence may develop with continuous use. Do not take for more than 7 consecutive nights without consulting a doctor. Seek medical advice if sleeplessness persists, as insomnia may be a symptom of serious underlying medical illness.

In patients with moderate to severe hepatic impairment and moderate to severe renal impairment, a lower dose might be required.

Should not be used in patients currently receiving monoamine oxidase inhibitors (MAOI) or those patients who have received treatment with MAOIs within the last two weeks.

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 whilst taking Nytol One-A-Night 50 mg Tablets.

Use in the elderly is not recommended because of the greater risk of adverse reactions (e.g. anticholinergic effects) (see section 4.8). Avoid use in elderly patients with confusion.

Cases of abuse and dependence were reported with diphenhydramine in adolescents or young adults for recreational use and/or in patients with psychiatric dis-orders and/or history of abuse disorders,

The onset of signs or symptoms raising abuse should be monitored.

Nytol One-A-Night 50 mg Tablets contain lactose: Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Antihistamines may suppress the cutaneous histamine response to allergen extracts and should be stopped several days before skin testing.

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, sedatives, hypnotics and tricyclic antidepressants).

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. Concomitant administration of Diphenhydramine with these drugs should be avoided. Diphenhydramine itself is a high affinity substrate of CYP2D6. Therefore, concomitant administration with CYP2D6 inhibitors should be avoided. The administration of diphenhydramine should occur with caution in (very) slow metabolisers.

The concomitant administration of medicines that prolong the QT interval of the ECG (such as Class Ia and Class III anti-arrhythmics) should be avoided.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is not adequate data from the use of diphenhydramine in pregnant women. Animal studies are insufficient with respect to effects on 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.

Use of diphenhydramine during the first trimester of pregnancy has been associated with an increased risk of fetal abnormalities.

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.

Patients should consult a doctor before use.

Breast-feeding

Diphenhydramine has been detected in breast milk, but the effect of this on breastfed infants is unknown. If administered during breastfeeding there is an increased risk of adverse effects of antihistamines, such as unusual excitation or irritability in infants. Nytol One-A-Night 50 mg Tablets are not recommended whilst breastfeeding without medical advice.

Fertility

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

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. If affected, do not drive or operate machinery.

4.8 Undesirable effects

Specific estimation of the frequency of adverse events for consumer 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 $\geq 1/100$ to $< 1/10$) or very common (occurring in $\geq 1/10$) 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 $\geq 1/1,000$ to $< 1/100$) or rare (occurring in $\geq 1/10,000$ to $< 1/1,000$).

Blood and lymphatic system disorders:

Rare: Thrombocytopenia

Immune system disorders:

Unknown: Hypersensitivity reactions including rash, urticaria, dyspnoea and angioedema

Psychiatric disorders*:

Unknown: confusion, paradoxical excitation (e.g. increased energy, restlessness, nervousness)

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

Nervous system disorders:

Common: sedation, drowsiness, disturbance in attention, unsteadiness, dizziness,

Unknown: convulsions, headache, paraesthesia, dyskinesias

Eye disorders

Unknown: blurred vision

Cardiac disorders

Unknown: tachycardia, palpitations

Respiratory, thoracic and mediastinal disorders:

Unknown: thickening of bronchial secretions

Gastrointestinal disorders:

Common: dry mouth

Unknown: gastrointestinal disturbance including nausea, vomiting

Musculoskeletal and connective tissue disorders:

Unknown: muscle twitching

Renal and urinary disorders:

Unknown: urinary difficulty, urinary retention

General disorders and administration site conditions:

Common: fatigue

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 HPRA Pharmacovigilance Earlsfort Terrace, IRL - Dublin 2; Tel: +353 16764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Symptoms and signs

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, such as QT prolongation and torsades de pointes. Large overdose may cause rhabdomyolysis, convulsions, delirium, toxic psychosis, arrhythmias, coma and cardiovascular collapse.

Management

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, aminoalkyl ethers, ATC code: R06A A02

Diphenhydramine is an ethanolamine-derivative antihistamine. It has anticholinergic and marked sedative effects. 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

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 body including CNS. 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.

Diphenhydramine is approx. 80-85% bound to plasma proteins.

Biotransformation

Diphenhydramine is rapidly and extensively metabolised, mainly in the liver. The drug is metabolised principally to Diphenylmethoxyacetic acid and is also dealkylated. The metabolites are conjugated with glycine and glutamine and excreted in urine. Multiple cytochrome P450 enzymes contribute to the metabolism of diphenhydramine, with the highest activity shown by CYP2D6. Diphenhydramine has been shown to competitively inhibit CYP2D6 activity.

Elimination

Only about 1% of a single dose is excreted unchanged in urine. 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

Diphenhydramine hydrochloride has a well-established safety profile. There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SmPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Anhydrous lactose
Stearic acid
Microcrystalline cellulose
Colloidal anhydrous silica
Maize starch

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store below 25°C

Store in the original packaging in order to protect from light and moisture.

6.5 Nature and contents of container

Nytol One-A-Night 50 mg Tablets are packaged into rigid UPVC/PVdC blister packs with a heat sealable aluminium foil. Strips of 4, 8, 10, 16 or 20 tablets. Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal

7 MARKETING AUTHORISATION HOLDER

Chefaro Ireland DAC
Treasury Building
Lower Grand Canal Street
Dublin 2

8 MARKETING AUTHORISATION NUMBER

PA1186/016/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26th May 2017

10 DATE OF REVISION OF THE TEXT