APPROVED PROFESSIONAL INFORMATION FOR

BETAHISTINE 24 UNICORN

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

BETAHISTINE 24 UNICORN tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

BETAHISTINE 24 UNICORN**:** Each tablet contains 24 mg betahistine dihydrochloride.

Excipients with known effect: Each tablet contains 61,80 mg mannitol (a sugar alcohol).

For the full list of excipients, see **section 6.1**.

3. PHARMACEUTICAL FORM

BETAHISTINE 24 UNICORN: White colour, round & biconvex uncoated tablet scored on one side with the embossing "II" on either sides of the score and plain on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

BETAHISTINE 24 UNICORN is indicated for the symptomatic treatment of vertigo associated with Ménière's syndrome.

4.2 Posology and method of administration

Posology:

The usual dose is 24 mg to 48 mg of BETAHISTINE 24 UNICORN per day in divided doses. One 24 mg tablet can be administered twice daily.

The dosage should be individually adapted according to the response.

Paediatric population

BETAHISTINE 24 UNICORN should not be used in children and patients under the age of 18 since safety and efficacy have not yet been established.

Method of administration:

For oral use.

4.3 Contraindications

BETAHISTINE 24 UNICORN is contraindicated in:

- Patients with known hypersensitivity to betahistine or to any of the ingredients contained in BETAHISTINE 24 UNICORN (see **section 6.1**).
- Patients with phaeochromocytoma. Betahistine, a synthetic analogue of histamine, may induce the release of catecholamines from the tumour resulting in severe hypertension.

4.4 Special warnings and precautions for use

- Caution is advised in the treatment of patients with peptic ulcer or a history of peptic ulceration, because of the occasional dyspepsia observed in patients taking betahistine dihydrochloride.
- Patients with bronchial asthma should be monitored carefully for the duration of the treatment with BETAHISTINE 24 UNICORN.
- Caution is advised in prescribing BETAHISTINE 24 UNICORN to patients with either urticaria, rashes or allergic rhinitis, due to the possibility of aggravating these symptoms.
- Caution is advised in patients with severe hypotension.
- Caution is advised in patients with porphyria.

- If BETAHISTINE 24 UNICORN is to be administered subsequent to the treatment with an antihistamine and this treatment is stopped abruptly, withdrawal symptoms such as sleep disorders and agitation could appear due to the sedative action of antihistamines. Treatment with the antihistamine should be tapered over approximately six days.

4.5 Interaction with other medicines and other forms of interaction

There are no studies on the interactions with the following medicines: vasodilators, psychotropic medicines, in particular sedatives, tranquillisers and neuroleptics, parasympatholytics, and vitamins.
Based on available data, no inhibition on cytochrome-P450 enzymes is anticipated.

As betahistine is an analogue of histamine, BETAHISTINE 24 UNICORN should not be concomitantly administered with antihistamines as betahistine may in theory affect the efficacy of one of these medicines (see **section 4.3**).
The metabolism of BETAHISTINE 24 UNICORN may be inhibited by medicines that inhibit monoamine-oxidase (MAO) including MAO subtype B (e.g. selegiline). Caution is recommended when using BETAHISTINE 24 UNICORN and MAO inhibitors (including MAO-B selective) concomitantly.

4.6 Fertility, pregnancy and lactation

Pregnancy:

The safety of BETAHISTINE 24 UNICORN during pregnancy and breastfeeding has not been established.
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 human milk, however it has shown to be excreted in rat milk, however studies are limited to very high doses.

Fertility:

There is no data on fertility with BETAHISTINE 24 UNICORN.

4.7 Effects on the ability to drive and use machines

Vertigo, tinnitus and hearing loss associated with Ménière's syndrome can negatively affect the ability to drive and use machines.

Occasional drowsiness may occur as a side effect associated with the use of BETAHISTINE 24 UNICORN. Patients should therefore not drive, use machinery or perform any tasks that require concentration, until they are certain that BETAHISTINE 24 UNICORN does not adversely affect their ability to do so (see **section 4.8**).

4.8 Undesirable effects

System Organ Class	**Frequent**	**Less frequent**	**Frequency unknown**
Immune system disorders			Hypersensitivity reactions, e.g. anaphylaxis
Nervous system disorders	Headache	Head pressure	Occasional drowsiness
Cardiac disorders		Palpitations, tightness of the chest	
Respiratory, thoracic and mediastinal disorders		Exacerbation of pre-existing bronchial asthma	
Gastrointestinal disorders	Nausea, dyspepsia	Retching, heartburn, gastric discomfort and pain, flatulence	Mild gastric disorders including vomiting, gastrointestinal pain, abdominal distension and bloating have been observed. This can normally be avoided by taking BETAHISTINE 24 UNICORN with or

System Organ Class	Frequent	Less frequent	Frequency unknown
			after a meal, or by reducing the dosage.
Skin and subcutaneous tissue disorders			Cutaneous and subcutaneous hypersensitivity reactions, in particular angioneurotic oedema, urticaria rash, and pruritus

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of BETAHISTINE 24 UNICORN is important. It allows continued monitoring of the benefit/risk balance of BETAHISTINE 24 UNICORN. Health care providers are asked to report any suspected adverse reactions via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

Report all side effects to Unicorn Pharmaceuticals (Pty) Ltd to enquiries@unicornpharma.co.za

4.9 Overdose

Symptoms

In case of overdose, the following symptoms, similar to histamine overdose, might occur: headache, redness of the face, vertigo, tachycardia, hypotension, bronchial spasm, oedema, in particular oedema of betahistine especially in combination with other overdosed medicines.

Treatment

There is no specific antidote to BETAHISTINE 24 UNICORN. Treatment of overdose should include standard supportive measures.

5. PHARMACOLOGICAL PROPERTIES

Category and class: A 5.6 Histamine

Pharmacotherapeutic group: Anti-vertigo preparations.

ATC Code: N07CA01

5.1 Pharmacodynamic properties

Pharmacodynamic properties:

Betahistine is an analogue of histamine.

Betahistine may increase blood flow to the cochlear region as well as to the whole brain:

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 affects the histaminergic system:

In pharmacological studies, betahistine was found to have weak H_1 receptor agonistic and considerable H_3 antagonistic properties in the central nervous system and the autonomic nervous system.

Betahistine facilitates vestibular compensation:

Betahistine accelerates the vestibular recovery after unilateral neurectomy in animals, by promoting and facilitating central vestibular compensation; this effect characterized by an up-regulation of histamine turnover and release, is mediated via the H_3 Receptor antagonism. In human subjects, recovery time after vestibular neurectomy was also reduced when treated with betahistine.

Betahistine alters neuronal firing in the vestibular nuclei:

Betahistine was also found to have a dose dependant inhibiting effect on spike generation of neurons in lateral and medial vestibular nuclei.

5.2 Pharmacokinetic properties:

Absorption

Following oral administration betahistine is well absorbed from all parts of the gastro-intestinal tract. After absorption, betahistine is rapidly 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 blood and urine.

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.

Distribution

There is little or no binding to plasma proteins. The percentage of betahistine that is bound by blood plasma proteins is less than 5 %.

Biotransformation

After oral administration of betahistine the plasma (and urinary) concentration of 2-PAA reaches its maximum within an hour after intake and declines with a half-life of about 3,5 hours.

Elimination

Betahistine is excreted in urine as the metabolite 2-pyridylacetic acid within 24 hours. No unchanged betahistine has been detected. Betahistine is excreted in breast milk at approximately the same level as found in plasma.

In the dose range of 8 - 48 mg, about 85 % of the original dose is recovered in the urine. Renal or faecal excretion of betahistine itself is of minor importance.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Inactive ingredients:

Citric acid anhydrous, mannitol, microcrystaline cellulose, colloidal anhydrous silica and talc.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years.

6.4 Special precautions for storage

Store at or below 25 °C.

Keep the blister strips in the outer carton until required for use.

6.5 Nature and contents of container

Pack size: 20 tablets

Blister pack

The tablets are packed in PVC/PVDC/Al foil blisters, which is standard pharmaceutical packaging. The blister pack comprises 25 µm hard temper lidding foil and 250 µm clear PVC film with 120gsm clear PVdC coating.

HDPE pack

Round white opaque high density polyethylene bottle with a polypropylene screw closure with an induction seal liner containing tablets.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Unicorn Pharmaceuticals (Pty) Ltd

Corner of Searle & Pontac Streets

Cape Town

South Africa 8001

8. REGISTRATION NUMBER

BETAHISTINE 24 UNICORN: 55/5.6/0469

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10 October 2023

10. DATE OF REVISION OF THE TEXT

Not applicable.