PRODUCT INFORMATION
SERC® TABLETS

NAME OF THE DRUG
Non-proprietary Name
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:

```
CH2CH2-NH-CH2-2HCl
```

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 as 16 mg uncoated tablets. The inactive ingredients in Serc 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 H1 receptor agonistic and considerable H3 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 MEDICINES’).

**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 ‘CONTRAINDICATIONS’) since there are 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 fetal damage.

**Use in Lactation**
Betahistine dihydrochloride should not be used during lactation (see ‘CONTRAINDICATIONS’).

**Paediatric Use**
Due to lack of clinical experience, betahistine dihydrochloride should not be used in children less than 18 years (see ‘CONTRAINDICATIONS’).

**Carcinogenicity and Genotoxicity**
No animal data is available on the carcinogenic or mutagenic potential of betahistine.

**INTERACTIONS WITH OTHER MEDICINES**

*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.

**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 systems 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, pruritus 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:**
  - *Common:* headache.
  - *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:**
  - *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 PRECAUTIONS).

- **Immune system disorders**
  - Hypersensitivity reactions, e.g. anaphylaxis, have been reported.

**DOSAGE AND ADMINISTRATION**

The recommended starting dose in adults is 8 to 16 mg 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 in symptoms may be observed in the first few days to 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 on 13 11 26 (Australia) for advice on management of overdosage.

PRESENTATION AND STORAGE CONDITIONS
Serc (betahistine dihydrochloride) 16 mg tablets: round, biconvex, scored, white to almost white uncoated tablet, one side inscribed with ‘267’ on either side of the score, in PVC/PVDC/aluminium blister packs containing 10 tablets (sample pack), 25 tablets and *100 tablets.

Serc (betahistine dihydrochloride) *8 mg tablets: round, flat, white to almost white uncoated tablet, one side inscribed with ‘256,’ in PVC/PVDC/aluminium blister packs containing 10 tablets and 120 tablets.

* Not currently distributed in Australia

16 mg tablets: AUST R 61687
8 mg tablets: AUST R 61688

Store below 30°C, protect from light.

NAME AND ADDRESS OF THE SPONSOR
Mylan Health Pty Ltd
Level 1, 30 The Bond
30-34 Hickson Road
Millers Point, NSW 2000
Australia
www.mylan.com.au
Phone: 1800 314 527

POISON SCHEDULE OF THE MEDICINE
Schedule 4

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (THE ARTG)
SERC 16 mg: 05th November 1997
SERC 8 mg: 05th November 1997

DATE OF MOST RECENT AMENDMENT
18th September 2017