PRODUCT INFORMATION

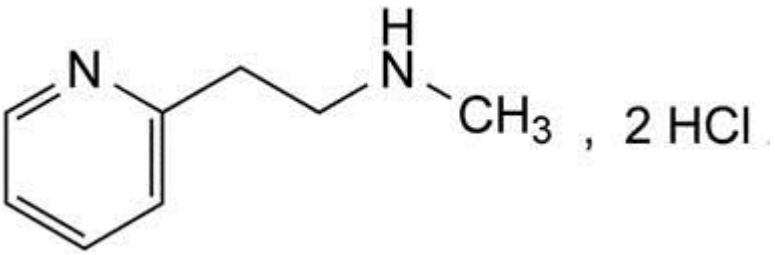
Betahistine Sandoz

NAME OF THE MEDICINE

Betahistine dihydrochloride is chemically identified as 2-[2-ethylamino)ethyl]pyridine dihydrochloride.

Molecular formula: $C_8H_{14}Cl_2N_2$ MW: 209.1

The chemical structure of betahistine dihydrochloride is:



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.

Chemically, betahistine has a close resemblance to histamine.

BETAHISTINE SANDOZ tablets contain Betahistine dihydrochloride 16 mg and the following excipients: Lactose, maize starch, microcrystalline cellulose, anhydrous citric acid, povidone, crospovidone and hydrogenated vegetable oil.

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 Meniere's syndrome or vestibular vertigo, however, remains unclear.

Pharmacokinetics

In humans, 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 radiolabelled betahistine have demonstrated a plasma half-life of 3.4 hours and a urinary half-life of 3.5 hours for the radiolabel. 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

- 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).

Carcinogenesis, mutagenesis, impairment of fertility

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

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

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 foetal damage.

Use in lactation

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

Use in children

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

INTERACTIONS WITH OTHER MEDICINES

An antagonism between betahistine dihydrochloride 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 greater than or equal to 1 and < 10%);

Uncommon (frequency greater than or equal to 0.1% and < 1%);

Rare (frequency greater than or equal to 0.01% and < 0.1%);

Very rare (frequency < 0.01%).

Skin	*Rare*: various types of rash, pruritus and urticaria/ angioedema. 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	*Common:* headache *Rare*: tiredness and malaise.
Gastrointestinal system	*Rare*: nausea, dyspepsia, vomiting, diarrhoea 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	*Rare*: dizziness. *Very rare*: 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	*Very rare*: vasodilation, postural hypotension and tachychardia.
Respiratory system	*Very rare*: dyspnoea, asthma and bronchospasms (see Precautions).

Immune system disorder. Hypersensitivity reactions, e.g. anaphylaxis have been reported.

DOSAGE AND ADMINISTRATION

The recommended starting dose in adults is one-half to one tablet (8 to 16 mg) taken three times a day. The maximum recommended daily dosage 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

Symptoms

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

Treatment should include standard supportive measures.

PRESENTATION AND STORAGE CONDITIONS

BETAHISTINE SANDOZ tablets contain betahistine dihydrochloride 16 mg as white flat tablets with bevelled edges and a breakline on one side.

BETAHISTINE SANDOZ tablets are presented in PVC/PE/PVDC/Al blister packs of 25 tablets.

Storage: Tablets should be stored below 25°C.

NAME AND ADDRESS OF THE SPONSOR

Southern Cross Pharma Pty Ltd

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Hawthorn VIC 3122

POISON SCHEDULE OF THE MEDICINE

S4 – Prescription Only Medicine

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

16 November, 2015

DATE OF MOST RECENT AMENDMENT

27 April 2017