SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the pharmaceutical product:

HISTY® SYRUP

Ebastine Syrup 5mg/5ml

2. Structure & Composition:

Each 5ml contains:

Ebastine BP 5 mg

Flavoured Syrupy Base q.s.

(for the full list of excipients, see section 6.1)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

3. Pharmaceutical form:

A Clear Colourless syrup

4. Clinical particulars

4.1. Therapeutic indications

Ebastine is indicated for the symptomatic treatment of:

• allergic rhinitis (seasonal and perennial) whether or not associated with allergic conjunctivitis

• Idiopathic chronic urticaria

4.2. Posology and method of administration

Posology

Children between 2 and 5 years: 2.5 ml (half teaspoonful) once daily (up to 5 ml in severe cases such as perennial allergic rhinitis).

Children between 6 and 11 years: 5 ml (one teaspoonful) once daily (up to 10 ml in severe cases such as perennial allergic rhinitis).

Adults and older children more than 11 years: 10 ml (two teaspoonfuls) once daily.

Method of administration

For oral use.

HISTY® SYRUP may be taken with or without food.

4.3. Contraindications

Hypersensitivity to the active substance or to any of the excipients.

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.

• Do not drive if you experience drowsiness after taking this medicine.

• Avoid alcohol intake with Ebastine.

• Ebastine should be used with caution in patients with severe hepatic insufficiency.

• It is probably unsafe to take this medicine if you are breastfeeding because no specific -information is available on the safety of this medicine.

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. Pregnancy and lactation

Pregnancy:

There are limited data amount of data from the use of ebastine in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure it is preferable to avoid the use of ebastine during pregnancy.

Breastfeeding

It is not known whether the Ebastine is excreted in human breast milk. As a precautionary measure, it is preferable to avoid the use of Ebastine during lactation.

4.7. Effects on ability to drive and use machines.

Ebastine has negligible influence on the ability to drive and use machines.

4.8. Undesirable effects

Cardiac disorders: Tachycardia, Palpitations

Gastrointestinal disorders: Dry mouth, Nausea, Abdominal pain, Dyspepsia, Vomiting

General disorders: Asthenia, Oedema

Hepatobiliary disorders: Abnormal liver function test

Respiratory, thoracic and mediastinal disorders: Pharyngitis, Rhinitis,

Sinusitis, Epistaxis

Nervous system disorders: Somnolence, Headache, Dizziness, Dysaesthesia
Psychiatric disorders: Insomnia, nervousness

Reproductive system and breast disorders: Menstrual disorders

Skin and subcutaneous tissue disorders: Urticaria, Rash, 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 pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org'.

4.9. Overdose.

In studies with a high dosage up to 100 mg once daily, no clinically significant symptoms or signs of overdose were seen. A specific antidote for Ebastine is not known. In the event of overdose, monitoring of vital functions, including ECG, symptomatic treatment are indicated.

5. Pharmacological properties

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: other anti-histamines for systemic use

ATC code: R06AX22

Pre-clinical:

Ebastine has been shown to produce a rapid and long-lasting inhibition of histamine- induced effect and to have a strong affinity towards H1receptors.

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 longlasting 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

Absorption

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

Biotransformation/Elimination

Ebastine is almost totally converted to its active metabolite, carebastine. After an oral dose of 10 mg ebastine, maximum plasma levels of 80 to 100 ng/ml carebastine were observed after 2.6 to 4 hours. The half-life of the metabolite is 15- 19 hours, 66% of which is excreted in urine in the form of conjugated metabolites. After repeated administration of a daily dose of 10 mg, steady state with plasma levels of 130- 160 ng/ml is reached after 3 to 5 days. After a single 20 mg oral dose, peak plasma levels of ebastine occur at 1 to 3 hours and achieve a mean level of 2.8 ng/ml. Peak plasma levels of the metabolite, carebastine, achieve a mean value of 157 ng/ml. More than 95% of both ebastine and carebastine is bound to plasma proteins. In vitro studies on human hepatic microsomes show that ebastine is metabolised to carebastine predominantly via the CYP450 (-2J2,-4F12 and-3A4) enzyme systems.

After concomitant administration of ketoconazole or erythromycin (both inhibitors of CYP450-3A4) significant increases in plasma ebastine and carebastine concentrations were observed.

In elderly patients, no changes in pharmacokinetics were observed compared with young adults. 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 ebastine, the plasma concentrations of ebastine and carebastine on the first and fifth day of treatment were similar to those obtained in healthy volunteers. In patients with renal insufficiency, the elimination half-life of the metabolite, carebastine is prolonged to 23 - 26 hours. In patients with hepatic insufficiency, the half-life is 27 hours.

5.3. Preclinical safety data

Non-clinical data in rats and mice reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction.

6. Pharmaceutical particulars

6.1. List of Excipients:

Sugar

Sodium Methyl Paraben

Sodium Propyl Paraben

Sucralose

Saccharin Sodium

Citric Acid

Sodium Benzoate

Acrysol 150

Glycerin

Flavour Liquid Mixed Fruit

Xanthan Gum FNCS

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

36 Months

6.4. Special precautions for storage

Store below 30°C, protect from direct sunlight, heat and moisture.

6.5. Nature and contents of container

Histy® Syrup is available in a pack of 60ml bottle.

6.6. Special precautions for disposal and other

Any unused medicine product or waste material should be disposed of in accordance with the local requirements.

7. MARKETING AUTHORISATION HOLDER

Krishna Chemists Ltd

3rd Floor Metrix Hardware, Lusaka Road, Industrial Area.

Nairobi, Kenya.

8. MARKETING AUTHORISATION NUMBER(S)

CTD5971

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorisation: 13.10.2021

10. DATE OF REVISION OF THE TEXT

13.10.2021