

# Data Sheet

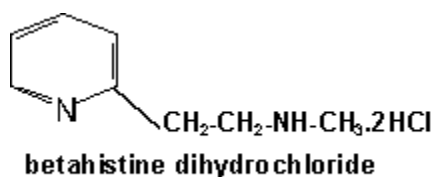
## Serc<sup>®</sup> Tablets

### Name of the Medicine

Betahistine dihydrochloride

### Chemical Structure

Betahistine dihydrochloride is chemically identified as 2-[2-(methylamino)ethyl]pyridine dihydrochloride. Chemically, betahistine has a close resemblance to histamine. It has the following chemical structure:



MW= 209.1

### CAS Number

5579-84-0

### Description

Betahistine dihydrochloride is a white to almost white crystalline powder, which is very hygroscopic. The product is very soluble in water, freely soluble in methanol and 96% ethanol, and slightly soluble in isopropanol. The pKa values are 3.5 and 9.7.

Serc (Betahistine dihydrochloride) is available in 8 mg and 16 mg tablets. The inactive ingredients in Serc 8 mg and 16 mg tablets are: colloidal anhydrous silica, microcrystalline cellulose, mannitol, citric acid monohydrate, and purified talc.

### Pharmacology

#### Pharmacodynamics

The mechanism of action of betahistine is not known. 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.

In further animal pharmacological studies, betahistine was found to have weak H<sub>1</sub> receptor agonistic and considerable H<sub>3</sub> antagonistic properties in the CNS and autonomic nervous system. Betahistine was also found to have a dose dependent inhibiting effect on spike generation of neurons in lateral and medial vestibular nuclei in cats. The importance of this observation in the action against Ménière's syndrome or vestibular vertigo, however, remains unclear.

#### Pharmacokinetics

In man, orally administered doses of betahistine dihydrochloride are rapidly and completely absorbed from the gastrointestinal tract. The drug is rapidly metabolised to one major metabolite - 2-pyridylacetic acid - and excreted in the urine. Studies with radio-labelled betahistine have demonstrated a plasma half life of 3.4 hours and a urinary half life of 3.5

hours for the radio-label. Urinary excretion of the label was about 90% complete within 24 hours of administration.

### **Indications**

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

- vertigo (with nausea/vomiting)
- hearing loss (hardness of hearing)
- tinnitus

### **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 Description)

### **Precautions**

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

Caution should be taken in the treatment of patients receiving antihistamines (see "Interactions with Other Drugs").

### **Effects on Fertility**

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

### **Use in Pregnancy**

#### **Category B2**

Betahistine dihydrochloride should not be used during pregnancy (see 'Contraindication') 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.

### **Use in Lactation**

Betahistine dihydrochloride should not be used during lactation (see 'Contraindication')

### **Paediatric Use**

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

### **Carcinogenicity/ Mutagenicity**

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

### **Effects on Ability to Drive and Use Machines**

Betahistine is presumed to be safe or unlikely to produce an effect on the ability to drive or use machinery.

## Interactions with other Medicines

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

## Adverse 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>Common:</i> headache <i>Rare:</i> tiredness and malaise
Gastrointestinal system:	<i>Rare:</i> nausea, dyspepsia, vomiting, diarrhoea, 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>Rare:</i> dizziness <i>Very rare:</i> 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 "Precautions")
Immune system disorders	Hypersensitivity reactions, e.g. anaphylaxis have been reported

## Dosage and Administration

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

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

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

### **Overdosage**

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.

Contact the Poisons Information Centre for advice on management of overdosage.

### **Presentation and Storage Conditions**

Serc (betahistine dihydrochloride) 8 mg\* tablets: round, flat, white to almost white tablet, one side inscribed with '256', in packs of 120 and 10 (sample pack).

Serc (betahistine dihydrochloride) 16 mg tablets: round, biconvex, scored, white to almost white tablet, one side inscribed with '267' on either side of the score, in packs of 100\*, 25 and 10\* (sample pack).

\* not currently distributed in New Zealand

### **Medicine Schedule**

Prescription Medicine

### **Further Information**

Nil

### **Name and Address of the Sponsor**

Abbott Laboratories NZ Ltd

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Auckland

New Zealand

### **Date of Preparation**

31 October 2011