Summary Product Characteristics for Pharmaceutical Products

1.Name of the medicinal product

Ebamine 10mg tablet
Ebastine Oral Solution 5 mg/5ml

2.Qualitative and quantitative composition

Ebamine 10mg tablet
Each film coated tablet contains Ebastine BP 10 mg

Ebastine Oral Solution 5 mg/5ml
Each 5 ml syrup contains: Ebastine BP 5 mg.

For the full list of excipients, see section 6.1

3. Pharmaceutical form

Ebamine 10mg tablet
Film coated tablet A light yellow colored, round shaped, biconvex film coated tablet, one side being scored and another side being IPI engraved.

Ebastine Oral Solution 5 mg/5ml
Colorless, clear, flavored syrup. Free from any visible foreign particles

4.Clinical particulars

4.1 Therapeutic indications

Ebamine is indicated for the symptomatic treatment of:
- Seasonal and perennial allergic rhinitis
- Idiopathic chronic urticaria

4.2 Posology and method of administration

For oral administration Posology
One tablet (10mg) once-a-day (up to 20 mg once-a-day in severe cases such as Perennial Allergic Rhinitis).
One tablet (10mg) once-a-day for Idiopathic chronic urticaria:

Children (2-5 years of age): 2.5 ml once daily (upto 5 ml in severe cases such as Perennial Allergic Rhinitis).
Children (6-12 years of age): 5 ml once daily (upto 10 ml in severe cases such as Perennial Allergic Rhinitis).
Method of administration
Ebastine may be taken with or without food.

4.3 Contraindications

Patients with a known hypersensitivity to Ebastine or any of its ingredients

4.4 Special warnings and precautions for use

It is advisable to exercise caution when using ebastine in patients

known to have the following conditions: long QT syndrome, hypokalaemia, treatment with any medicine known to produce an increase in QT interval or inhibit CYP3A4 enzyme systems such as azole antifungals and macrolide antibiotics. Use in Pregnancy and Lactation The safety of ebastine during pregnancy and lactation has not been established. Ebastine should not be used during pregnancy only if clearly needed. It is not known whether ebastine is excreted in milk, therefore, ebastine should not be used during lactation

4.5 Interaction with other medicinal products and other forms of interaction

The interaction of ebastine in combination with either ketoconazole or erythromycin (both known to prolong the QTc interval) has been evaluated. A significant pharmacokinetic and pharmacodynamic interaction has been observed with this combination; an 18-19 msec (4.7% – 5%) increase in QTc has been reported with either combination. Ebastine does not interact with the kinetics of theophylline, warfarin, cimetidine, diazepam or alcohol. The sedation effect of alcohol and diazepam may be enhanced. When ebastine is administered with food, there is a 1.5 to 2.0 fold increase in the plasma levels and the AUC of the main active acid metabolite of ebastine. This increase does not alter the Tmax. The administration of ebastine with food does not cause a modification in its clinical effect.

4.6 Fertility, pregnancy and lactation

The safety of Ebastine during human pregnancy has not been established.

No teratogenic effects have been identified in animals. However, there are no well controlled studies in pregnant women and reproductive studies are not always predictive of human response.

Therefore, ebastine should be used during pregnancy only if clearly needed, category B1.

Ebastine is not recommended for nursing women, because it is not known whether is excreted in human milk.

4.7 Effects on ability to drive and use machines

Ebastine at recommended therapeutic doses does not affect the ability to drive or operate machines.

4.8 Undesirable effects

The adverse reactions reported in association with the use of Ebastine presented according to system organ classes in a decreasing frequency, are listed below. According to frequency, reported adverse reactions have been classified in the category very rare (<1/100000).

Cardiac disorders: Palpitations, tachycardia.

Gastrointestinal disorders: Dry mouth, dyspepsia, abdominal pain, nausea, vomiting.

General disorders and administration site conditions: Asthenia, oedema.

Hepatobiliary disorders: Liver function test abnormal.
Infections and Infestations: Pharyngitis, rhinitis, sinusitis.
Nervous system disorder: Somnolence, headache, dizziness, dysaesthesia.
Psychiatric disorders: Insomnia, nervousness.
Reproductive system and breast disorders: Menstrual disorders.
Respiratory, thoracic and mediastinal disorders: Epistaxis.
Skin and subcutaneous tissue disorders: Rash, urticaria, dermatitis

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system

4.9 Overdose

No clinically meaningful signs or symptoms were observed up to 100 mg given once daily. There is no specific antidote for Ebastine. In case of accidental overdoses, gastric lavage, monitoring of vital functions including ECG and symptomatic treatment should be carried out.

5.Pharmacological properties

5.1 Pharmacodynamic properties

Ebastine has been shown to produce a rapid and long-lasting inhibition of histamine induced effect and to have a strong affinity towards H1-receptors.

Following oral administration neither ebastine nor its metabolites cross the blood brain barrier. This characteristic is consistent with the low sedative profile seen in the results of experiments studying the effects of ebastine on the central nervous system.

In vitro and in vivo data demonstrate that ebastine is a potent, long lasting and highly selective histamine H1- receptor antagonist devoid of untoward CNS actions and anticholinergic effects.

Clinical: Histamine skin wheal studies have shown a statistically and clinically significant anti-histamine effect beginning at 1 hour and lasting in excess of 48 hours. After the discontinuation of the administration of a 5 day-course of treatment with ebastine, the anti-histamine activity remained apparent for more than 72 hours. This activity parallels the plasma levels of the main active acid metabolite, carebastine.

After repeated administration, inhibition of the peripheral receptors remained at a constant level, without tachyphylaxis. These results suggest that ebastine at a dose of at least 10 mg produces a rapid, intense and long-lasting inhibition of peripheral H1-histamine receptors, consistent with a once-a-day administration.

Sedation was studied through pharmaco-EEG, cognitive performance, visual-motor co-ordination tests and subjective estimates. There was no significant increase of sedation at the recommended dose. These results are consistent with those from double-blind clinical trials; the incidence of sedation is comparable between placebo and ebastine. The actions of ebastine on the heart have been investigated in clinical trials. No influence on the heart, including prolongation of the QT interval, has been observed at the recommended doses. In two studies using repeated doses up to 100 mg per day or 500 mg as a single dose, with a limited number of subjects (n=24 and n=5) small increases in heart rate of a few beats per minute resulted in a shortening of the QT interval with no significant effect of the appropriately corrected QTc

5.2 Pharmacokinetic properties

Ebastine is rapidly absorbed and undergoes extensive first pass metabolism following oral administration. Ebastine is almost totally converted to the pharmacologically active acid metabolite, carebastine.

After a single 10 mg oral dose, peak plasma levels of the metabolite occur at 2.6 to 4 hours and achieve levels of 80 to 100 mg/ml.

The half-life of the acid metabolite is between 15 to 19 hours with 66% of the drug

being excreted in the urine mainly as conjugated metabolites. Following the repeated administration of 10 mg once-daily, steady state was achieved in 3 to 5 days with peak plasma levels ranging from 130 to 160 mg/ml.

In vitro studies with human liver microsomes show that ebastine is metabolised to carebastine predominantly via the CYP3A4 pathway. Concurrent administration of ebastine with ketaconazole or erythromycin (both CYP3A4 inhibitors) to healthy volunteers was associated with significantly increased plasma concentrations of ebastine and carebastine

Both ebastine and carebastine are highly protein bound, >95%.

In elderly subjects, no statistically significant changes were observed in the pharmacokinetics compared to those of young adult volunteers.

In patients with mild, moderate or severe renal insufficiency and in patients with mild to moderate hepatic insufficiency treated with daily doses of 20 mg of ebastine, as well as in patients with severe hepatic insufficiency treated with 10 mg of ebastine, the pharmacokinetic behaviour was not relevantly modified in comparison with healthy subjects. In patients with mild to moderate renal insufficiency, mean carebastine exposure was higher than that observed in healthy volunteers, whereas the plasma concentrations of this metabolite in patients with severe renal failure and in patients with mild, moderate or severe hepatic insufficiency were similar to those observed in healthy subjects. The elimination half-lives of ebastine and carebastine in all groups of patients were in the same range as those of healthy subjects.

Taking into account the high intraindividual variability of both parent drug and metabolite, as well as the wide therapeutic margin, the variations observed in the pharmacokinetic parameters are not likely to be of any clinical significance.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development. Fertility and the duration of gestation were not impaired.

6.Pharmaceutical particulars

6.1 List of excipients

Ebamine 10mg tablet

Microcrystalline Cellulose (PH 102)
Crospovidone (Type-A)
Sodium Starch Glycolate (Type A)
Sodium Lauryl Sulfate
Colloidal Silicon Dioxide
Magnesium Stearate
Hypromellose
Propylene Glycol
Titanium Dioxide
Lemon Yellow Colour
Methanol
Methylene Chloride

Ebastine Oral Solution 5 mg/5ml

Glycerin
Sucrose
Liquid Sorbitol
Methylparaben
Propylparaben
Citric Acid Monohydrate
Saccharin Sodium
Propylene Glycol
Polysorbate 80
Flavour Raspberry Liquid
Purified Water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 Months

6.4 Special precautions for storage:

Store below 30°C.Protected from direct sunlight.

6.5 Nature and contents of container

Ebamine 10mg tablet

Alu-Alu blister pack of 1x10s, packed in a unit boxes, with literature

insert.
Ebastine Oral Solution 5 mg/5ml
50ml Amber coloured PET bottle , packed in a unit boxes, with literature insert

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

7. Marketing authorisation holder and manufacturing site addresses

Marketing authorization holder:
Medcure Healthcare Limited.
Address: P.O Box 14609-00400 Nairobi-Kenya.

Manufacturing site address:
The IBN SINA Pharmaceutical Industry Ltd.
Address: Shafipur, Kaliakoir, Gazipur, Bangladesh People's Republic of Bangladesh

8. Marketing authorization number

9. Date of first registration
Day-Month- Year

10. Date of revision of the text:

11. Dosimetry:
Not Applicable

12. Instructions for Preparation of Radiopharmaceuticals:
Not Applicable