Ebastine

Kestine® 20 mg Film-coated Tablet

Antihistamine

FORMULATION:
Each Ebastine (Kestine®) Film-coated tablet contains:
Ebastine ……..…….. 20mg

Excipients: microcrystalline cellulose, pregelatinised maize starch, lactose monohydrate, croscarmellose sodium, magnesium stearate, hypromellose, macrogol and titanium dioxide.

PHARMACEUTICAL FORM AND CONTENT OF PACKAGE:
Round, white film-coated tablets with one side marked E20. Boxes containing 10 (1x10), 20 (2x10) 30 (3x10), 50 (5x10) and 100 (10x10) tablets in PVC/Aluminium blisters.
Not all the presentations are available in all markets.

INDICATION:
EBASTINE (Kestine®) is indicated in the treatment of allergic rhinitis (seasonal and perennial) with or without allergic conjunctivitis.

MECHANISM OF ACTION:
EBASTINE (Kestine®) produces rapid and prolonged inhibition of the effects induced by histamines, showing a strong afinity for binding to H1 receptors. After oral administration, neither EBASTINE (Kestine®) nor it's metabolites cross the blood-brain barrier. This characteristic is consistent with the low sedation observed in the results of experiments in which the effects of EBASTINE (Kestine®) on the central nervous system were studied.
The in vitro and in vivo data demonstrate that EBASTINE (Kestine®) is a powerful antagonist with a prolonged effect and highly selective of the histamine H1 receptors, free of CNS side effects and anticholinergic effects.

PHARMACOKINETIC PROPERTIES:
Absorption

- Ebastine is rapidly absorbed and undergoes extensive hepatic and intestinal first pass metabolism after oral administration.

- Ebastine is almost totally converted into the pharmacologically active metabolite, carebastine.

- Administration of ebastine with food increases the plasma levels of carebastine 1.5 to 2.0 fold.

- After a single 10 mg oral dose, peak plasma level of the metabolite (Cmax) occurs at 2 to 4 hours and achieves a mean value of 80 to 100 ng/mL.

- The half-life of carebastine is between 15 and 19 hours with 66% of the drug being excreted in the urine mainly as conjugated metabolites.

- Following repeated administration of 10 mg once-daily, steady state is achieved in 3 to 5 days with peak plasma levels ranging from 130 to 160 ng/mL. Given the linear and dose proportional

pharmacokinetic behavior of ebastine, the plasma levels of the metabolite following administration of 20 mg oral doses are 2-fold higher than those of 10 mg.

- Ebastine and carebastine are highly protein bound : > 97%.

Elderly

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

Patients with renal and hepatic impairment

Ebastine and carebastine plasma concentrations obtained on the first and fifth day of treatment in patients in studies of slight, moderate or severe renal impairment (daily doses of 20 mg), and in those of slight and moderate hepatic impairment (both with doses of 20 mg/day) or severe hepatic impairment (dose of 10 mg/day) were similar to those reached in healthy volunteers, indicating that the pharmacokinetic profile of ebastine and its metabolite do not undergo significant changes in patients with various degrees of hepatic or renal impairment.

DOSAGE AND ADMINISTRATION:

For oral use. EBASTINE (Kestine®) 20 mg film-coated tablets may be taken with or without food. Tablets must be swallowed whole with a small amount of water.

Adults and children over 12 years of age	- The usual dose is 10 mg of ebastine once daily, but some patients may require a dose of 20mg once daily.
Children 12 years old and below	- The safety of ebastine film-coated tablets has not been established for children under 12 years of age.
For Elderly	- not necessary to adjust dose.
For patients with Renal Impairment	- not necessary to adjust dose
For patients with Liver Impairment	- not necessary to adjust dose but in patients with liver failure a dose of 10 mg /day should not be exceeded

SPECIAL PRECAUTIONS:

Administer with caution in patients with known cardiac risk such as prolongation of the QT interval, hypokalemia, concomitant treatment with drugs which increase the QT interval or which inhibit the CYP3A4 enzyme, such as azole antifungal and macrolide antibiotics.
Given that Ebastine (Kestine®) achieves its therapeutic effect between 1 and 3 hours after administration, it should not be used to treat acute allergic emergencies.
Pharmacokinetic interactions could occur when administering ebastine with rifampicin.

Ebastine should be used with caution in patients with severe hepatic impairment.

Warnings about excipients:
This medicine contains lactose. Patients with hereditary galactose intolerance, Lapp lactase deficiency or glucosegalactose malabsorption should not take this medicinal product.

FERTILITY, PREGNANCY AND LACTATION:
Fertility: There are no fertility data associated with ebastine in humans.
Pregnancy: The safety of EBASTINE (Kestine®) for use during pregnancy has not been established. Therefore, EBASTINE (Kestine®) should only be used during pregnancy if the potential benefit justifies the potential risk to the foetus.
Lactation: It is not known whether ebastine is excreted in mother's milk. The high degree of binding to proteins (> 97%) of ebastine and its main metabolite, carebastine, suggests that the medication is not excreted in mother's milk. As a precautionary measure it is preferable to avoid the use of EBASTINE (Kestine®) during lactation.

UNDESIRABLE EFFECTS:
The following adverse effects have been observed in clinical trials and in post-marketing experience:

Very frequent (they could affect more than 1 in every 10 persons):
- Headache

Frequent (they could affect up to 1 in every 10 persons):
- Drowsiness
- Dry mouth

Rare (they could affect up to 1 in every 1,000 persons):
- Hypersensitivity reactions (like anaphylaxis and angioedema)
- Restlessness, insomnia
- Dizziness, decreased sensation of touch or sensitivity, decreased or altered taste
- Palpitations, tachycardia
- Abdominal pain, vomiting, nausea, digestive problems
- Liver disorders, anomalies in hepatic function analytic tests (raised transaminases, gamma-GT, alkaline phosphatase and bilirubin)
- Urticaria, rash, dermatitis
- Menstrual irregularities
- Oedema, fatigue

Consult your doctor or pharmacist if you observe any adverse reaction, even if it is not described in this patient information leaflet.
EFFECTS OF ABILITY TO DRIVE AND USE OF MACHINERY:
Psychomotor function has been studied extensively in humans without any effect being observed at the recommended therapeutic doses.
Based on these results, at recommended therapeutic doses, EBASTINE (Kestine®) does not affect the ability to drive or operate machines.
However, in sensitive subjects who react unusually to ebastine, it is advisable to know the individual reactions before a patient drives or carries out complicated activities: somnolence or dizziness may occur.

INTERACTION WITH OTHER MEDICINAL PRODUCTS:
The interaction of EBASTINE (Kestine®) in combination with Ketoconazole or Erythromycin has been studied. With both combinations, a pharmacokinetic and pharmacodynamic interaction has been observed, leading to an increase in the plasma levels of EBASTINE, although the increase in QTc was only approximately 10 ms greater than that observed with Ketoconazole and Erythromycin alone. It is therefore recommended that EBASTINE (Kestine®) be administered with caution to patients on concomitant treatment with Ketoconazole and Erythromycin.

When EBASTINE (Kestine®) is administered with food, both the plasma levels and the AUC of the principal metabolite of EBASTINE increased between 1.5 and 2-fold. This increase does not alter the Tmax. The administration of EBASTINE (Kestine®) with food does not alter its clinical effect.
EBASTINE (Kestine®) may interfere with the results of allergy skin tests, and it is therefore recommended that 5-7 days be allowed after stopping treatment before carrying out these tests. It may enhance the effects of other antihistamines.

Pharmacokinetic interactions have been observed when administering ebastine with rifampicin. These interactions can give rise to a decrease in plasma concentrations and a reduction of the antihistamine effects.

There are no described interactions between ebastine and theophylline, warfarin, cimetidine, diazepam and alcohol.

OVERDOSAGE:
In studies carried out with high doses, no clinically significant signs or symptoms were observed at doses of up to 100mg once a day. There is no specific antidote for EBASTINE. The need for performing a gastric lavage, monitoring vital signs, including ECG, and symptomatic treatment, should be considered.

CONTRAINDICATION:
Hypersensitivity to EBASTINE or any of the excipients.

CAUTION:
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

STORAGE:
Store at temperatures not exceeding 30°C.

Reg. No.:
SIN: XXXXXXXX
MAL: XXXXXXXX

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Date of revision of the text: 02/2015