

 **14 February 2025**

**SUMMARY OF PRODUCT CHARACTERISTICS**

**for**

**Betahistinhydrochlorid "Stada", tablets**

**0. D.SP.NO.**

33421

**1. NAME OF THE MEDICINAL PRODUCT**

Betahistinhydrochlorid "Stada"

**2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Betahistindihydrochlorid "Stada" 8 mg tablet

Each tablet contains 8 mg betahistine dihydrochloride

Betahistindihydrochlorid "Stada" 16 mg tablet

Each tablet contains 16 mg betahistine dihydrochloride

Betahistindihydrochlorid "Stada" 24 mg tablet

Each tablet contains 24 mg betahistine dihydrochloride

For the full list of excipients, see section 6.1.

**3. PHARMACEUTICAL FORM**

Tabletter

Betahistindihydrochlorid "Stada" 8 mg tablet

White to off-white round (diameter approximately 7 mm), flat tablets debossed with ‘JI’ on one side and plain on the other side.

Betahistindihydrochlorid "Stada" 16 mg tablet

White to off-white round (diameter approximately 9 mm), biconvex tablets debossed with ‘J2’ on one side and a score line on other side.

The tablet can be divided into equal doses.

Betahistindihydrochlorid "Stada" 24 mg tablet

White to off-white round (diameter approximately 10 mm), biconvex tablets debossed with ‘J4’ on one side and a score line on 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 and hearing loss.

**4.2 Posology and method of administration**

Dosage

*Adults*

Initial oral treatment is 16 mg three times daily.

Maintenance doses are generally in the range 24 - 48 mg daily and it should be divided into two or three individual doses to achieve a more even plasma concentration.

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.

*Special populations*

*Renal and hepatic impairment*

There are no specific clinical trials available in these patient groups, but according to post-marketing experience no dose adjustment appears to be necessary. Caution should be advised in these patient groups.

*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 population.

*Paediatric population*

Betahistine tablets are not recommended for use in children and adolescents below age 18 due to lack of data on safety and efficacy.

Method of administration

Take the tablets preferably with meals or after meals with a glass of water.

**4.3 Contraindications**

* hypersensitivity to the active substance or to any of the excipients listed in section 6.1
* betahistine is contraindicated in patients with phaeochromocytoma. As betahistine is a synthetic analogue of histamine it may induce the release of catecholamines from the tumour 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 in bronchial asthma patients has been shown in a relatively few patients. These patients need to be monitored carefully during the treatment with betahistine.

Caution is advised in prescribing betahistine to patients with either urticaria, rashes or allergic rhinitis, because of the possibility of aggravating these symptoms.

Caution is advised in patients with severe hypotension.

**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 monoamine 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 an analogue of histamine, 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 are insufficient with respect to effects on pregnancy, embryonal/foetal development, parturition and postnatal development. The potential risk for humans is unknown. 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

There are no adequate fertility data for betahistine.

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

No traffic warning.

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. However, betahistine may cause drowsiness which can affect the ability to drive and use machines.

**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: 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); very rare (< 1/10 000).

***Gastrointestinal disorders***

*Common*: nausea and dyspepsia

***Nervous system disorders***

*Common*: headache

In addition to those events reported during clinical trials, the following undesirable effects have been reported spontaneously during post-marketing use and in scientific literature. A frequency cannot be estimated from the available data and is therefore classified as “not known”.

***Immune system disorders***

Hypersensitivity reactions, e.g. anaphylaxis have been reported.

***Gastrointestinal disorders***

Mild gastric complaints (e.g. vomiting, gastrointestinal pain, abdominal distension and bloating) have been observed. These can normally be dealt with by taking the dose during meals or by lowering the dose.

***Skin and subcutaneous tissue disorders***

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:

Lægemiddelstyrelsen

Axel Heides Gade 1

DK-2300 København S

Website: www.meldenbivirkning.dk

**4.9 Overdose**

Symptoms

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). Other symptoms of betahistine overdose are vomiting, dyspepsia, ataxia and seizures. More serious complications (convulsion, pulmonary or cardiac complications) were observed in cases of intentional overdose of betahistine especially in combination with other overdosed drugs.

Management

No specific antidote. Gastric lavage and symptomatic treatment are recommended within one hour after intake. Treatment of overdose should include standard supportive measures.

**4.10 Legal status**

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**5. PHARMACOLOGICAL PROPERTIES**

**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Other nervous system drugs, Antivertigo preparations,

ATC code: N07CA01

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 in animals, by promoting and facilitating central vestibular compensation; this effect is 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.

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

The efficacy of betahistine was shown in studies in patients with vestibular vertigo and with Ménière'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 gastro-intestinal tract. After absorption, the drug is rapidly and almost completely metabolised into 2-pyridylacetic acid. Plasma levels of betahistine are very low. Pharmacokinetic analyses are therefore based on 2-PAA measurements in plasma and urine.

Under fed conditions Cmax 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.

Excretion

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 faecal excretion of betahistine itself 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 effects in the nervous system were seen in dogs and baboons after intravenous doses at and above 120 mg/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**

Mannitol (E 421)

Microcrystalline cellulose

Silica, colloidal anhydrous

Povidone

Citric acid, anhydrous

Crospovidone

Talc

Stearic acid

**6.2 Incompatibilities**

Not applicable.

**6.3 Shelf life**

4 years.

**6.4 Special precautions for storage**

Store in the original package in order to protect from moisture.

**6.5 Nature and contents of container**

Blisters and unit-dose blisters of clear PVC/PVDC-Aluminium:

8 mg: 20, 30, 50, 60, 100, 50×1

16 mg and 24 mg: 20, 30, 50, 60, 100, 20×1

Not all pack sizes may be marketed.

**6.6 Special precautions for disposal and other handling**

No special requirements.

**7. MARKETING AUTHORISATION HOLDER**

STADA Arzneimittel AG

Stadastrasse 2-18

61118 Bad Vilbel

Tyskland

**Representative**

Stada Nordic ApS

Marielundvej 46a

2730 Herlev

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

8 mg: 69417

16 mg: 69418

24 mg: 69420

**9. DATE OF FIRST AUTHORISATION**

14 February 2025

**10. DATE OF REVISION OF THE TEXT**

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