

PRODUCT INFORMATION

BETAHISTINE MYLAN TABLETS

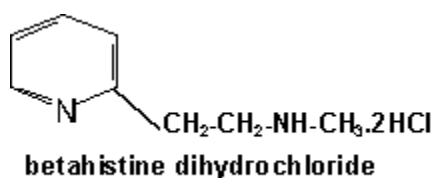
NAME OF THE DRUG

Non-proprietary Name

Betahistine dihydrochloride

Chemical Structure

Betahistine dihydrochloride is chemically identified as 2-[2-(methylamino)ethyl]pyridine dihydrochloride. Chemically, betahistine has a close resemblance to histamine. It has the following chemical structure:



MW= 209.1

CAS Number

5579-84-0

DESCRIPTION

Betahistine dihydrochloride is a white to almost white crystalline powder, which is very hygroscopic. The product is very soluble in water, freely soluble in methanol and 96% ethanol, and slightly soluble in isopropanol. The pKa values are 3.5 and 9.7.

BETAHISTINE MYLAN (betahistine dihydrochloride) is available as 16 mg uncoated tablets. The inactive ingredients in BETAHISTINE MYLAN 16 mg tablets are: colloidal anhydrous silica, microcrystalline cellulose, mannitol, citric acid monohydrate and purified talc.

PHARMACOLOGY

Pharmacodynamics

The mechanism of action of betahistine is not known. Pharmacological testing in animals has shown that the blood circulation in the striae vascularis of the inner ear improves, probably by means of a relaxation of the precapillary sphincters of the microcirculation of the inner ear.

In further animal pharmacological studies, betahistine was found to have weak H₁ receptor agonistic and considerable H₃ antagonistic properties in the CNS and autonomic nervous system. Betahistine was also found to have a dose dependent inhibiting effect on spike generation of neurons in lateral and medial vestibular nuclei in cats. The importance of this observation in the action against Ménière's syndrome or vestibular vertigo, however, remains unclear.

Pharmacokinetics

In man, orally administered doses of betahistine dihydrochloride are rapidly and completely absorbed from the gastrointestinal tract. The drug is rapidly metabolised to one major metabolite - 2-pyridylacetic acid - and excreted in the urine. Studies with radio-labelled betahistine have demonstrated a plasma half life of 3.4 hours and a urinary half life of 3.5

hours for the radio-label. Urinary excretion of the label was about 90% complete within 24 hours of administration.

INDICATIONS

Meniere's Syndrome as defined by the following core symptoms:

- vertigo (with nausea/vomiting)
- hearing loss (hardness of hearing)
- tinnitus

CONTRAINDICATIONS

BETAHISTINE MYLAN (betahistine dihydrochloride) Tablets are contraindicated as follows:

- during pregnancy and lactation.
- in children less than 18 years.
- in patients suffering from phaeochromocytoma
- in patients with active peptic ulcer or a history of this condition
- in patients with hypersensitivity to any component to the product (see 'Description').

PRECAUTIONS

Patients with bronchial asthma need to be carefully monitored during therapy.

Caution should be taken in the treatment of patients receiving antihistamines (see 'Interactions with Other Drugs').

Effects on Fertility

Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of fetal damage.

Use in Pregnancy

Category B2

Betahistine dihydrochloride should not be used during pregnancy (see 'Contraindications') since there are insufficient data on the use of this drug during pregnancy to evaluate possible harmful effects. Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of fetal damage.

Use in Lactation

Betahistine dihydrochloride should not be used during lactation (see 'Contraindications').

Paediatric Use

Due to lack of clinical experience, betahistine dihydrochloride should not be used in children less than 18 years (see 'Contraindications').

Carcinogenicity and Genotoxicity

No animal data are available on the carcinogenic or mutagenic potential of betahistine.

INTERACTIONS WITH OTHER MEDICINES

In vitro data indicate an inhibition of betahistine metabolism by drugs that inhibit monoamine-oxidase (MAO) including MAO subtype B (e.g. selegiline). Caution is recommended when using betahistine and MAO inhibitors (including MAO-B selective) concomitantly.

An antagonism between BETAHISTINE MYLAN and antihistamines could be expected on a theoretical basis. However, no such interactions have been reported.

ADVERSE EFFECTS

Most of the reported adverse reactions pertain to the skin, gastrointestinal tract, body as a whole, nervous system, respiratory system and cardiovascular system.

Events are listed within body systems and categorised by frequency according to the following definitions: *Common* (frequency ≥ 1 and < 10 %), *Uncommon* (frequency ≥ 0.1 % and < 1 %), *Rare* (frequency ≥ 0.01 % and < 0.1 %), *Very rare* (frequency < 0.01 %)

Skin and subcutaneous tissue disorders:	<i>Rare</i> : various types of rash, pruritis and urticaria/angioneurotic oedema. These reactions are probably related to the histamine like structure of betahistine. There was a single case of Stevens Johnson syndrome.
Body as a whole:	<i>Common</i> : headache <i>Rare</i> : tiredness and malaise.
Gastrointestinal system:	<i>Common</i> : nausea and dyspepsia <i>Rare</i> : vomiting, diarrhoea, abdominal distension, bloating and epigastric pain have been reported. These symptoms were usually mild. Gastrointestinal disturbances may be relieved by reducing the dose or by taking betahistine with meals.
Nervous system:	<i>Rare</i> : dizziness <i>Very rare</i> : convulsions, somnolence, confusion and hallucinations. Some of these symptoms may also be observed as part of the disease condition and are usually resolved without changes to the treatment schedule. Patients with neurological events usually presented with confounding factors.
Cardiovascular system:	<i>Very rare</i> : vasodilation, postural hypotension and tachycardia.
Respiratory system:	<i>Very rare</i> : dyspnoea, asthma and bronchospasms (see 'Precautions')
Immune system disorders	Hypersensitivity reactions, e.g. anaphylaxis have been reported

DOSAGE AND ADMINISTRATION

The recommended starting dose in adults is 8 to 16 mg three times a day. The maximum recommended daily dose is 48 mg.

The tablets may be taken with or without food. However, if gastrointestinal upset occurs, it is recommended that the tablets be taken with meals.

The dosage should be individually adapted according to the response. Improvement in symptoms may be observed in the first few days to weeks of treatment.

OVERDOSAGE

There have been a few cases of overdosage reported. Although in most cases no overdose symptoms were reported, some patients have experienced mild to moderate symptoms of overdosage including nausea, dry mouth, epigastric pain and sleepiness at doses above 200 mg. A case of convulsion was reported at a dose of 728 mg. In all cases recovery was complete. Treatment should include standard supportive measures.

Contact the Poisons Information Centre on 131126 (Australia) for advice on management of overdosage.

PRESENTATION AND STORAGE CONDITIONS

BETAHISTINE MYLAN (betahistine dihydrochloride) 16 mg tablets: round, biconvex, scored, white to almost white uncoated tablet, one side inscribed with '267' on either side of the score, in PVC/PVDC/aluminium blister packs containing 25 tablets.

Betahistine Mylan 16 mg Tablets: AUST R 286806

Store below 30°C, protect from light.

NAME AND ADDRESS OF THE SPONSOR

Mylan Health Pty Ltd
Level 1, 30-34 Hickson Road
Millers Point, NSW 2000
Australia
Phone: 1800 314 527

POISON SCHEDULE OF THE MEDICINE

Schedule 4

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (THE ARTG)

29th August 2017