AUSTRALIAN PRODUCT INFORMATION – APO-BETAHISTINE (BETAHISTINE DIHYDROCHLORIDE)

1 NAME OF THE MEDICINE
Betahistine dihydrochloride.

2 AND 3 QUALITATIVE AND QUANTITATIVE COMPOSITION AND PHARMACEUTICAL FORM
Each tablet contains 16mg of betahistine dihydrochloride as the active ingredient.

List of excipients with known effect: contains sucrose as lactose monohydrate. Each tablet contains the following inactive ingredients: povidone, microcrystalline cellulose, lactose monohydrate, colloidal anhydrous silica, crospovidone and stearic acid.

16 mg Tablets:
White or almost white, round, flat bevelled edged tablets embossed B16 on one side and scored on the other side.

4 CLINICAL PARTICULARS
4.1 THERAPEUTIC INDICATIONS
Meniere’s Syndrome as defined by the following core symptoms:
- vertigo (with nausea/vomiting)
- hearing loss (hardness of hearing)
- tinnitus

4.2 DOSE AND METHOD OF 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.

4.3 CONTRAINDICATIONS
Betahistine is 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 Section 2 and 3 Qualitative and quantitative composition and pharmaceutical form).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE
Patients with bronchial asthma need to be carefully monitored during therapy.
Caution should be taken in the treatment of patients receiving antihistamines (See Section 4.5 Interactions with other medicines and other forms of interactions).

Use in hepatic impairment
No data available.

Use in renal impairment
No data available.

Use in the elderly
No data available

Paediatric Use
Due to lack of clinical experience, betahistine dihydrochloride should not be used in children less than 18 years (See Section 4.3 Contraindications).

Effects on laboratory tests
No data available

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

In vitro data indicate an inhibition of betahistine metabolism by drugs that inhibit monoamineoxidase (MAO) including MAO subtype B (e.g. selegiline). Caution is recommended when using betahistine and MAO inhibitors (including MAO-B selective) concominantly. An antagonism between betahistine and antihistamines could be expected on a theoretical basis. However, no such interactions have been reported.

4.6 FERTILITY, PREGNANCY AND LACTATION

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 Section 4.3 Contraindications) since there is 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 Section 4.3 Contraindications).
4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE 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 disorder
Rare: 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
Common: headache
Rare: tiredness and malaise.

Gastrointestinal system
Common: nausea and dyspepsia
Rare: 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
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 tachycardia.

Respiratory system
Very rare: dyspnoea, asthma and bronchospasms (See Section 4.4 Special warnings and precautions for use)

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

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare

4.9 OVERDOSE

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.

For information on the management of overdose, contact the Poison Information Centre on 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

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.

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

In man, orally administered doses of betahistine dihydrochloride are rapidly and completely absorbed from the gastrointestinal tract.

Distribution

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.

Metabolism

The drug is rapidly metabolised to one major metabolite - 2-pyridylacetic acid - and excreted in the urine.

Excretion

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

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No animal data is available on the mutagenic potential of betahistine.
Carcinogenicity
No animal data is available on the carcinogenic potential of betahistine.

6 PHARMACEUTICAL PARTICULARS
6.1 LIST OF EXCIPIENTS
Refer to section 2 and 3 – Qualitative and quantitative composition and pharmaceutical form.

6.2 INCOMPATIBILITIES
Incompatibilities were either not assessed or not identified as part of the registration of this medicine, see section 4.5-Interactions with other medicines and other forms of interactions.

6.3 SHELF LIFE
In Australia, the information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE
Store below 25°C. Store in original container.

6.5 NATURE AND CONTENTS OF CONTAINER
16 mg Tablets
Blisters (Clear PVC/PVDC/Aluminium silver foil) of 25 tablets
AUST R 217105

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL
In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES
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.

Chemical structure

![Chemical structure of betahistine dihydrochloride]
Chemical Name: 2-[2-methylamino)ethyl]pyridine dihydrochloride
Chemical Formula: C₈H₁₂N₂·2HCl
Molecular Weight: 209.1

CAS number
5579-84-0

7 MEDICINE SCHEDULE (POISONS STANDARD)
S4 – Prescription Only Medicine

8 SPONSOR
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9 DATE OF FIRST APPROVAL
20 October 2014

10 DATE OF REVISION
21 September 2018

Summary table of changes

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