DEST

5mg Tablets U.S.P.
0.5mg/mL Syrup

(Desloratadine)

QUALITATIVE AND QUANTITATIVE COMPOSITION
DEST 5mg Tablets U.S.P.
Each film-coated tablet contains:
Desloratadine U.S.P. 5mg
DEST Syrup 0.5mg/mL
Each mL contains:
Desloratadine U.S.P. 0.5mg

DESCRIPTION: Desloratadine is a non-sedating, long-acting histamine antagonist with selective peripheral H_1-receptor antagonist activity.

Pharmacodynamic properties

Pharmacotherapeutic group: antihistamines – H_1 antagonist

Mechanism of action: Desloratadine is a non-sedating, long-acting histamine antagonist with selective peripheral H1-receptor antagonist activity. After oral administration, desloratadine selectively blocks peripheral histamine H_1-receptors because the substance is excluded from entry to the central nervous system. Desloratadine has demonstrated antiallergic properties from in vitro studies. These include inhibiting the release of proinflammatory cytokines such as IL-4, IL-6, IL-8, and IL-13 from human mast cells/basophils, as well as inhibition of the expression of the adhesion molecule P-selectin on endothelial cells. The clinical relevance of these observations remains to be confirmed.

PHARMACOKINETICS

Absorption: Desloratadine plasma concentrations can be detected within 30 minutes of administration. Desloratadine is well absorbed with maximum concentration achieved after approximately 3 hours; the terminal phase half-life is approximately 27 hours. The degree of accumulation of desloratadine was consistent with its half-life (approximately 27 hours) and a once daily dosing frequency. The bioavailability of desloratadine was dose proportional over the range of 5 mg to 20 mg. In a series of pharmacokinetic and clinical trials, 6 % of the subjects reached a higher concentration of desloratadine. The prevalence of this poor metaboliser phenotype was comparable for adult (6 %) and paedi-atric subjects 2- to 11-year old (6 %), and greater among Blacks (18 % adult, 16 % paediatric) than Caucasians (2 % adult, 3 % paediatric) in both populations. In a pharmacokinetic trial in which patient demographics were comparable to those of the general seasonal allergic rhinitis population, 4 % of the subjects achieved a higher concentration of desloratadine. This percentage may vary according to ethnic background. Maximum desloratadine concentration was about 3-fold higher at approximately 7 hours with a terminal phase half-life of approximately 89 hours. The safety profile of these subjects was not different from that of the general population. Similar pharmacokinetic parameters were observed in a multiple-dose pharmacokinetic study conducted with the Oral Solution formulation in paediatric poor metaboliser subjects 2- to 11-year old diagnosed with allergic rhinitis. The exposure (AUC) to desloratadine was about 6-fold higher and the Cmax was about 3 to 4 fold higher at 3-6 hours with a terminal half-life of approximately 120 hours. Exposure was the same in adult and paediatric poor metabolisers when treated with age-appropriate doses. The overall safety profile of these subjects was not different from that of the general population. The effects of desloratadine in poor metabolizers < 2 years of age have not been studied. In separate single dose studies, at the recommended doses, paediatric patients had comparable AUC and C_{max} values of desloratadine to those in adults who received a 5 mg dose of desloratadine Oral Solution. **Distribution:** Desloratadine is moderately bound (83%-87%) to plasma proteins. There is no evidence of clinically relevant medicine accumulation following once daily dosing of desloratadine (5 mg to 20 mg) for 14 days. In a single dose, crossover study of desloratadine, the tablet and the Oral Solution formulations were found to be bioequivalent. As oral solution contains the same concentration of desloratadine, no bioequivalence study was required and it is expected to be equivalent to the Oral Solution and tablet. **Biotransformation:** The enzyme responsible for the metabolism of desloratadine has not been identified yet, and therefore, some interactions with other medicinal products cannot be fully excluded. Desloratadine does not inhibit CYP3A4 in vivo, and in vitro studies have shown that the medicinal product does not inhibit CYP2D6 and is neither a substrate nor an inhibitor of P-glycoprotein. **Elimination:** In a single dose trial using a 7.5 mg dose of desloratadine, there was no effect of food (high-fat, high caloric breakfast) on the disposition of desloratadine. In another study, grapefruit juice had no effecton the disposition of desloratadine. **Renally impaired patients:** The pharmacokinetics of desloratadine in patients with chronic renal insufficiency (CRI) was compared with that of healthy subjects in one single dose study and one multiple dose study. In the single dose study, the exposure to desloratadine was approximately 2 and 2.5-fold greater in subjects with mild to moderate and severe CRI, respectively, than in healthy subjects. In the multiple-dose study, steady state was reached after Day 11, and compared to healthy subjects the exposure to desloratadine was ~1.5-fold greater in subjects with mild to moderate CRI and ~2.5-fold greater in subjects with severe CRI. In both studies, changes in exposure (AUC and Cmax) of desloratadine and 3-hydroxydesloratadine were not clinically relevant.

INDICATION: DEST Tablet is indicated in adults and adolescents aged 12 years and older and DEST Oral Solution is indicated in adults, adolescents and children over the age of 1 year for the relief of symptoms associated with:
- allergic rhinitis
- urticaria

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

INTERACTIONS: Caution is recommended if alcohol is taken concomitantly.
Paediatric population: Interaction studies have only been performed in adults.

USE IN SPECIFIC POPULATION
Pregnancy Category C: A large amount of data on pregnant women (more than 1,000 pregnancy outcomes) indicate no malformative nor foeto/ neonatal toxicity of desloratadine. 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 Desloratadine during pregnancy. **Breast feeding:** Desloratadine has been identified in breastfed newborns/infants of treated women. The effect of desloratadine on newborns/infants is unknown. A decision must be made whether to discontinue breastfeeding or to discontinue/abstain from Desloratadine therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman. **Fertility:** There are no data available on male and female fertility.

WARNINGS AND PRECAUTIONS: In the case of severe renal insufficiency, Desloratadine should be used with caution. Desloratadine should be administered with caution in patients with medical or familial history of seizures, and mainly young children, being more susceptible to develop new seizures under desloratadine treatment. Healthcare providers may consider discontinuing desloratadine in patients who experience a seizure while on treatment. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose galactose malabsorption should not take this medicine. Paediatric population In children below 2 years of age, the diagnosis of allergic rhinitis is particularly difficult to distinguish from other forms of rhinitis. The absence of upper respiratory tract infection or structural abnormalities, as well as patient history, physical examinations, and appropriate laboratory and skin tests should be considered. Approximately 6% of adults and children 2- to 11-year old are phenotypic poor metabolisers of deslorata-dine and exhibit a higher exposure. The safety of desloratadine in children 2- to 11-years of age who are poor metabolisers is the same as in children who are normal metabolisers. The effects of desloratadine in poor metabolisers < 2 years of age have not been studied.

ADVERSE REACTIONS: Increased appetite, Hallucinations, Abnormal behaviour, aggression Headache, Dizziness, somnolence, insomnia, psychomotor hyperactivity, seizures, Tachycardia, palpitations, QT prolongation, Dry mouth, Abdominal pain, nausea, vomiting, dyspepsia, diarrhoea, Elevations of liver enzymes, increased bilirubin, hepatitis Jaundice, Photosensitivity, Myalgia, Fatigue Hypersensitivity reactions (such as anaphylaxis, angioedema, dyspnoea, pruritus, rash, and urticaria), Weight increased, Asthenia

DOSAGE AND ADMINISTRATION
Posology Tablet: Adults and adolescents (12 years of age and over) The recommended dose of Desloratadine is one tablet once a day. Intermittent allergic rhinitis (presence of symptoms for less than 4 days per week or for less than 4 weeks) should be managed in accordance with the evaluation of patient's disease history and the treatment could be discontinued after symptoms are resolved and reinitiated upon their reappearance. In persistent allergic rhinitis (presence of symptoms for 4 days or more per week and for more than 4 weeks), continued treatment may be proposed to the patients during the allergen exposure periods. **Paediatric population:** There is limited clinical trial efficacy experience with the use of desloratadine in adolescents 12 through 17 years of age. The safety and efficacy of Desloratadine 5 mg film coated tablets in children below the age of 12 years have not been established. **Posology Syrup:** Adults and adolescents (12 years of age and over) The recommended dose of Desloratadine is 10 ml (5 mg) oral solution once a day. **Paediatric population:** The prescriber should be aware that most cases of rhinitis below 2 years of age are of infectious origin and there are no data supporting the treatment of infectious rhinitis with Desloratadine. **Children 1 through 5 years of age:** 2.5 ml (1.25 mg) Desloratadine oral solution once a day. **Children 6 through 11 years of age:** 5 ml (2.5 mg) Desloratadine oral solution once a day. The safety and efficacy of Desloratadine 0.5 mg/ml oral solution in children below the age of 1 year have not been established. There is limited clinical trial efficacy experience with the use of desloratadine in children 1 through 11 years of age and adolescents 12 through 17 years of age. Intermittent allergic rhinitis (presence of symptoms for less than 4 days per week or for less than 4 weeks) should be managed in accordance with the evaluation of patient's disease history and the treatment could be discontinued after symptoms are resolved and reinitiated upon their reappearance. In persistent allergic rhinitis (presence of symptoms for 4 days or more per week and for more than 4 weeks), continued treatment may be proposed to the patients during the allergen exposure periods. **Method of administration:** Oral use. The dose can be taken with or without food. **Overdose:** The adverse event profile associated with overdosage, as seen during post marketing use, is similar to that seen with therapeutic doses, but the magnitude of the effects can be higher. **Treatment:** In the event of overdose, consider standard measures to remove unabsorbed active substance. Symptomatic and supportive treatment is recommended. Desloratadine is not eliminated by haemodialysis; it is not known if it is eliminated by peritoneal dialysis. **Symptoms:** Based on a multiple dose clinical trial, in which up to 45 mg of desloratadine was administered (nine times the clinical dose), no clinically relevant effects were observed. **Paediatric population:** The adverse event profile associated with over dosage, as seen during post marketing use, is similar to that seen with therapeutic doses, but the magnitude of the effects can be higher.

INSTRUCTIONS
TABLET: Dosage as directed by the physician. Store below 30°C. Protect from heat, light and moisture.
SYRUP (For oral use only): Dosage as directed by the physician. Store below 30°C. Protect from heat and light. Shake well before use. Tighten the cap securely after use.

Keep all medicines out of the reach of children. Do not freeze. To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:
DEST 5mg tablets U.S.P. are available in Alu-Alu Blister 1x10's pack with leaf insert.
DEST 0.5mg/mL Syrup is available in 60mL Amber Pet bottle with leaf insert.

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