Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

Betahistine ratiopharm 8 mg tablets
Betahistine ratiopharm 16 mg tablets
Betahistine ratiopharm 24 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 tablet of Betahistine ratiopharm 8 mg tablets contains 8 mg betahistine dihydrochloride.
1 tablet of Betahistine ratiopharm 16 mg tablets contains 16 mg betahistine dihydrochloride.
1 tablet of Betahistine ratiopharm 24 mg tablets contains 24 mg betahistine dihydrochloride.

Betahistine ratiopharm 8 mg tablets
Excipient with known effect: 70 mg lactose monohydrate.

Betahistine ratiopharm 16 mg tablets
Excipient with known effect: 140 mg lactose monohydrate.

Betahistine ratiopharm 24 mg tablets
Excipient with known effect: 210 mg lactose monohydrate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

tablet

Appearance:
Betahistine ratiopharm 8 mg tablets
White to almost white, cylindrical, flat tablets, bevelled edge on both sides and marked with “B8”.

Betahistine ratiopharm 16 mg tablets
White to almost white, cylindrical, flat tablets with a bevelled edge on both sides, scored on one side and marked with “B16” on the other side.
The tablet can be divided into equal doses.

Betahistine ratiopharm 24 mg tablets
White to almost white, round, convex tablets, scored on one side.
The tablet can be divided into equal doses.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications

Menière's disease or partial symptoms of Menière-like syndrome:

- vertigo with nausea and vomiting
- tinnitus
- hearing loss

4.2 Posology and method of administration

Dosage

The recommended initial dose is 24 mg betahistine dihydrochloride daily in 2 or 3 single doses. If this dosage is insufficient, the daily dose can be increased to a maximum of 48 mg betahistine dihydrochloride.

*Betahistine ratiopharm 8 mg tablets*

**adult and elderly patients**

Twice daily 3 tablets (in the morning and in the evening) or 3 times daily either 1 or 2 tablets (in the morning, at midday and in the evening) *Betahistine ratiopharm 8 mg tablets* (which equals 24-48 mg betahistine dihydrochloride).

For the higher dosage, *Betahistine ratiopharm 16 mg tablets* and *Betahistine ratiopharm 24 mg tablets* are also available.

*Betahistine ratiopharm 16 mg tablets*

**adult and elderly patients**

Twice daily 1½ tablets (in the morning and in the evening) or 3 times daily either 1 or 1½ tablet (in the morning, at midday and in the evening) *Betahistine ratiopharm 16 mg tablets* (which equals 24-48 mg betahistine dihydrochloride).

For the low dosage, *Betahistine ratiopharm 8 mg tablets* and for the higher dosage *Betahistine ratiopharm 24 mg tablets* are also available.

*Betahistine ratiopharm 24 mg tablets*

**adult and elderly patients**

Twice daily ½-1 tablet (in the morning and in the evening) *Betahistine ratiopharm 24 mg tablets* (which equals 24-48 mg betahistine dihydrochloride).

For the low dosage, *Betahistine ratiopharm 8 mg tablets* and *Betahistine ratiopharm 16 mg tablets* are also available.

*Children and adolescents*

*Betahistine ratiopharm x mg tablets* are not recommended for the treatment of children and adolescents below 18 years of age. Safety and efficacy in this patient group have not been established in studies.

Method of administration

The tablets should be taken with some fluid, either during or after meals.
Duration of administration
To ensure a satisfactory result, treatment should be continued for several months.

4.3 Contraindications

- hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- phaeochromocytoma: As betahistine dihydrochloride is a synthetic histamine analogue, it can induce catecholamine release from the tumour, which can lead to severe hypertension.
- during pregnancy and lactation (see section 4.6 “Pregnancy and lactation”)

4.4 Special warnings and precautions for use

Caution is advised in the treatment of patients with:

- peptic ulcer (including a history of this disorder), as dyspepsia may occasionally occur in patients undergoing betahistine dihydrochloride treatment;
- bronchial asthma;
- urticaria, exanthema or allergic rhinitis, as these symptoms may worsen;
- pronounced hypotension.
- concurrent administration of antihistamines (see section 4.5 “Interaction with other medicinal products and other forms of interaction”)

Betahistine ratiopharm x mg tablets are not recommended for the treatment of children and adolescents below 18 years of age. Safety and efficacy in this patient group have not been established in studies.

This medicinal product contains lactose. Patients with rare, hereditary metabolic disorders such as galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption should not take Betahistine ratiopharm x mg tablets.

4.5 Interaction with other medicinal products and other forms of interaction

As betahistine dihydrochloride is a histamine analogue, concurrent administration of H₁ antagonists may cause a mutual attenuation of effect of the active agents.

4.6 Fertility, pregnancy and lactation

Betahistine ratiopharm x mg tablets must not be administered during pregnancy and lactation, as no adequate animal studies are available and there has been no experience with use during human pregnancy and lactation.

4.7 Effects on ability to drive and use machines

While taking Betahistine ratiopharm x mg tablets side effects as tiredness might occur. Under these circumstances the ability to react may be reduced, thus impairing the ability to drive and the ability to operate machinery.

4.8 Undesirable effects

The following undesirable effects have been reported at the approximate frequencies shown.
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)
Not known (cannot be estimated from the available data)

Cardiac disorders
rare: beating of the heart

Nervous system disorders:
rare: Headache, somnolence

Respiratory, thoracic and mediastinal disorders:
rare: Pre-existing bronchial asthma may worsen.

Gastrointestinal disorders:
rare: Gastric discomfort and pain, heartburn, vomiting, nausea, indigestion. Pre-existing gastrointestinal ulcer may worsen.

Skin and subcutaneous tissue disorders:
rare: rash, urticaria, pruritus

General disorders
rare: sensation of heat

4.9 Overdose

The symptoms of betahistine dihydrochloride overdose are dryness of the mouth, nausea, vomiting, dyspepsia, ataxia and - following intake of very high doses – convulsions may also occur.

In analogy to Histamine following symptoms can occur: redness of the face, dizziness, increased beating of the heart, low blood pressure, bronchial spasm and oedema.

There is no specific antidote. In addition to general measures aimed at toxin elimination (gastric lavage, administration of activated charcoal), treatment is symptomatic.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antivertiginous drugs
ATC code: N07CA01

Betahistine dihydrochloride is a synthetic histamine analogue for oral administration. The precise mechanism of action has not been fully elucidated.

In pharmacological animal studies, betahistine dihydrochloride was shown to have \( H_3 \)-antagonistic and weak \( H_1 \)-agonistic activities on the CNS and autonomic nervous system. Furthermore, it was shown that betahistine dihydrochloride has a dose-dependent inhibitory effect on the activity of the medial and lateral vestibular nuclei. In addition, an improved blood circulation was shown in the vascular stria and a reduced endolymphatic pressure in the inner ear, probably due to relaxation of the precapillary
sphincters of the microcirculation of the inner ear. The onset of effect varies between a few days and weeks.

5.2 Pharmacokinetic properties

To date, pure betahistine dihydrochloride could not be demonstrated in the human body (below the limit of detection). Thus, the plasma concentrations and the plasma half-life are determined using radiolabelled betahistine dihydrochloride and the urinary concentration of the inactive major metabolite, 2-pyridylacetic acid.

Absorption
Following oral administration, betahistine dihydrochloride is rapidly and completely absorbed. Peak plasma concentrations of C14-labelled betahistine dihydrochloride are reached approximately 1 hour after oral administration in fasting volunteers. The absolute bioavailability of betahistine dihydrochloride is not known.

Distribution
The volume of distribution of betahistine dihydrochloride is not known. Human plasma protein binding is under 5%.

Biotransformation
Betahistine dihydrochloride is rapidly metabolised in the liver to the inactive major metabolite, 2-pyridylacetic acid and to demethyl-betahistine.

Elimination
Elimination of betahistine dihydrochloride is 90% renal in the form of the major metabolite. Only traces of desmethyl-betahistine dihydrochloride are recovered in the urine. Biliary elimination is not a significant route of elimination for the active agent or any of its metabolites.

5.3 Preclinical safety data

There are no findings from preclinical chronic toxicity studies that suggest any increased risk associated with use in humans. Betahistine dihydrochloride has been inadequately investigated for its toxicity in relation to reproduction. No adequate mutagenicity or carcinogenicity studies are available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Povidone K 90
microcrystalline cellulose
lactose monohydrate
colloidal anhydrous silica
crospovidone
stearic acid

6.2 Incompatibilities

Not applicable.
6.3 **Shelf life**

*Betahistine ratiopharm 8 mg/16 mg tablets*
3 years

*Betahistine ratiopharm 24 mg tablets*
2 years

6.4 **Special precautions for storage**

Do not store above 25 °C.
Store in the original package.

6.5 **Nature and contents of container**

PVC/PVDC-Alu blister

*Betahistine ratiopharm 8 mg tablets*
30, 50, 60, 100 und 120 tablets

*Betahistine ratiopharm 16 mg tablets*
20, 30, 50, 60, 100 und 120 tablets

*Betahistine ratiopharm 24 mg tablets*
20, 50, 60, 100 und 120 tablets

Not all pack sizes may be marketed.

6.6 **Special precautions for disposal**

No special requirements

7. **MARKETING AUTHORISATION HOLDER**

To be completed nationally.

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

To be completed nationally

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

To be completed nationally

10. **DATE OF REVISION OF THE TEXT**
To be completed nationally