Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Betahistine dihydrochloride 8mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains
Betahistine dihydrochloride 8 mg

Excipient(s) with known effect:
Each tablet contains 50 mg lactose monohydrate

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

White, round, flat, 6.5.mm tablets with bevelled edges with the inscription 'BE' on one side and a breakline on the other side. The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Betahistine is indicated for treatment of Ménière's syndrome, symptoms of which may include vertigo, tinnitus, hearing loss and nausea.

4.2 Posology and method of administration

Dosage

Adults
Initial oral treatment is 8 to 16 mg three times daily, taken preferably with meals.
Maintenance doses are generally in the range 24 - 48 mg daily. Daily dose should not exceed 48 mg.
Dosage can be adjusted to suit individual patient needs. Sometimes improvement could be observed only after a couple of weeks of treatment.

Hepatic impairment:
There are no specific clinical trials available in this patient group, but according to post-marketing experience no dose adjustment appears to be necessary.

Renal impairment
There are no specific clinical trials available in this patient group, but according to post-marketing experience no dose adjustment appears to be necessary.

Elderly:
Although there are limited data from clinical studies in this patient group, extensive post marketing experience suggests that no dose adjustment is necessary in this patient population.

Paediatric population
Betahistine tablets are not recommended in children and adolescents below age 18. The safety and efficacy of betahistine tablets in children and adolescents below 18 years have not been established.

4.3 Contraindications

- hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.
- phaeochromocytoma. As betahistine is a synthetic analogue of histamine it may induce the release of catecholamines from the tumor resulting in severe hypertension.

4.4 Special warnings and precautions for use

Caution is advised in the treatment of patients with peptic ulcer or a history of peptic ulceration, because of the occasional dyspepsia encountered in patients on betahistine.

Clinical intolerance to Betahistine may occur in bronchial asthma patients. These patients should therefore be monitored carefully during the treatment with betahistine.

Caution is advised in patients with severe hypotension.

Excipient warning:
This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.3 Contraindications

- hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.

- phaeochromocytoma. As betahistine is a synthetic analogue of histamine it may induce the release of catecholamines from the tumor resulting in severe hypertension.

4.4 Special warnings and precautions for use

Caution is advised in the treatment of patients with peptic ulcer or a history of peptic ulceration, because of the occasional dyspepsia encountered in patients on betahistine.

Clinical intolerance to Betahistine may occur in bronchial asthma patients. These patients should therefore be monitored carefully during the treatment with betahistine.

Caution is advised in patients with severe hypotension.

Excipient warning:
This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

No *in-vivo* interaction studies have been performed. Based on *in-vitro* data, no *in-vivo* inhibition on Cytochrome P450 enzymes is expected.

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

As betahistine is a histamine analogue, interaction of betahistine with antihistamines may in theory affect the efficacy of one of these drugs.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are insufficient data on the use of betahistine in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity at clinically relevant therapeutic exposure. As a precautionary measure, it is preferable to avoid the use of Betahistine during pregnancy.

Lactation
It is not known whether betahistine is excreted in human breast milk. Betahistine is excreted in rat milk. The effects seen post-partum in animal studies were limited to very high doses. The importance of taking the medicine by the mother must be weighed against the benefits of breastfeeding and the potential risk for the child.

Fertility
Animal studies show no influence on fertility in rats.

4.7 Effects on ability to drive and use machines

Vertigo, tinnitus and hearing loss associated with Ménière's syndrome can negatively affect the ability to drive and use machines.

In clinical studies specifically designed to investigate the ability to drive and use machines betahistine had no or negligible effects

4.8 Undesirable effects

"The following undesirable effects have been experienced with the below indicated frequencies in betahistine-treated patients in placebo-controlled clinical trials with frequency listed below: very common (≥ 1/10); common (≥ 1/100 to <1/10); uncommon (≥ 1/1,000 to <1/100); rare (≥ 1/10,000 to <1/1,000) and very rare (<1/10,000).

Nervous system disorders:
Common: headache.

Gastrointestinal disorders:
Common: dyspepsia, nausea.

In addition to these adverse reactions reported during clinical trials, the following unexpected adverse reactions have been reported spontaneously in the scientific literature during post-marketing use. A frequency cannot be estimated from the available data and therefore these side effects are classified as "Not known".

Immune system disorders
Not known: hypersensitivity reactions, e.g. anaphylaxis.

Gastrointestinal disorders
Not known: mild gastric complaints (e.g. vomiting, gastrointestinal pain, abdominal distension and bloating). These can normally be dealt with by taking the dose during meals or by lowering the dose.

Skin and subcutaneous tissue disorders
Not known: cutaneous and subcutaneous hypersensitivity reactions, in particular angioneurotic oedema, urticarial, rash and pruritus

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,
Website: www.hpra.ie.

4.9 Overdose

A few overdose cases have been reported. Some patients experienced mild to moderate symptoms with doses up to 640 mg (e.g. nausea, somnolence, abdominal pain).

More serious complications (convulsion, pulmonary or cardiac complications) were observed in cases of intentional overdose of betahistine especially in combination with other overdosed drugs. Treatment of overdose should include standard supportive measures.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antivertigo preparation,
ATC code: N07C A01

The mechanism of action of betahistine is only partly understood. There are several plausible hypotheses that are supported by animal studies and human data.

- Betahistine affects the histaminergic system:In biochemical studies, betahistine was found to have weak H1 receptor agonistic and strong H3 antagonistic properties in the central nervous system and autonomic nervous system. The H2 receptor activity appeared to be negligible (e.g. stimulation of gastric acid secretion).Betahistine increases the turnover and release of histamine most likely by blocking presynaptic H3 receptors and inducing the downregulation of H3 receptors.

- Betahistine may increase blood flow to the inner ear:It has been shown in pharmacological animal experiments that betahistine improves the flow in the stria vascularis of the inner ear, probably by relaxing the precapillary sphincters of the microcirculation in the inner ear.
- Betahistine facilitates vestibular compensation:Betahistine accelerates vestibular healing after unilateral neurectomy in animals by stimulating and facilitating vestibular compensation; this effect, characterised by increases in histamine turnover and release, is mediated via H3 receptor antagonism. The recovery period after vestibular neurectomy was also reduced by betahistine in humans.

- Betahistine alters the release of neuron action potentials in the vestibular nuclei:Betahistine also has a dose-dependent inhibitory effect on the release of action potentials of neurons in the lateral and medial vestibular nuclei.

Meniere's syndrome is characterized by attacks of dizziness, tinnitus, headache, nausea. Over time, hearing loss can occur. Clinical studies show that betahistine can prevent an attack and reduce the severity of attacks.

5.2 Pharmacokinetic properties

Absorption

Betahistine is rapidly and completely absorbed from all parts of the gastrointestinal tract after oral administration. After absorption, it is rapidly and almost completely metabolized to 2-pyridylacetic acid. Plasma levels of betahistine are very low. Pharmacokinetic analyses are therefore based on 2-PAA measurements in plasma and urine. After oral administration of betahistine, the plasma concentration of 2-PAA reaches its maximum after 1 hour.
During food intake the Cmax is lower than during fasting. However, the total absorption of betahistine is similar under both conditions, indicating that food alone delays the absorption of betahistine.

Distribution
The percentage of betahistine that is bound by blood plasma proteins is less than 5%.

Metabolism
Following the absorption, the drug is rapidly and almost completely metabolised to 2-PAA (2-pyridylacetic acid). 2- PAA has a half-life of approximately 3.5 hours.

Elimination

The 2-pyridylacetic acid is rapidly excreted in the urine. In the dose range between 8 and 48 mg, about 85% of the original dose was recovered in the urine. Renal or fecal excretion of betahistine is of minor importance.

Linearity
Recovery rates are constant over the oral dose range of 8-48 mg indicating that the pharmacokinetics of betahistine are linear and suggesting that the involved metabolic pathway is not saturated.

5.3 Preclinical safety data

Chronic toxicity
Adverse reactions affecting the central nervous system were seen in dogs and baboons after intravenous doses of 120 mg / kg and higher.

Studies on chronic oral toxicity over a period of 18 months in rats at a dose of 500 mg / kg and for 6 months in dogs at a dose of 25 mg / kg indicate that betahistine is well tolerated without definitive toxicity.

Mutagenic and carcinogenic potential
Betahistine has no mutagenic potential.

In an 18-month chronic toxicity study in rats at doses up to 500 mg / kg, there was no evidence of carcinogenic potential.

Reproductive toxicity
During reproductive toxicity studies, effects were only seen at exposures considered to be well above the maximum human exposure, indicating minimal relevance during clinical use.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Povidone K25,
Anhydrous citric acid
Maize starch,
Microcrystalline cellulose
Crospovidone
Hydrogenated vegetable oil

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store below 30 ºC.
Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

The tablets are packaged in blister strips (PVC/PVdC-aluminium).
Pack size of 14, 20, 30, 50, 60, 84, 90 and 120 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Accord Healthcare Ireland Ltd.
Euro House
Euro Business Park
Little Island
Cork T45 K857
Ireland

8 MARKETING AUTHORISATION NUMBER

PA2315/078/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 7th October 2011
Date of last renewal: 30th August 2015

10 DATE OF REVISION OF THE TEXT

June 2025