SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

For a full list of excipients see section 6.1

3. PHARMACEUTICAL FORM

Betaserc® tablet, 8 mg:
A round, flat, white to almost white tablet with beveled edges. The diameter is 7 mm; the tablet weight is about 125 mg. The inscription is 256 on one side and S on the other side.

Betaserc® tablet, 16 mg:
A round, biconvex, scored, white to almost white tablet with beveled edges. The diameter is 8.5 mm; the tablet weight is about 250 mg. The inscription is 267 on either side of the score and S on the other side.
The tablet can be divided into equal halves.

Betaserc® tablet, 24 mg:
A round, biconvex, scored, white to almost white tablet with beveled edges and relevant inscriptions. The diameter is 10 mm; the tablet weight is about 375 mg. The inscription is 289 on either side of the score and S on the other side.
The scoreline is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Ménière's Syndrome as defined by the following trias 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

Betaserc® tablets 8mg/ Betaserc® tablets 16mg:

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

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

Betaserc® tablets 24mg:
The dosage for adults is 48mg 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 only be observed after a couple of weeks of treatment. The best results are sometimes obtained 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.

Paediatric population:
Betaserc® is not recommended for use in children below 18 years due to insufficinet data on safety and efficacy.

Geriatric population:
Although there are limited data from clinical studies in this patient group, extensive post marketing experiance 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 post-marketing experience no dose adjustment appears to be necessary.

Hepatic impairment
There are no specific clinical trials available in this patient group, but according to post-marketing 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 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 on Cytochrome P450 enzymes is expected.

As betahistine is an analogue of histamine, 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 from the use of betahistine in pregnant women.
There are insufficient data from animal studies regarding effects on pregnancy, embryonal/fetal development, parturition and postnatal development. The potential risk for humans is not known. Betahistine should not be used during pregnancy unless clearly necessary.

Lactation
It is not known whether betahistine is excreted in human breast milk, neither has the excretion of betahistine in milk been studied in animals. Before administering betahistine to a breast-feeding mother, the potential risks to the infant must be carefully evaluated.

4.7 Effect 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 in comparison to 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 post-marketing 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 have been reported.

Gastrointestinal disorders
Mild gastric complaints (e.g. vomiting, gastrointestinal pain, abdominal distension and bloating) have been observed. 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 have been reported, in particular angioneurotic oedema, urticaria, rash, and prurituss

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 considerable H_3 antagonistic properties in the CNS and autonomic nervous system.
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 found to have a dose dependent inhibiting effect on spike generation of neurons in lateral and medial vestibular nuclei.
Betahistine accelerates the vestibular recovery after unilateral neurectomy, by promoting and facilitating central vestibular compensation; this effect characterized by an up-regulation of histamine turnover and release, is mediated via the H3 Receptor antagonism.
Taken together these properties contribute to its beneficial therapeutic effects in Ménière's disease and vestibular vertigo.
Betahistine increases histamine turnover and release by blocking presynaptic H3-receptors and inducing H3-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. Pharmacokinetic analyses are based on 2 PAA measurements in plasma and urine. The plasma concentration of 2 PAA reaches its maximum 1 hour after intake and declines with a half-life of about 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 faecal excretion of betahistine 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 affected. 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.

5.3 Preclinical safety data

Oral dosing up to 250 mg/kg/day betahistine dihydrochloride in rats 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/day. Emesis was seen after dosing at and above 120 mg/kg/day in dogs and sporadically in baboons.
Betahistine has not shown any mutagenic effect.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Betaserc® tablets contain microcrystalline cellulose, mannitol E421, citric acid monohydrate, colloidal anhydrous silica and talc.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

When stored in its original undamaged packaging, betahistine tablets are stable for 5 years at 25 °C (climate zones I and II) and for 3 years at 30 °C (climate zones III and IV).

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

Press-through strips PVC/PVDC and aluminium foil

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.
CJ. van Houtenlaan 36
NL-1381 CP Weesp
The Netherlands

8. MARKETING AUTHORISATION NUMBER

Betaserc 8mg – MA013/00502
Betaserc 16mg – MA013/00501
Betaserc 24mg – MA013/00503

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Betaserc 8mg – MA013/00502: 23 May 2006/ 14 December 2010
Betaserc 16mg – MA013/00501 23 May 2006/ 14 December 2010
Betaserc 24mg – MA013/00503 7 February 2008

10. DATE OF REVISION OF THE TEXT

November 2010