

## SUMMARY OF PRODUCT CHARACTERISTICS

### 1. NAME OF THE MEDICINAL PRODUCT

Betahistin Actavis 16mg Tablets

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One tablet contains 16 mg Betahistine dihydrochloride

One tablet contains 140 mg lactose monohydrate.

For a full list of excipients, see section 6.1

### 3. PHARMACEUTICAL FORM

Tablet.

White or almost white round tablet. Embossed B16 on one side, scored reverse.

The tablet can be divided into equal halves.

### 4. CLINICAL PARTICULARS

#### 4.1 Therapeutic indications

Betahistine is indicated for the treatment of Ménière's syndrome, symptoms of which may include vertigo, tinnitus, hearing loss and nausea

#### 4.2 Posology and method of administration

*Dosage*

Adults (including the elderly):

Initial oral treatment is 8 to 16 mg three times daily, taken with food.

Maintenance doses are generally in the range of 24 - 48 mg daily. Dosage can be adjusted to suit individual patient needs. Sometimes improvement can be observed after only a couple of weeks of treatment.

Children and adolescents:

Betahistine tablets are not recommended for use in children and adolescents below the age of 18 years due to lack of data on safety and efficacy.

#### 4.3 Contraindications

Betahistine is contraindicated in patients with phaeochromocytoma. As betahistine is a synthetic analogue of histamine it may induce the release of catecholamines from the tumor resulting in severe hypertension.

Also contraindicated in the cases of:

- hypersensitivity to the active substance or to any of the excipients.

#### **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 reported in patients taking betahistine.

Caution should be exercised when administering the drug to patients with bronchial asthma.

Caution is advised in prescribing betahistine to patients with either urticaria, rashes or allergic rhinitis, because of the possibility of aggravating these symptoms.

Caution is advised in the treatment of patients with severe hypotension.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

#### **4.5 Interaction with other medicinal products and other forms of interaction**

There are no proven cases of hazardous interactions.

There is a case report of an interaction when betahistine was taken with ethanol as well as a compound containing both pyrimethamine and dapsone, and another report of the potentiation of the effect of betahistine when it was taken together with salbutamol.

As betahistine is an analogue of histamine, interaction with antihistamines is theoretically possible, but none have been reported.

#### **4.6 Pregnancy and lactation**

Animal studies are insufficient with respect to effects on pregnancy, embryonal/foetal development, parturition and postnatal development (see section 5.3). The potential risk for humans is unknown.

Betahistin Actavis 16mg Tablets is not recommended for use in pregnant women.

Betahistine is excreted in breast milk in concentrations similar to those found in plasma. The toxic effects of betahistine in neonates at these concentrations are not known. The use of betahistine should therefore be avoided in patients who are breast feeding. See section 5.3.

#### **4.7 Effects on ability to drive and use machines**

Rare reports of drowsiness associated with betahistine have been made. Patients should be advised that if they are affected in this way they should avoid activities requiring concentration, such as driving and operating machinery.

#### **4.8 Undesirable effects**

Immune system disorders:

Very rare (<1/10,000): skin rashes and pruritus

Nervous system disorders:  
Unknown: headaches, and occasional drowsiness

Gastrointestinal disorders:  
Rare (>1/10,000, <1/1,000): gastro-intestinal upset, nausea and dyspepsia

#### **4.9 Overdose**

The symptoms of betahistine overdose are nausea, vomiting, dyspepsia, ataxia and seizures at higher doses. There is no specific antidote. Gastric lavage and symptomatic treatment are recommended.

### **5 PHARMACOLOGICAL PROPERTIES**

#### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: antivertigo preparation, ATC code: N07C A01

Betahistine's H<sub>1</sub>-agonist activity at histamine receptors in peripheral blood vessels has been demonstrated in man by the abrogation of betahistine-induced vasodilation with the histamine antagonist diphenhydramine. Betahistine has minimal effects on gastric acid secretion (an H<sub>2</sub>-receptor mediated response).

The mechanism of action of betahistine in Ménière's syndrome is unclear. The efficacy of betahistine in the treatment of vertigo may be due to its ability to modify the circulation of the inner ear or due to a direct effect on the neurons of the vestibular nucleus.

Single oral doses of up to 32mg betahistine in normal subjects produced maximal suppression of induced vestibular nystagmus 3 to 4 hours post-dose, with larger doses being more effective in reducing the nystagmus duration.

Pulmonary epithelial permeability in man is increased by betahistine. This has been demonstrated by a reduction in the time of clearance from the lung to blood of a radioactive marker. This action is prevented by oral pre-treatment with terfenadine, a known H<sub>1</sub>-receptor blocker.

Whilst histamine has positive inotropic effects on the heart, betahistine is not known to increase cardiac output and its vasodilator effect may produce a small fall in blood pressure in some patients.

In man, betahistine has little effect on exocrine glands

#### **5.2 Pharmacokinetic properties**

Betahistine is completely absorbed after oral administration, and in fasting subjects peak plasma concentrations of <sup>14</sup>C-labelled betahistine are attained after approximately one hour of oral administration.

Elimination of betahistine takes place mainly by metabolism and the metabolites are subsequently eliminated mainly by renal excretion. 85-90% of the radioactivity of an 8 mg dose appears in the urine over 56 hours, with maximum excretion rates attained within 2 hours of administration. After oral administration, betahistine plasma levels

are very low. Therefore, the assessment of the pharmacokinetics of betahistine is based on the plasma concentration data of the only metabolite 2-pyridylacetic acid.

There is no evidence of presystemic metabolism and biliary excretion is not considered to be an important route of elimination for the drug or any of its metabolites. Little or no binding occurs with human plasma proteins, however betahistine is subject to metabolism in the liver. Approximately 80-90% of the administered dose is excreted in the urine.

### **5.3 Preclinical safety data**

Repeated dose toxicity studies of six months duration in dogs and 18 months duration in albino rats revealed no clinically relevant harmful effects at dose levels in the range 2.5 to 120 mg.kg<sup>-1</sup>. Betahistine is devoid of mutagenic potential and there was no evidence of carcinogenicity in rats. Tests conducted on pregnant rabbits showed no evidence of teratogenic effects.

## **6 PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Povidone K90, microcrystalline cellulose, lactose monohydrate, colloidal anhydrous silica, crospovidone and stearic acid.

### **6.2 Incompatibilities**

Not applicable.

### **6.3 Shelf life**

3 years

### **6.4 Special precautions for storage**

Store below 25°C in the original package.

### **6.5 Nature and contents of container**

Alu/PVC/PVDC blister strips. Available in packs of 20, 42, 50, 60 and 84 tablets. Not all pack sizes may be marketed.

### **6.6 Special precautions for disposal**

No special requirements.

## **7 MARKETING AUTHORISATION HOLDER**

Actavis Group Hf  
Reykjavikurvegur 76-78  
220 Hafnarfjordur  
Iceland

**8      MARKETING AUTHORISATION NUMBER**

MA651/00202

**9      DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION**

20-12-2006

**10     DATE OF REVISION OF THE TEXT**