

**SERC®**

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## 1. Product Name

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SERC, 8 mg, 16 mg tablet.

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## 2. Qualitative and Quantitative Composition

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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.

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## 3. Pharmaceutical Form

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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.

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## 4. Clinical Particulars

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### 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  $\geq 1$  and  $< 10$  %)*

*Uncommon (frequency  $\geq 0.1\%$  and  $< 1$  %)*

*Rare (frequency  $\geq 0.01\%$  and  $< 0.1$  %)*

*Very rare (frequency  $< 0.01$  %)*

|                                         |                                                                                                                                                                       |
|-----------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Skin and subcutaneous tissue disorders: | <i>Rare:</i> 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: | <i>Rare:</i> tiredness and malaise |
|------------------|------------------------------------|

|                          |                                     |
|--------------------------|-------------------------------------|
| Gastrointestinal system: | <i>Common:</i> 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: | <i>Common:</i> 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: | <i>Very rare:</i> vasodilation, postural hypotension and tachycardia. |
|------------------------|-----------------------------------------------------------------------|

|                     |                                                                        |
|---------------------|------------------------------------------------------------------------|
| Respiratory system: | <i>Very rare:</i> dyspnoea, asthma and bronchospasms (see section 4.4) |
|---------------------|------------------------------------------------------------------------|

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|-------------------------|-----------------------------------------------------------------|
| 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).

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## 5. Pharmacological Properties

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### 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<sub>1</sub>-receptor agonist and histamine H<sub>3</sub>-receptor antagonist also in neuronal tissue, and has negligible H<sub>2</sub>-receptor activity. Betahistine increases histamine turnover and release by blocking presynaptic H<sub>3</sub>-receptors and inducing H<sub>3</sub>-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<sub>3</sub> 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.

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## **6. Pharmaceutical Particulars**

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### **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.

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## **7. Medicines Schedule**

Prescription Medicine

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## **8. Sponsor Details**

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## **9. Date of First Approval**

14 January 1999

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## **10. Date of Revision of the Text**

24 January 2022

### **Summary table of changes**

| <b>Section</b> | <b>Summary of new information</b>              |
|----------------|------------------------------------------------|
| 3              | Halving statement introduced for 16 mg tablet. |

Serc® is a Viatris company trade mark.