NEW ZEALAND DATA SHEET

SERC ®

1. Product Name

SERC, 8 mg, 16 mg tablet.

2. Qualitative and Quantitative Composition

Each 8 mg tablet contains 8 mg betahistine dihydrochloride corresponding to 5.21mg betahistine,

Each 16 mg tablet contains 16 mg betahistine dihydrochloride corresponding to 10.42 mg betahistine.

For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

8 mg tablet: round, flat, white to almost white tablet with bevelled edges, one side inscribed with '256'.

16 mg: round, biconvex, scored, white to almost white tablet with bevelled edges, one side inscribed '267' on either side of the score.

SERC 16 mg tablets can be divided into equal doses.

4. Clinical Particulars

4.1 Therapeutic indications

Ménière's Syndrome as defined by the following core symptoms:

- Vertigo (with nausea/vomiting)
- Hearing loss (hardness of hearing)
- Tinnitus

4.2 Dose and method of administration

Dose

The recommended starting dose is 8 to 16 mg taken three times a day. The maximum recommended daily dose is 48 mg.

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

Special populations

Paediatric

Due to lack of clinical experience, betahistine dihydrochloride should not be used in children less than 18 years (see section 4.3).

Method of administration

The tablets may be taken with or without food. However, if gastrointestinal upset occurs, it is recommended that the tablets be taken with meals.

4.3 Contraindications

Serc (betahistine dihydrochloride) Tablets are contraindicated as follows:

- During pregnancy and lactation
- In children less than 18 years
- In patients suffering from phaeochromocytoma
- In patients with active peptic ulcer or a history of this condition
- In patients with hypersensitivity to any component to the product (see Section 6.1)

4.4 Special warnings and precautions for use

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

Caution should be taken in the treatment of patients receiving antihistamines (see section 4.5).

4.5 Interaction with other medicines and other forms of interaction

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.

An antagonism between Serc and antihistamines could be expected on a theoretical basis. However, no such interactions have been reported.

4.6 Fertility, pregnancy and lactation

Pregnancy

Category B2

Betahistine dihydrochloride should not be used during pregnancy (see section 4.3) since there is insufficient data on the use of this drug during pregnancy to evaluate possible harmful effects.

Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of foetal damage.

Breast-feeding

Betahistine dihydrochloride should not be used during lactation (see section 4.3)

Fertility

For pre-clinical fertility data refer to section 5.3.

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. This 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

Most of the reported adverse reactions pertain to the skin, gastrointestinal tract, body as a whole, nervous system, respiratory system and cardiovascular system.
Events are listed within body system and categorised by frequency according to the following definitions:
Common (frequency ≥1 and <10 %)
Uncommon (frequency ≥0.1% and < 1 %)
Rare (frequency ≥0.01% and < 0.1 %)
Very rare (frequency < 0.01 %)

Skin and subcutaneous tissue disorders:	*Rare*: various types of rash, pruritis and urticaria/angioneurotic oedema. These reactions are probably related to the histamine like structure of betahistine. There was a single case of Stevens Johnson syndrome.
Body as a whole:	*Rare:* tiredness and malaise
Gastrointestinal system:	*Common:* nausea and dyspepsia *Rare:* vomiting, diarrhoea, abdominal distension, bloating and epigastric pain have been reported. These symptoms were usually mild. Gastrointestinal disturbances may be relieved by reducing the dose or by taking betahistine with meals.
Nervous system:	*Common:* headache *Rare:* dizziness *Very rare:* convulsions, somnolence, confusion and hallucinations. Some of these symptoms may also be observed as part of the disease condition and are usually resolved without changes to the treatment schedule. Patients with neurological events usually presented with confounding factors.
Cardiovascular system:	*Very rare*: vasodilation, postural hypotension and tachycardia.
Respiratory system:	*Very rare:* dyspnoea, asthma and bronchospasms (see section 4.4)
Immune system disorders	Hypersensitivity reactions, e.g. anaphylaxis have been reported

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/.

4.9 Overdose

There have been a few cases of overdosage reported. Although in most cases no overdose symptoms were reported, some patients have experienced mild to moderate symptoms of

overdosage including nausea, dry mouth, epigastric pain and sleepiness at doses above 200 mg. A case of convulsion was reported at a dose of 728 mg. In all cases recovery was complete.

Treatment should include standard supportive measures.

For further advice on management of overdose please contact the National Poisons Information Centre (0800 POISON or 0800 764 766).

5. Pharmacological Properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-vertigo preparations, ATC code: N07CA01

Mechanism of action

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

Betahistine acts both as a partial histamine H_1-receptor agonist and histamine H_3-receptor antagonist also in neuronal tissue, and has negligible H_2-receptor activity. Betahistine increases histamine turnover and release by blocking presynaptic H_3-receptors and inducing H_3-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 characterized by an upregulation of histamine turnover and release, is mediated via the H_3 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 effects

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 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 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 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 metabolized 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 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

Carcinogenicity/ Mutagenicity

No animal data is available on the carcinogenic or mutagenic potential of betahistine.

Fertility

Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of fetal damage.

6. Pharmaceutical Particulars

6.1 List of excipients

SERC tablets also contains:

- colloidal anhydrous silica,
- microcrystalline cellulose,
- mannitol,
- citric acid monohydrate,
- purified talc.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store at or below 30°C.

6.5 Nature and contents of container

8 mg tablet: Blister packs of 120 and 10 (sample pack).

16 mg tablet: Blister packs of 100, 25 and 10 (sample pack).

Not all pack types and sizes and strengths may be marketed.

6.6 Special precautions for disposal and other handling

Not applicable.

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

7. Medicines Schedule

Prescription Medicine

8. Sponsor Details

Viatris Ltd
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AUCKLAND
www.viatris.co.nz
Telephone 0800 168 169

9. Date of First Approval

14 January 1999

10. Date of Revision of the Text

24 January 2022

Summary table of changes

Section	Summary of new information
3	Halving statement introduced for 16 mg tablet.

Serc® is a Viatris company trade mark.