PROFESSIONAL INFORMATION

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

SERC® 24 Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains betahistine dihydrochloride 24 mg.

Contains sugar (75 mg mannitol per tablet).

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.

A round, biconvex, white to almost white tablet with bevelled edges, the standard inscription is 289 on either side of the score on one tablet-side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Symptomatic treatment of the vertigo associated with Ménière's syndrome.

4.2 Posology and method of administration

Posology

The daily dosage is 24 – 48 mg in divided doses. One 24 mg tablet can be administered twice daily.

The dosage should be individually adapted according to the response. Improvement can sometimes only be observed after a couple of weeks of treatment.

Paediatric population

SERC 24 is not recommended for use in children below 18 years, due to insufficient data on safety and efficacy.

Method of administration

For oral use.

Preferably to be swallowed with water during meals.

4.3 Contraindications

- Hypersensitivity to betahistine dihydrochloride or any excipients listed in section 6.1.
- Patients with active peptic ulcer.
- Patients with phaeochromocytoma.

4.4 Special warnings and precautions for use

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

4.5 Interaction with other medicines and other forms of interaction

No *in vivo* interaction studies have been performed. Based on *in vitro* data, no *in vivo* inhibition of cytochrome P450 enzymes is to be expected.

In vitro data indicate inhibition of betahistine metabolism by medicines that inhibit monoamine oxidase (MAO), including MAO subtype B (e.g. selegiline). Caution is recommended with concomitant use of SERC 24 and MAO inhibitors (including selective MAO-B inhibitors).

Concomitant use with antihistamines should be avoided.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety and efficacy in pregnancy and lactation has not been demonstrated.

It is not recommended to use SERC 24 during pregnancy.

Breastfeeding

It is not known whether betahistine is excreted in human milk. Therefore, SERC 24 should not be used during breastfeeding.

Fertility

Animal studies show no influence on fertility in rats.

4.7 Effects on ability to drive and use machines

Ménière's syndrome can negatively affect the ability to drive and use machines. In clinical studies specially devised to investigate the influence of SERC 24 on the ability to drive and use machines, no negative effects or negligible negative effects were observed.

4.8 Undesirable effects

Adverse reactions reported as more than isolated case is listed below by system organ class and by frequency.

Frequencies are defined as: very common (≥ 1/10), common (≥ 1/100, < 1/10), uncommon (≥ 1/1 000, < 1/100), rare (< 1/1 000); very rare (≤ 1/ 10 000), including isolated cases.

Immune system disorders:

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

Nervous system disorders*:*

Common: Headache

Gastrointestinal disorders:

Common: Nausea and dyspepsia

Skin and subcutaneous tissue disorders:

Very rare: Cutaneous and subcutaneous hypersensitivity reactions have been reported, in particular angioedema, rash, pruritus and urticaria.

In addition to these undesirable effects, which were reported during clinical trials, the following undesirable effects have been spontaneously reported during post-marketing use and in scientific literature. Frequency cannot be estimated from the available data and these undesirable effects are therefore classified as "not known".

Gastrointestinal disorders:

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.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of this medicine is important. It allows continued monitoring of the benefit/risk balance of this medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications:
https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

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 medicines.

Treatment of overdose

Treatment of overdose should include standard supportive measures.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A. 5.6 Histamine.

Pharmacotherapeutic group: antivertigo preparations, ATC code: N07CA01.

Mechanism of action

The mechanism of action of betahistine is only partially known. There are various plausible hypotheses which are supported by animal studies and by human data:

Betahistine influences the histaminergic system:

Betahistine works both as a partial histamine H_1-receptor agonist and as a histamine H_3-receptor antagonist, also in neuronal tissue, and has negligible H_2-receptor activity.

Betahistine increases synthesis and release of histamine by blocking presynaptic H_3-receptors and inducing H_3-receptor downregulation.

Betahistine can cause an increase in the blood flow to both the cochlear environment and to the brain as a whole:

Pharmacological studies in animals have shown that the blood flow in the stria vascularis of the inner ear improves, probably by means of a relaxation of the precapillary sphincters of the microcirculation of the inner ear. It has also been shown that betahistine increases cerebral blood flow in humans.

Betahistine facilitates vestibular compensation:

Betahistine accelerates vestibular healing after unilateral neurectomy in animals by stimulating and facilitating central vestibular compensation; this effect, which is characterised by an increase in the

synthesis and release of histamine, is mediated via the H_3-receptor antagonism.

Betahistine alters the neuron firing in the vestibular nuclei:

It has also been discovered that betahistine has a dose-dependent inhibiting effect on the occurrence of neuron peaks in the lateral and medial vestibular nuclei.

The importance of this observation in the action against Ménière's syndrome or vestibular vertigo, however, remains unclear.

5.2 Pharmacokinetic properties

Absorption

Orally administered betahistine is readily and fully absorbed from all parts of the gastro-intestinal tract. After absorption, it is rapidly and almost completely metabolised into 2-pyridylacetic acid (2-PAA). Plasma levels of betahistine are very low (i.e., below the detection limit of 100 pg/mL). All pharmacokinetic analyses are therefore based on 2-PAA measurements in plasma and urine.

The C_{max} is lower during food consumption than it is during fasting. However, total absorption of betahistine is similar under both conditions, which indicates 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 quickly and almost completely metabolised into 2-PAA (which has no pharmacological activity).

After oral administration of betahistine, the plasma (and urine) concentrations of 2-PAA reach their maximum levels 1 hour after administration and decline with a half-life of approximately 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 excreted in the urine. There is minor renal or fecal excretion of betahistine itself.

Linearity/non-linearity

Recovery rates over the oral dose range of 8 – 48 mg are constant, which indicates that the pharmacokinetics of betahistine are linear and suggests that the involved metabolic trajectory is not saturated.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric acid monohydrate

Colloidal anhydrous silica

Mannitol (E421)

Microcrystalline cellulose

Talc

6.2 Incompatibilities

None known.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store below 25 °C in the original container.

6.5 Nature and contents of container

Press through strips of PVC/PVDC/Aluminium containing 20 tablets.

6.6 Special precautions for disposal and other handling

None.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Abbott Laboratories S.A. (Pty) Ltd

Abbott Place, 219 Golf Club Terrace

Constantia Kloof, 1709

Johannesburg, South Africa

8. REGISTRATION NUMBER

South Africa: 38/5.6/0040

Namibia: 10/5.6/0034 (NS2)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

25 November 2005

10. DATE OF REVISION OF THE TEXT

22 November 2022