

# SUMMARY OF PRODUCT CHARACTERISTICS

## 1 NAME OF THE MEDICINAL PRODUCT

Betahistine dihydrochloride 24mg Tablets

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 24 mg betahistine dihydrochloride.

Excipient(s) with known effect:  
Each tablet contains 150 mg lactose monohydrate.

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Tablet

White to off white, round, approximately 10mm in diameter, biconvex, uncoated tablets with inscription 'GRI' on one side and breakline on other side.

The tablet can be divided into equal doses.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Ménière's syndrome as defined by the following trias of core symptoms:

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

### 4.2 Posology and method of administration

Posology

### Adults:

Initial oral treatment is 24-48mg daily divided over three equal doses, taken preferably with meals. For this purpose 8 and 16mg formulations are available. Maintenance doses are generally in the range 24 - 48mg daily. If a high daily maintenance dose is needed, the 24mg strength can be used 2 times a day (1 tablet in the morning and evening). Daily dose should not exceed 48 mg.

The dosage should be individually adapted according to the response.

### *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. Caution is recommended in this group of patients.

### *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. Caution is recommended in this group of patients.

### *Elderly population*

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 for use in children below 18 years due to insufficient data on safety and efficacy.

### Method of administration

Preferably during meal, with some water.

### **Duration of treatment**

Improvement can sometimes only be observed after a couple of weeks of treatment. The best results are sometimes obtained after a few months. There are indications that treatment from the onset of the disease prevents the progression of the disease and/or the loss of hearing in later phases of the disease.

## **4.3 Contraindications**

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

## **4.4 Special warnings and precautions for use**

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

Patients with gastric or duodenal ulcer or a history of peptic ulceration need to be carefully monitored during the therapy, because of the occasional dyspepsia encountered in patients on Betahistine.

Caution is advised in prescribing betahistine to patients with either urticaria, rashes or allergic rhinitis, because of the possibility of aggravating these symptoms. Such patients should be carefully monitored for early signs of hypersensitivity reactions to Betahistine.

Caution is advised in patients with severe hypotension

Betahistine dihydrochloride 24 mg tablets 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 no adequate data from 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.

##### Breast-feeding

It is not known whether betahistine is excreted in human milk.

Betahistine is excreted in rat milk. Effects seen post-partum in animal studies were limited to very high doses. The importance of the drug to the mother should be weighed against the benefits of nursing and the potential risks for the child.

##### Fertility

Animal studies did not show effects on fertility in rats.

#### **4.7 Effects on ability to drive and use machines**

Betahistine is indicated for Ménière's syndrome defined by the triad of core symptoms vertigo, hearing loss, tinnitus. The disease 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 frequency of undesirable effects [is described as follows: very common ( $\geq 1/10$ ); common ( $\geq 1/100$  to  $< 1/10$ ); uncommon ( $\geq 1/1,000$  to  $< 1/100$ ); rare ( $\geq 1/10,000$  to  $< 1/1,000$ ); very rare ( $< 1/10,000$ )].

### Adverse reactions observed during clinical trials

#### *Gastrointestinal disorders*

Common: nausea and dyspepsia.

#### *Disorders of the nervous system*

Common: headache.

In addition to these events reported in clinical trials, the following adverse events have been reported spontaneously during post-marketing experience and published in the scientific literature. Frequency cannot be determined from available data and is therefore classified as “frequency unknown”.

#### Immune system disorders:

*Not known:* Hypersensitivity reactions, e.g. anaphylaxis

#### Gastrointestinal disorders:

*Not known:* Mild gastric complaints (e.g. vomiting, abdominal pain, flatulence). 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 have been reported, in particular angioneurotic oedema, urticaria, 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 the Yellow Card Scheme Website: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the Google Play or Apple App Store.

## 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 (e.g. 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: Other nervous system drugs, Antivertigo preparation, ATC code: N07C A01

### Mechanism of action

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

- Betahistine affects the histaminergic system:

Betahistine acts both as a partial histamine H1-receptor agonist and histamine H3-receptor antagonist also in neuronal tissue, and has negligible H2-receptor activity.

Betahistine increases histamine turnover and release by blocking presynaptic H3- receptors and inducing H3-receptor downregulation.

- Betahistine may increase blood flow to the cochlear region as well as to the whole brain:

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. Betahistine was also shown to increase cerebral blood flow in humans.

- Betahistine facilitates vestibular compensation:

Betahistine accelerates the vestibular recovery after unilateral neurectomy, by promoting and facilitating central vestibular compensation; this effect characterised by an up-regulation of histamine turnover and release, is mediated via the H3 Receptor antagonism. In human subjects, recovery time after vestibular neurectomy was also reduced when treated with betahistine.

- Betahistine alters neuronal firing in the vestibular nuclei:

Betahistine was also found to have a dose-dependent inhibiting effect on spike generation of neurons in lateral and medial vestibular nuclei.

### Pharmacodynamic effect

The pharmacodynamic properties as demonstrated in animals may contribute to the therapeutic benefit of betahistine in the vestibular system.

### Clinical efficacy and safety

The efficacy of betahistine was shown in studies in patients with vestibular vertigo and with Meniere's disease as was demonstrated by improvements in severity and frequency of vertigo attacks.

## **5.2 Pharmacokinetic properties**

### Absorption

Orally administered betahistine is readily and almost completely absorbed from all parts of the gastrointestinal tract. After absorption, the drug is rapidly and almost completely metabolized into 2-pyridylacetic acid. Plasma levels of betahistine are very low. Pharmacokinetic analyses are based on 2-PAA measurements in plasma and urine. Under fed conditions C<sub>max</sub> is lower compared to fasted conditions. However, total absorption of betahistine is similar under both conditions, indicating that food intake only slows down the absorption of betahistine.

### Distribution

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

### Biotransformation

After absorption, betahistine is rapidly and almost completely metabolised into 2- PAA (which has no pharmacological activity). After oral administration of betahistine the plasma (and urinary) concentration of 2- PAA reaches its maximum 1 hour after intake and declines with a half-life of about 3.5 hours.

#### Elimination:

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

#### Linearity/non-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 effects in the nervous system were seen in dogs and baboons after intravenous doses at and above 120mg/kg.

Chronic oral toxicity testing for 18 months in rats at a dose of 500 mg/kg and 6 months in dogs at a dose of 25 mg/kg showed betahistine to be well tolerated with no definitive toxicities.

#### Mutagenic and carcinogenic potential

Betahistine does not have mutagenic potential.

In an 18 months chronic toxicity study in rats betahistine up to a dose of 500 mg/kg did not show any evidence for carcinogenic potential.

#### Reproduction toxicity

Effects in reproductive toxicity studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.

## **6 PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Lactose monohydrate  
Povidone K25  
Anhydrous citric acid (E330)  
Maize starch  
Cellulose, microcrystalline  
Crospovidone (Type B)  
Hydrogenated vegetable oil

### **6.2 Incompatibilities**

Not applicable.

### **6.3 Shelf life**

2 years

### **6.4 Special precautions for storage**

This medicinal product does not require any special temperature storage conditions. Store in the original package in order to protect from moisture.

### **6.5 Nature and contents of container**

Tablets are available in PVC-PVdC/Aluminium blisters. Pack size of 20, 30, 50, 60, 84, 90 and 100 tablets in a carton.

Not all pack sizes may be marketed.

### **6.6 Special precautions for disposal**

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

## **7 MARKETING AUTHORISATION HOLDER**

Accord Healthcare Limited  
Sage House  
319 Pinner Road  
North Harrow  
Middlesex  
HA1 4HF  
United Kingdom

## **8 MARKETING AUTHORISATION NUMBER(S)**

PL 20075/0666

## **9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

30/05/2023

**10 DATE OF REVISION OF THE TEXT**

27/10/2025