SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Eslotin 2.5 mg/5 ml Syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Substance:

Desloratadine	2.5 mg/5 ml

Excipients:

Sodium methyl parahydroxybenzoate

Sodium propyl parahydroxybenzoate

Saccharose

Sunset yellow (E 110)

Glycerol

Propylene glycol

Citric acid monohydrate

Trisodium Citrate

Disodium edetate

For excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Syrup

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ESLOTIN is indicated in relieving the symptoms such as sneeze, nasal discharge and itching, congestion / nasal congestion, itching, lachrymation and redness on eyes, itching on the palate and coughing related to allergic rhinitis.

ESLOTIN is also indicated in relieving the symptoms such as itching co-existing with urticaria, exanthema and redness on skin.

4.2 Posology and method of administration

Posology/ frequency and time of administration

Intermittent allergic rhinitis, which presence of symptoms for less than 4 days per week or for less than 4 weeks, should be treated 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, which 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

The drug is presented with a transparent plastic measuring cup one side striped 2.5-5-7.5-10-15-20, the other side striped 1.25- 6.25-8.75-11.25-13.75-16.25 in the box.

Children 6 through 11 months of age: 2.0 ml (1 mg) ESLOTIN once a day with or without food in order to relieve symptoms associated with allergic rhinitis including intermittent and persistent allergic rhinitis, urticaria.

Use the measuring cup by filling up to 2 ml.

Children 1 through 5 years of age: 2.5 ml (1.25 mg) ESLOTIN once a day with or without food in order to relieve symptoms associated with allergic rhinitis including intermittent and persistent allergic rhinitis, urticaria.

Use the measuring cup by filling up to 2.5 ml.

Children 6 through 11 years of age: 5.0 ml (2.5 mg) ESLOTIN once a day with or without food in order to relieve symptoms associated with allergic rhinitis including intermittent and persistent allergic rhinitis, urticaria.

Use the measuring cup by filling up to 5 ml.

In adults and adolescents (12 years of age and over): 10.0 ml (5 mg) ESLOTIN once a day with or without food in order to relieve symptoms associated with allergic rhinitis including intermittent and persistent allergic rhinitis, urticaria.
Use the measuring cup by filling up to 10 ml.

Additional information relating to specific populations

Renal impairment

It should be used carefully in patients with severe renal impairment.

Liver impairment

There is no data related to use in patients with liver impairment.

Pediatric population

Method of administration for pediatric population is presented above.

Geriatric population

Efficacy and safety in geriatric population have not been determined yet.

4.3 Contraindications

It is contraindicated in patients with hypersensitivity to the active substance, to any of the excipients, or to loratadine.

4.4 Special warnings and precautions for use

Efficacy and safety of Desloratadine in children under 6 months of age have not been established. (See. Section 5.1)
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 medical 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 desloratadine 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 under age of 2 years of age have not been examined.

ESLOTIN should be used carefully in patients with severe renal impairment. (See section 5.2).

Sodium methyl parahydroxybenzoate and Sodium propyl parahydroxybenzoate:

It may cause allergic reactions (probably delayed). This medicinal product contains sodium less than 1 mmol (23 mg); in other words ‘it does not contain sodium ‘ basically.

Saccharose:

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not use this medicine.

Sunset Yellow (E110):

It may cause allergic reactions.

Glycerol:

This medicinal product contains 250 mg/5 ml glycerol. Since it contains glycerol less than 10 g/dose, it does not require any warning.

Propylene glycol:

This medicinal product contains 420 mg/5 ml propylene glycol. Since it contains propylene glycol less than 200 mg/kg for children and 400 mg/kg for adults, it does not require any warning.

4.5 Interaction with other medicinal products and other forms of interaction

No clinically relevant interactions were observed in clinical trials with desloratadine in which erythromycin or ketoconazole were co-administered.

In a clinical pharmacology trial, desloratadine taken concomitantly with alcohol did not potentiate the performance impairing effects of alcohol (see section 5.1).

Desloratadine interacts with contraceptive drugs taken orally. Therefore, an alternative, efficient and safe birth control method should be administrated during the treatment.

4.6 Pregnancy and lactation

General advice

Its pregnancy category is C.

Women of childbearing potential / Birth control (Contraception)

Desloratadine interacts with contraceptive drugs taken orally. Therefore, an alternative, efficient and safe birth control method should be administrated during the treatment.

Gestation period

There is no enough information about use of Desloratadine for pregnant women. There is no reproductive toxicity in animal studies.

Potential risk for human is unknown (See section 5.3). Therefore, the use of ESLOTIN during pregnancy is not recommended.

Lactation period

In case of administration of Desloratadine at therapeutic doses, desloratadine is excreted into breast milk and that may cause effect on child in the breast. ESLOTIN is not used breastfeeding period.

Reproductive ability/ Fertility

There is not reproductive toxicity in studies performed on animals.

Potential risk for human is not known.

4.7 Effects on ability to drive and use machines

The effect of desloratadine on the ability to drive and machine was not observed. However,

patients should be informed that very rarely some people experience drowsiness, which may affect their ability to drive or use machines.

4.8 Undesirable effects

In clinical trials in a paediatric population, the desloratadine was given to a total of 246 children aged 6 months through 11 years. The overall incidence of adverse events in children 2 through 11 years of age was similar for groups used the desloratadine and the placebo. In infants and toddlers aged 6 to 23 months, the most frequent adverse events reported in excess of placebo were diarrhoea (3.7 %), fever (2.3 %) and insomnia (2.3 %).

At the recommended dose, in clinical trials involving adults and adolescents in a range of indications including allergic rhinitis and chronic idiopathic urticaria, undesirable effects were reported in 3 % of patients used desloratadine in excess of those treated with placebo. The most frequent of adverse events reported in excess of placebo were fatigue (1.2 %), dry mouth (0.8 %) and headache (0.6 %).

Undesirable cases are listed in below according to system organ class. Frequencies are defined as;

For different organ systems,

Very common (≥ 1/10), common (≥ 1/100 and < 1/10), uncommon (≥ 1/1,000 and <1/100), rare (≥1/10,000 and <1/1,000), very rare (<1/10,000), unknown (it may not be predicted with available data).

Nervous system disorders

Common: Fatigue

Uncommon: Headache

Gastrointestinal disorders

Uncommon: Dry mouth

Post-marketing experience:

Other undesirable effects reported very rarely at the post-marketing period are listed below.

Psychiatric disorders

Very rare: Hallucinations

Nervous system disorders

Very rare: Dizziness, somnolence, insomnia, psychomotor hyperactivity, seizures

Cardiac disorders

Very rare: Tachycardia, palpitations

Gastrointestinal disorders

Very rare: Abdominal pain, nausea, vomiting, dyspepsia, diarrhoea

Hepatobiliary disorders

Very rare: Elevations of liver enzymes, increased bilirubin and hepatitis

Musculoskeletal disorders, connective tissue and bone diseases

Very rare: Myalgia

General disorders and administration site conditions

Very rare: Hypersensitivity reactions (such as anaphylaxis, angioedema, dyspnoea, pruritus, rash, and urticaria)

4.9 Overdose

In the event of overdose, standard measures should be taken to remove unabsorbed active substance.

Symptomatic and supportive treatment is recommended.

Based on a multiple dose clinical trial in adults and adolescents, in which up to 45 mg of desloratadine was administered (nine times of the clinical dose), no clinically relevant effects were observed.
Desloratadine is not eliminated by haemodialysis; it is not known whether or not it is eliminated by peritoneal dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: other antihistamines used systemic
ATC code: R06AX27

Mechanism of action:
Desloratadine is a non-sedating, long-acting histamine antagonist with selective peripheral H_1-receptor antagonist activity. After oral administration, desloratadine selectively blocks peripheral histamine H_1-receptors because it is excluded from entry to the central nervous system.

Desloratadine has demonstrated antiallergic properties in *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 has not been confirmed yet.

Efficacy of desloratadine syrup has not been investigated in separate paediatric trials. The safety of Desloratadine was demonstrated in three paediatric trials. Children, 6 month through 1 years of age, who were candidates for antihistamine treatment received a daily desloratadine dose of 1 mg (6 through 11 month), 1.25 mg (1 through 5 years of age) or 2.5 mg (6 through 11 years of age).

Treatment was well tolerated as documented by clinical laboratory tests, vital signs, and ECG interval data, including QTc (corrected QT). When given at the recommended doses, the pharmacokinetic activity of desloratadine was comparable in the paediatric and adult populations. Since the course of allergic rhinitis/chronic idiopathic urticaria and the profile of desloratadine are similar in adults and paediatric patients, efficacy of desloratadine in adults may be extrapolated to the paediatric population.

In a multiple dose clinical trial in which up to 20 mg of desloratadine was administered daily for 14 days, no statistically or clinically relevant cardiovascular effect was observed. In a clinical pharmacology trial in which desloratadine was administered to adults at a dose of 45 mg daily (nine times of the clinical dose) for ten days, no prolongation of QTc (duration between Q wave and T wave in ECG) interval was seen.

Desloratadine does not readily penetrate the central nervous system. There was no excess incidence of somnolence as compared to placebo at the recommended dose of 5 mg daily. Desloratadine tablets, daily dose of 7.5 mg, did not affect psychomotor performance in clinical trials. In a single dose study, desloratadine 5 mg did not affect standard measures of flight performance including exacerbation of subjective sleepiness or tasks related to flying.

In clinical pharmacology trials in adults, co-administration with alcohol did not increase the alcohol-induced impairment in performance or increase in sleepiness. No significant differences were found in the psychomotor test results between desloratadine and placebo groups. When desloratadine are taken whether alone or with alcohol, it has not increased the performance deterioration of alcohol.

No clinically relevant changes in desloratadine plasma concentrations were observed in multiple-dose ketoconazole and erythromycin interaction trials.

In adult and adolescent patients with allergic rhinitis, desloratadine tablets were effective in relieving symptoms such as sneezing, nasal discharge and itching, as well as ocular itching, tearing and redness, and itching of palate.

Allergic rhinitis may alternatively be classified as intermittent allergic rhinitis and persistent allergic rhinitis according to the duration of symptoms. Intermittent allergic rhinitis may be defined as the presence of symptoms for less than 4 days per week or for less than 4 weeks. Persistent allergic rhinitis may be defined as the presence of symptoms for 4 days or more per week and for more than 4 weeks.

Desloratadine tablets were effective in alleviating the burden of seasonal allergic rhinitis as shown by the total score of the rhino-conjunctivitis quality of life questionnaire. The greatest amelioration was seen in the domains of practical problems and daily activities limited by symptoms.

Chronic idiopathic urticaria was studied as a clinical model for urticarial conditions, since the underlying pathophysiology is similar, regardless of etiology, and because chronic patients may be more easily recruited prospectively. Since histamine release is a causal factor in all urticarial diseases, desloratadine is expected to be effective in providing symptomatic relief for other urticarial conditions, in addition to chronic idiopathic urticaria, as advised in clinical guidelines.

In two placebo-controlled six week trials in patients with chronic idiopathic urticaria, desloratadine was effective in relieving pruritus and decreasing the size and number of hives by the end of the first dosing interval. In each 2 trials, the effects were sustained over the 24 hour dosing interval. As with other antihistamine trials in chronic idiopathic urticaria, the minority of patients who were identified as non-responsive to antihistamines was excluded. An improvement in pruritus of more than 50 % was observed in 55 % of patients treated with desloratadine compared with 19 % of patients treated with placebo. Treatment with Desloratadine also significantly reduced interference with sleep and daytime function, as measured by a four-point scale used to assess these variables.

5.2 Pharmacokinetic properties

General properties

Absorption:

Desloratadine plasma concentrations may be detected within 30 minutes of desloratadine administration in adults and adolescents. Desloratadine is well absorbed with maximum concentration achieved after approximately 3 hours. The terminal phase half-life of Desloratadine 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.

Distribution:

In a series of pharmacokinetic and clinical trials, 6 % of the volunteers reached a higher concentration of desloratadine. The prevalence of this poor metaboliser phenotype was comparable for adult (6 %) and paediatric 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 multiple-dose pharmacokinetic study conducted with the tablet formulation in healthy adult subjects, four volunteers were found to be poor metabolisers of desloratadine. These volunteers had a C_{max} concentration about 3-fold higher at approximately 7 hours with a terminal phase half-life of approximately 89 hours.

Similar pharmacokinetic parameters were observed in a multiple-dose pharmacokinetic study conducted with the syrup 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 C_{max} 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 in these patients was not different from that of

the general population. The effects of desloratadine in poor metabolizers under age of 2 years have not been examined.

Desloratadine is moderately bound (83 % - 87 %) to plasma proteins. There is no evidence of clinically relevant active substance accumulation following once daily adult and adolescent dosing of desloratadine (5 mg to 20 mg) for 14 days.

In a single dose, crossover study with desloratadine, the tablet and the syrup formulations were found to be bioequivalent.

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 syrup.

Biotransformation:

The enzyme responsible for the metabolism of desloratadine has not been identified yet, therefore, some interactions with other medicinal products can not be fully excluded. *In vitro* studies with specific inhibitors of CYP3A4 and CYP2D6 have shown that the enzymes are not effective in desloratadine metabolism. Desloratadine does not inhibits CYP3A4 or 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 effect on the disposition of desloratadine.

5.3 Preclinical safety data

Desloratadine is the primary active metabolite of loratadine. Non-clinical studies conducted with desloratadine and loratadine demonstrated that there are no qualitative or quantitative differences

in the toxicity profile of desloratadine and loratadine at comparable levels of exposure to desloratadine.

Non-clinical data with desloratadine reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, and toxicity to reproduction. The lack of carcinogenic potential was demonstrated in studies conducted with loratadine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycerol

Sodium methyl parahydroxybenzoate

Sodium propyl parahydroxybenzoate

Propylene glycol

Citric acid monohydrate

Saccharose

Trisodium citrate dehydrate

Disodium edetate

Orange flavor

Sunset yellow (E110)

Purified water

6.2 Incompatibilities

Not valid for this product.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store below 30°C at room temperature.

6.5 Nature and contents of container (for 100 mL)

100 ml packaging

Syrup is filled in 125 ml size Type III amber coloured glass bottles. Bottle is closed with white PE cap. Each cardboard box contains a leaflet, a bottle and a transparent plastic measuring cup.

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 AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization:
Date of renewal of the authorization:

10. DATE OF REVISION OF THE TEXT