SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Ebastine Tablet 20 mg

EROSTIN 20

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains:

Ebastine BP ……20 mg

Excipient(s) with known effect: 93.000 mg of lactose monohydrate/tablet

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Film-coated tablets

Light yellow colored, circular, biconvex, film-coated tablet**s**

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the symptomatic treatment of severe seasonal and perennial allergic rhinitis or rhinocojunctivitis.

4.2 Posology and method of administration

Dosage

The following dosage recommendations apply to adults: 1 film-coated tablet (20 mg ebastine) once a day in the case of severe symptoms of allergic rhinitis. For patients with milder symptoms, 1 film-coated tablet containing 10 mg ebastine once a day is recommended.

Ebastine 20 mg film-coated tablets are available for this purpose.

Children and adolescents

For children over 12 years of age, the same dosage recommendations apply as for adults.

Elderly patients

No dose adjustment is necessary.

Patients with hepatic or renal impairment

No dose adjustment is required in patients with mild, moderate or severe renal or hepatic impairment.

There is no experience with doses above 10 mg in patients with severe hepatic impairment; therefore, a dosage of 10 mg should not be exceeded in these patients.

Method of administration

For oral use. The film-coated tablets should be swallowed whole with some liquid. Ebastine can be taken with or without food.

Duration of use

The doctor decides on the duration of use. Clinical application experience of up to one year is available for allergic rhinitis.

4.3 Contraindications

Hypersensitivity to the active ingredient or to any of the excipients included in section 6.1.

4.4 Special warning and precautions

Pharmacokinetic interactions may occur when ebastine is co-administered with imidazole-type antifungals such as ketoconazole and itraconazole, or macrolide antibiotics such as erythromycin, or anti-tuberculosis drugs such as rifampicin (see section 4.5). Therefore, Ebastine should be prescribed with caution in combination with medicines containing these active ingredients.

Caution is advised in patients with severe hepatic impairment (see sections 4.2 and 5.2). Ebastine film-coated tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Interaction studies of ebastine with ketoconazole, itraconazole or erythromycin (drugs known to prolong the QTc interval) have shown interactions in the form of higher plasma levels of ebastine and, to a lesser extent, higher levels of carebastine. However, the latter were not associated with clinically significant pharmacodynamic effects. Compared to the administration of ketoconazole or erythromycin alone, only about 10 msec longer increase in the QTc interval was observed. However, as a precautionary measure, particular attention should be paid to the prescription of ebastine in patients receiving concomitant imidazole-type antifungal drugs such as ketoconazole and itraconazole, or macrolide antibiotics such as erythromycin. Pharmacokinetic interactions occurred when ebastine was administered with rifampicin. These interactions could lead to lower plasma levels and a reduction in the antihistaminic effect. Interactions of ebastine with theophylline, warfarin, cimetidine, diazepam or alcohol have not been observed.

With food, there is a 1.5- to 2.0-fold increase in plasma levels of carebastine, the major active metabolite of ebastine, and in AUC, while T_{max} remains unchanged. However, this does not affect the clinical efficacy.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are limited data for Ebastine in pregnant women. Animal studies do not indicate direct or indirect harmful effects on reproductive toxicity. As a precaution, ebastine should be avoided during pregnancy.

Breast- feeding

It is not known whether ebastine is excreted in human milk. The high protein binding (< 97%) of ebastine and the major metabolite carebastine do not suggest excretion of the drug in breast milk. As a precaution, ebastine should be avoided while breastfeeding.

Fertility

There are no human fertility data for ebastine.

4.7 Effects on ability to drive and use machine

The psychomotor functions in humans have been extensively studied, but no effects could be determined. At the recommended therapeutic doses, Ebastine has no or negligible influence on the ability to drive and use machines. However, in order to identify susceptible individuals who react unusually to ebastine, it is advisable to know the individual reactions before a patient drives a car or performs complicated activities: somnolence and dizziness may occur (see section 4.8).

4.8 Undesirable effects

In a joint analysis of placebo-controlled clinical trials carried out in 5,708 patients treated with ebastine, the most frequently reported adverse reactions were headache, dry mouth and drowsiness.

The adverse reactions notified in clinical trials in children (n = 460) were similar to those observed in adults.

Adverse reactions associated with ebastine that have been reported in clinical trials and post-marketing surveys are listed below according to MedDRA system organ class and in descending order of frequency. Frequencies are defined as follows: 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), not known (cannot be estimated from the available data).

system organ class	**frequency**	**side effect**
diseases of the immune system	Rarely	Hypersensitivity reactions (such as anaphylaxis and angioedema)
Metabolic and nutritional disorders	Not known	appetite increase
Psychiatric Illnesses	Rarely	nervousness, insomnia
Diseases of the nervous system	Very often	headache
	Frequently	sleepiness
	Rarely	Dizziness, hypoaesthesia, taste disturbance
heart diseases	Rarely	palpitations, tachycardia
Diseases of the gastrointestinal tract	Frequently	dry mouth
	Rarely	Abdominal pain, vomiting, nausea, dyspepsia
Liver and	Rarely	Hepatitis, cholestasis,

biliary diseases		liver function test abnormal (transaminases, gamma-GT, alkaline phosphatase and bilirubin increased)
Skin and subcutaneous tissue disorders	Rarely	Urticaria, rash, dermatitis
Diseases of the reproductive system and the mammary gland	Rarely	menstrual cramps
General disorders and administration site conditions	Rarely	edema, asthenia
investigations	Not known	weight gain

4.9 Overdose

In studies with high doses up to 100 mg once daily, there were no clinically relevant symptoms or signs of overdose.

A specific antidote for ebastine is not known. In the event of overdose, monitoring of vital signs including ECG monitoring with QT interval assessment for at least 24 hours, symptomatic treatment and gastric lavage are indicated.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Other antihistamines for systemic use, ATC code: R06A X22

Preclinical

In in vitro and in vivo studies, ebastine exhibits high affinity for H_1 receptors, which are inhibited selectively and rapidly for a prolonged period.

There is only a slight impairment of central functions; the risk of anticholinergic effects occurring is low, but cannot be completely ruled out by the available studies. After oral administration, neither ebastine nor the active metabolite cross the blood-brain barrier. This finding is consistent with the only minor sedative effects found in studies of the possible effects of ebastine on the CNS.

In vitro and in vivo data indicate that ebastine is a potent and long-acting, highly selective histamine H_1 antagonist with no CNS affecting effects and no anticholinergic effects.

Clinical Characteristics

Wheal tests demonstrated a statistically and clinically significant antihistamine effect that started after 1 hour and lasted for more than 48 hours. After stopping a 5-day ebastine medication, the antihistamine effect remained detectable for more than 72 hours. This effect was mirrored in plasma levels of the major active metabolite, carebastine.

After repeated administration, inhibition of peripheral receptors remained at a constant level, without tachyphylaxis. These results suggest that ebastine produces rapid, intense and long-lasting inhibition of peripheral H_1 -histamine receptors at doses of at least 10 mg, allowing for once-daily dosing.

The sedating effect was examined using pharmaco-EEG, perception tests, visual-motor coordination tests and by means of subjective assessment. At the therapeutically recommended dose, there was no significant increase in sedation. These findings are consistent with the results of double-blind clinical studies: the frequency of sedative effects of ebastine is comparable to that of placebo.

The cardiac effects of ebastine have been studied in clinical studies. No cardiac side effects, including QT interval prolongation, have been observed at the prescribed dose.

Repeated administration of up to 100 mg daily or 500 mg as a single dose resulted in a small increase in heart rate of a few beats per minute. This resulted in a shortening of the QT interval with no significant effect on the correspondingly corrected QTc interval.

5.2 Pharmacokinetic Properties

Ebastine is rapidly absorbed and undergoes extensive first-pass metabolism after oral administration. It is almost completely converted to the active metabolite, carebastine. The half-life of the active metabolite is 15-19 hours, 66% of which is excreted in the urine as conjugated metabolites.
After a single oral administration of a single dose of 20 mg ebastine, the highest plasma levels of ebastine occurred after 1 to 3 hours with a mean value of 2.8 ng/ml. The highest plasma levels of the metabolite carebastine reached a mean of 157 ng/ml.

Compared to 2 x 10 mg ebastine, taking a 20 mg tablet results in higher plasma levels. In particular, the value for C_{max} (90% confidence interval: 107.3 - 132.5) exceeded the limits usually defined for bioequivalence.

Protein binding of both ebastine and carebastine is greater than 97%.
In vitro studies with human liver microsomes show that the metabolism of ebastine to carebastine occurs primarily via the CYP450-3A4 enzyme system. Significant increases in plasma levels of ebastine and carebastine have been observed with concomitant administration of ketoconazole or erythromycin (both CYP450 3A4 inhibitors) (see section 4.5).
Elderly patients

The pharmacokinetics are not altered in elderly patients compared to younger adults.
Patients with hepatic or renal impairment.

In patients with mild, moderate, or severe renal impairment, as well as in patients with mild to moderate hepatic impairment, treated with ebastine 20 mg daily, the plasma concentrations of

ebastine and carebastine were similar on the first and fifth day of treatment similar to those obtained in healthy volunteers.

In patients with mild, moderate or severe renal impairment treated with a daily dose of ebastine 20 mg and in patients with mild to moderate hepatic impairment treated with a daily dose of ebastine 20 mg or in patients who have severe hepatic impairment and treated with 10 mg ebastine, the plasma levels of ebastine and carebastine on the first and fifth day of treatment were comparable to those in healthy volunteers. It can be concluded that the pharmacokinetic profile of ebastine and its metabolites does not change significantly in patients with different degrees of renal or hepatic insufficiency.

5.3 Preclinical safety Data

The findings occurring in animal studies on the toxicity of repeated administration to rats and dogs at higher doses are not expected at doses for human therapeutic use.

Reproductive toxicity studies on rats and mice gave no indication of embryotoxic effects. There was no impairment of fertility and gestation duration.

Ebastine has been tested in vitro and in vivo in a standard battery of mutagenicity tests. The tests were negative and gave no indication of a mutagenic potential. Likewise, long-term carcinogenicity studies on rats and mice did not provide any indication of a carcinogenic potential.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose
Pregelatinised starch
Lactose
Croscarmellose sodium
Magnesium stearate

Hypromellose HPMC 15 CPS)
Talc
Titanium dioxide
Iron oxide yellow
Polyethylene glycol 6000

6.2 Incompatibilities

Not applicable

6.3 Shelf life:

36 Months

6.4 Special precautions for storage

Keep below 30°C. Keep out of reach of children.

6.5 Nature and contents of container

Blister pack of 10 tablets

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 Authorization Holder

MICRO LABS LIMITED
31, Race Course Road
Bangalore-560001
INDIA

8. Marketing Authorization Numbers

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9. Date of first authorization

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10. Date of revision of the text

July 2022