SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Betaserc 24 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
Betahistine dihydrochloride……24 mg
Equivalent to betahistine……15.63 mg

For the full list of excipients see section 6.1.

3. PHARMACEUTICAL FORM

A round, biconvex, scored, white to almost white tablet with beveled edges and relevant inscriptions. The diameter is about 10 mm; the tablet weight is about 375 mg. The standard inscription is 289 on either side of the score on one tablet-side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Symptomatic treatment of recurrent vertigo with or without cochlear signs.
Ménière's Syndrome as defined by the following core symptoms:
• vertigo (with nausea/vomiting)
• hardness of hearing or hearing loss
• tinnitus Symptomatic treatment of vestibular vertigo

4.2 Posology and method of administration

Posology:
The recommended starting dose is 24 mg betahistine.
If this dosage is insufficient, the maximum daily dose can be increased to 48 mg betahistine.

If the maximum daily dose of 48 mg is indicated, adults should take one 24 mg tablet twice per day (in the morning and in the evening).
The dosage should be individually adapted according to the response.

Paediatric population
The use of Betaserc 24 is not recommended in children up to the age of 18 years, because of a lack of sufficient data on safety and efficacy.

Older population
Although there is limited data available from clinical trials related to this patient group, extensive post-marketing experience suggests that no dose adjustment is necessary in this patient population.

Renal impairment

There is no specific data from clinical trials available for this patient group, but post-marketing experience suggests that no dose adjustment is necessary.

Hepatic impairment
There is no specific data from clinical trials available for this patient group, but post-marketing experience suggests that no dose adjustment is necessary.

Method of administration

Preferably to be swallowed with water during

meals.

Treatment duration

Improvement may sometimes only be observed after a few weeks of treatment. The best results are sometimes obtained after a number of months. There are indications that treatment from the beginning of the condition prevents the progression of the illness and/or hearing loss at a later phase of the illness.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1. Pheochromocytoma.

4.4 Special warnings and precautions for use

Patients with bronchial asthma and a history of peptic ulcer must be carefully monitored during treatment.

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 to be expected.

In vitro data indicate inhibition of betahistine metabolism by medicines that inhibit monoamine- oxidase (MAO), including MAO subtype B (e.g. selegiline). Caution is recommended with concomitant use of betahistine and MAO inhibitors (including selective MAO-B inhibitors).

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 Fertility, pregnancy and lactation

Pregnancy:
There are insufficient data on the use of betahistine in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity at clinically relevant therapeutic exposure.
As a precautionary measure, it is preferable to avoid the use of betahistine during pregnancy.

Breastfeeding:

It is not known whether betahistine is excreted in breast milk in humans. Betahistine is excreted in rat milk. The effects post-partum seen in animal studies were limited to very high doses. The importance of taking the medicine by the mother must be weighed against the benefits of breastfeeding and the potential risk for the child.

Fertility
Animal studies show no influence on fertility in rats.

4.7 Effects on ability to drive and use machines

Betahistine is indicated for Ménière's syndrome, which is defined by the following triad of core symptoms: vertigo, loss of hearing and tinnitus. The disease can negatively affect the ability to drive and use machines. In clinical studies specially devised to investigate the influence of betahistine on the ability to drive and use machines, no negative effects or negligible negative effects were observed.

4.8 Undesirable effects

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

Gastrointestinal disorders:
Common: nausea and dyspepsia.

Nervous system
disorders
Common:
headache.

In addition to these undesirable effects, which were reported during clinical trials, the following undesirable effects have been spontaneously reported during post-marketing use and in scientific literature. Frequency cannot be estimated from the available data and these undesirable effects are 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 usually be prevented by taking the dose during meals or reducing the dose.

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

Reporting of suspected adverse reactions

Reporting of suspected adverse reactions: Healthcare professionals are requested to report any suspected adverse reactions via the Pharmacy and Poisons Reporting System (PVERS) https://pv.pharmacyboardkenya.org

4.9 Overdose

A few cases of overdose have been reported. Some patients have experienced mild to moderate symptoms on doses of up to 640 mg (e.g. nausea, somnolence, abdominal pain).
More serious complications (e.g. convulsions, pulmonary or cardiac complications) have been observed following intentional overdose of betahistine, especially in combination with other overdosed medications.
Treatment of overdose should include standard supportive measures.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antivertigo preparations, ATC-code:

N07CA01 Mechanism of action
The mechanism of action of betahistine is only partially known. There are various plausible hypotheses which are supported by animal studies and by human data:

- Betahistine influences the histaminergic system:
  Betahistine works both as a partial histamine H1-receptor agonist and as a histamine H3-receptor antagonist, also in neuronal tissue, and has negligible H2-receptor activity. Betahistine increases the synthesis and release of histamine by blocking the presynaptic H3-receptors and inducing H3-receptor downregulation.
- Betahistine can cause an increase in the blood flow to both the cochlear environment and to the brain as a whole:
  Pharmacological studies in animals have shown that the blood flow in the stria vascularis of the inner ear improves, probably due to a relaxant effect on the precapillary sphincters of the microcirculation in the inner ear. It has also been shown that betahistine increases cerebral blood flow in humans.

- Betahistine facilitates vestibular compensation:
  Betahistine accelerates vestibular healing after unilateral neurectomy in animals by stimulating and facilitating central vestibular compensation; this effect, which is characterised by an increase in the synthesis and release of histamine, is mediated via the H3-receptor antagonism. The recovery period after vestibular neurectomy has also been reduced after treatment with betahistine in humans.

- Betahistine alters the neuron firing in the vestibular nuclei:
  It has also been discovered that betahistine has a dose-dependent inhibiting effect on the occurrence of neuron peaks in the 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.

Clinical efficacy and safety
The efficacy of betahistine has been demonstrated in studies of patients with vestibular vertigo and with Ménière's disease, as evidenced by improvements in the severity and frequency of vertigo attacks.

5.2 Pharmacokinetic properties

Absorption
Orally administered betahistine is readily and fully absorbed from all parts of the gastro-intestinal tract. After absorption, it is quickly and almost completely metabolised into 2-pyridylacetic acid (2- PAA). Plasma levels of betahistine are very low. Pharmacokinetic analyses are therefore based on 2-PAA measurements in plasma and urine.

The C_{max} is lower during food consumption than it is during fasting. However, the total absorption of betahistine is comparable in both circumstances, which indicates that food only slows 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 quickly and almost completely metabolised into 2-PAA (which has no pharmacological activity).
After oral administration of betahistine, the plasma (and urine) concentrations of 2-PAA reach their maximum levels 1 hour after administration and decline with a half-life of approximately 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 excreted in the urine. There is minor renal or faecal excretion of betahistine itself.

Linearity/non-linearity
Recovery rates over the oral dosage range of 8-48 mg are constant, which indicates that the pharmacokinetics of betahistine are linear and suggests that the metabolic trajectory involved is not saturated.

5.3 Preclinical safety data

Chronic toxicity
Adverse reactions affecting the central nervous system were seen in dogs and baboons after intravenous doses of 120 mg / kg and higher.

Studies on chronic oral toxicity over a period of 18 months in rats with a dose of 500 mg / kg and for 6 months in dogs with a dose of 25 mg / kg indicate that betahistine is well tolerated without definitive toxicity.

Mutagenic and carcinogenic potential Betahistine has no mutagenic capacity.

In an 18-month chronic toxicity study in rats with a dose up to 500 mg / kg, there was no evidence of carcinogenic potential.

Reproductive toxicity
During reproductive toxicity studies, effects were only seen at exposures considered to be well above the maximum human exposure, indicating minimal relevance during clinical use.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Betaserc 24 tablets contain microcrystalline cellulose, mannitol (E421), citric acid monohydrate, colloidal anhydrous silica and talc.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 30^0C. Store in the original container.

6.5 Nature and contents of container

Betaserc 24 tablets come in packs of 20, 50, 60 and 100 tablets, packaged in PVC/PVDC blister packs containing 10 to 20 tablets with a grey aluminum cover foil.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESS

Marketing Authorization Holder:

Abbott Laboratories S.A. (Pty) Ltd

Abbott Place, 219 Golf Club
Terrace Constantia Kloof
1709

South Africa.

Manufacturing Site Address:

Mylan Laboratories SAS

Route de Belleville, Lieu dit

Maillard, 01400 Chatillon-

sur-Chalaronne France.

8. MARKETING AUTHORISATION NUMBER

Country	**Registration Number**	**Distribution Category**
Kenya	H2021/CTD7355/14502	P.O.M
Tanzania	TZ19H0408	P.O.M

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE REGISTRATION

Date of first authorization: 9th February 2021

10. DATE OF REVISION OF THE TEXT

01/04/2026