1. NAME OF THE MEDICINAL PRODUCT

Betaserc® 8 mg tablets
Betaserc® 16 mg tablets
Betaserc® 24 mg tablets

Serc® 8 mg tablets
Serc® 16 mg tablets
Serc® 24 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Betaserc/Serc tablets contain 8, 16 or 24 mg betahistine dihydrochloride.

For a full list of excipients see section 6.1.

3. PHARMACEUTICAL FORM

Betaserc/Serc tablet, 8 mg:
A round, flat, almost white to white tablet with beveled edges. The diameter is 7 mm, the tablet weight is approximately 125 mg. The tablet inscriptions are "256" on one side and " Ş" on the other side.

Betaserc/Serc tablet, 16 mg:
A round, biconvex, scored, almost white to white tablet with beveled edges. The diameter is 8.5 mm, the tablet weight is approximately 250 mg. The tablet inscriptions are "267" on either side of the score line and " Ş" on the other side.

The tablet can be divided into equal halves.

Betaserc/Serc tablet, 24 mg:
A round, biconvex, scored, almost white to white tablet with beveled edges. The diameter is 10 mm, the tablet weight is approximately 375 mg. The tablet inscriptions are "289" on either side of the score line and " Ş" on the other side.

The purpose of the scoreline is only to facilitate breaking for ease of swallowing and not intended to divide the tablet into two equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications
Ménière's Syndrome as defined by the following triad of core symptoms:

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

Symptomatic treatment of vestibular vertigo.

4.2 Posology and method of administration

8 and 16 mg tablets:
The dosage for adults is 24-48 mg divided over the day.

8 mg tablets	16 mg tablets
1 – 2 tablets 3 times/day	½ - 1 tablet 3 times/day

24 mg tablets:
The dosage for adults is 48 mg divided over the day.

24 mg tablets
1 tablet 2 times/day

The dosage should be individually adapted according to the response. Improvement can sometimes be observed only after a couple of weeks of treatment. The best results are sometimes obtained only after a few months. There are indications that treatment from the onset of the disease prevents the progression of the disease and/or the loss of hearing in later phases of the disease.

Pediatric population:
Betaserc/Serc is not recommended for use in children below 18 years of age due to insufficient data on safety and efficacy.

Geriatric population:
Although there are limited data from clinical studies in this patient group, extensive post marketing experience suggests that no dose adjustment is necessary in this patient population.

Renal impairment:
There are no specific clinical trials available in this patient group, but according to postmarketing experience no dose adjustment appears to be necessary.

Hepatic impairment:
There are no specific clinical trials available in this patient group, but according to postmarketing experience no dose adjustment appears to be necessary.

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients.
Phaeochromocytoma.

4.4 Special warnings and precautions for use
Patients with bronchial asthma and/or history of peptic ulcer need to be carefully monitored during the therapy.

4.5 Interaction with other medicinal products 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 expected.

As betahistine is an analogue of histamine, the interaction of betahistine with antihistamines may in theory affect the efficacy of one of these drugs.

4.6 Pregnancy and lactation
Pregnancy:
There are no adequate data for the use of betahistine in pregnant women.
Animal studies are insufficient with respect to effects on pregnancy, embryonal/foetal development, parturition and postnatal development. The potential risk for human foetuses and newborns is unknown. Betahistine should not be used during pregnancy unless clearly necessary.

Lactation:
It is not known whether betahistine is excreted in human milk. There are no animal studies on the excretion of betahistine in milk. The importance of the drug to the mother should be weighed against the benefits of nursing and the potential risks to the child.

4.7 Effects on ability to drive and use machines
Betahistine is regarded to have no or negligible influence on the ability to drive and use machines as no effects potentially influencing this ability were found to be related to betahistine in clinical studies.

4.8 Undesirable effects
The following undesirable effects have been experienced with the below indicated frequencies in betahistine-treated patients in placebo-controlled clinical trials: *very common* (≥1/10); *common* (≥1/100 to <1/10); *uncommon* (≥1/1,000 to <1/100); *rare* (≥1/10,000 to <1/1,000); *very rare* (<1/10,000).

Gastrointestinal disorders
Common: nausea and dyspepsia

Nervous system disorders
Common: headache*

*The incidence of headache in placebo-treated patients (5.9% in a pool of 457 patients) was similar to that of betahistine-treated patients (5.1% in a pool of 468 patients).

In addition to those events reported during clinical trials, the following undesirable effects have been reported spontaneously during postmarketing use and in scientific literature. A frequency cannot be estimated from the available data and is therefore classified as "not known".

Immune System disorders
Hypersensitivity reactions, e.g. anaphylaxis.

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.

Skin and subcutaneous tissue disorders
Cutaneous and subcutaneous hypersensitivity reactions, in particular angioneurotic oedema, urticaria, rash and pruritus.

4.9 Overdose
A few 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 drugs.

Treatment of overdose should include standard supportive measures.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Anti-vertigo preparations. ATC-Code: N07CA01

The mechanism of action of betahistine is partly known.

In biochemical studies, betahistine was found to have weak H_1 receptor agonistic and potent H_3 antagonistic properties in the CNS and autonomic nervous system. Pharmacological testing in animals has shown that 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 found to have a dose dependent inhibiting effect on spike generation of neurons in lateral and medial vestibular nuclei.

Betahistine accelerates vestibular recovery after unilateral neurectomy by promoting and facilitating central vestibular compensation; this effect, which is characterized by an up-regulation of histamine turnover and release, is mediated through H_3 Receptor antagonism.

Taken together, these properties contribute to the beneficial therapeutic effects of betahistine in Ménière's disease and vestibular vertigo.

Betahistine increases histamine turnover and release by blocking presynaptic H_3-receptors and inducing H_3-receptor downregulation. This effect on the histaminergic system provides explanation for the efficacy of betahistine in the treatment of vertigo and vestibular diseases.

5.2 Pharmacokinetic properties

Orally administered betahistine is readily and almost completely absorbed from all parts of the gastro-intestinal tract. After absorption, the drug is rapidly and almost completely metabolized into 2-PAA (which has no pharmacological activity). 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 plasma concentration of 2-PAA reaches its maximum 1 hour after intake. The half-life is approximately 3.5 hours. 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. 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. Under fed conditions C_{max} 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.

5.3 Preclinical safety data

Oral dosing up to and above 250 mg/kg in dogs and in rats respectively, of betahistine dihydrochloride administered during 3 months did not result in adverse effects. Side effects in the nervous system were seen in dogs and baboons after intravenous doses at and above 120 mg/kg. Emesis was observed at 300 mg/kg and 120 mg/kg following oral and IV dosing respectively in dogs and sporadically in baboons.
Betahistine has not shown any mutagenic effect.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Betaserc/Serc tablets contain microcrystalline cellulose, mannitol (E421), citric acid monohydrate, colloidal anhydrous silica and talc.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life
5 years.

6.4 Special precautions for storage
Store below 25°C.

Store in the original package in order to protect from light.

6.5 Nature and contents of container
Betaserc/Serc tablets are supplied in packages containing 10, 20, 30, 50, 60, 90, 100, 120, 500 or 1000 tablets (8 mg) or 10, 14, 15, 20, 28, 30, 40, 50, 56, 60, 100, 200, 300, 400 or 500 tablets (16 mg) or 10, 20, 30, 40, 50, 60 or 100 tablets (24 mg), packaged in press-through strips of PVC/PVDC and aluminum lidding foil.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling
Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Abbott Healthcare Products B.V., the Netherlands
C.J. van Houtenlaan 36, 1381 CP Weesp, The Netherlands

8. MARKETING AUTHORISATION NUMBER
-

9. DATE OF FIRST AUTHORISATION / RENEWAL OF AUTHORISATION
-

10. DATE OF REVISION OF THE TEXT