SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
ALORES 2.5mg/5ml Syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 5 ml (1 spoonful) syrup contains;

Active substance:

Desloratadine	2.5 mg

Excipients:

Sorbitol 70% (E420)	1750 mg
Sucrose	1300 mg
Sodium citrate	25 mg
Sodium benzoate (E211)	5 mg
Sodium edetate	5 mg
Sodium hydroxide	5.26 mg
Propylene glycol	80 mg
FDC yellow no: 6 (E110)	0.25 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Syrup
Yellow-orange clear solution with characteristic odor (strawberry)

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
ALORES is indicated for the relief of symptoms associated with allergic rhinitis such as , sneezing, nasal discharge and itching, congestion/nasal congestion, as well as eye itching, tearing and redness, itching of the palate and coughing.

ALORES is also indicated for the relief of symptoms associated with hives such as itching, swelling and redness of the skin.

4.2 Posology and method of administration
Posology/frequency of administration and duration of the treatment:
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
Children 1 through 5 years of age: for allergic rhinitis including intermittent and persistent allergic rhinitis or relief of urticaria symptoms use ALORES 2.5 ml once a day (1.25 mg) with or without food.

Children 6 through 11 years of age: for allergic rhinitis including intermittent and persistent allergic rhinitis or relief of urticaria symptoms use ALORES 5 ml once a day (2.5 mg) with or without food.

In adults and adolescents (12 years of age and over): for allergic rhinitis including intermittent and persistent allergic rhinitis or relief of urticaria symptoms use ALORES 10 ml once a day (5 mg) with or without food.

Additional information for special populations:
Renal failure:
ALORES should be used with caution in patients with severe renal impairment.

Hepatic failure:
No data are available for use in patients with hepatic impairment.

Pediatric population:
The route of administration in the pediatric population is given above.

Geriatric population:
Efficacy and safety in the geriatric population has not yet been established.

4.3 Contraindications
It is contraindicated in patients with hypersensitivity to the active substance, to any of the excipients listed in Section 6.1, or to loratadine.

4.4 Special warnings and precautions for use
Efficacy and safety of ALORES in children under 6 months of age have not yet 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 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 metabolizers of desloratadine and exhibit a higher exposure. The safety of ALORES in children 2- to 11-years of age who are poor metabolizers is the same as in children who are normal metabolizers. The effects of ALORES in children under 2 years of age who are poor metabolizers of desloratadine have not been studied.

In the case of severe renal insufficiency, ALORES should be used with caution (see section 5.2).

Sucrose and sorbitol (E420):
This medicinal product contains sucrose and sorbitol; thus, patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

FDC yellow No. 6 (E110):
This medicinal product can cause allergic reactions due to the content of FDC yellow dye no:6 (E110).

Sodium:
This medicinal product contains less than 1 mmol (23 mg) sodium. In fact, it is "sodium-free" and does not expect any side effects.

4.5 Interaction with other medicinal products and other forms of interaction
In clinical trials with erythromycin or ketoconazole in combination with desloratadine, no clinical interaction was observed.

In a clinical pharmacology study, the administration of ALORES in combination with alcohol did not increase the performance-reducing effects of alcohol. (See Section 5.1).

ALORES interact with oral contraceptives. Therefore, during treatment alternative, effective and reliable method of birth control should be applied.

4.6 Fertility, Pregnancy and lactation
General advise:
Pregnancy category: C

Women of child bearing potential/ Birth control (contraception):
ALORES interact with oral contraceptives. Therefore, during treatment alternative, effective and reliable method of birth control should be applied.

Pregnancy:
There is limited data on the use of desloratadine in pregnant women (results of less than 300 pregnancies) or no data available. Animal studies do not show direct or indirect harmful effects in terms of reproductive toxicity (see section 5.3).

The potential risk for humans is unknown. ALORES should not be used during pregnancy unless necessary.

Breastfeeding:
Desloratadine was detected in newborns / infants breastfed by treated women. The effect of desloratadine on newborns / infants is not known. Taking into consideration the benefit of breastfeeding for the child and the benefit of the treatment for the woman, a decision should be made between discontinuing / not using ALORES or stopping breastfeeding.

Reproductive ability / Fertility
There is no data on male and female fertility.

4.7 Effects on ability to drive and use machines
According to clinical studies, ALORES has no effect or negligible effect on the ability to drive and use machines. Patients should be informed that most people do not experience drowsiness. However, since the response to all medicinal products is different among individuals, patients should be advised not to engage in activities that require mental alertness, such as driving or using machines, until they fully understand their response to the medicinal product.

4.8 Undesirable effects
Summary of safety profile
In clinical trials in a pediatric population, desloratadine syrup formulation was administered to a total of 246 children aged 6 months through 11 years. The incidence of adverse events in children 2 through 11 years of age was similar for the desloratadine and the

placebo groups. In patients aged 6 to 23 months, the most common adverse events reported more than placebo are diarrhea (3.7%), fever (2.3%) and insomnia (2.3%). In another study, no adverse events were observed in children aged 6-11 years who received a single dose of 2.5 mg of desloratadine oral solution.

In clinical trials in adults and adolescents, including a range of indications, including allergic rhinitis and chronic idiopathic urticaria, 3% of patients receiving oral solutions at the recommended dose had more undesirable effects than placebo. The most common adverse events reported more than placebo were fatigue (1.2%), dry mouth (0.8%), and headache (0.6%).

Other undesirable effects reported more frequently than in placebo in clinical studies and reported very rarely in post-marketing period are shown below.

Undesirable effects were listed below according to the system organ class. The frequency of them are defined as below: Very common (≥1/10); common (≥1/100, < 1/10); uncommon (≥/l.000, <1/100); rare (≥1/10.000, <1/1.000); very rare (<1/10.000), not known (cannot be estimated based on available data).

Psychiatric disorders
Very rare: Hallucinations

Nervous system disorders
Common: Headache, insomnia (in children under 2 years)
Very rare: Dizziness, drowsiness, insomnia, psychomotor hyperactivity, stroke, seizure

Cardiac disorders
Very rare: Tachycardia, palpitations
Not known: Prolonged QT

Gastrointestinal disorders
Common: Dry mouth, diarrhea (children under 2 years)
Very rare: abdominal pain, nausea, vomiting, indigestion, diarrhea

Hepato-biliary disorders
Very rare: Elevated liver enzymes, hepatitis, increase in bilirubin
Not known: Jaundice

Skin and subcutaneous disorders
Not known: Sensitivity to light

Musculoskeletal disorders, connective tissue and bone diseases
Very rare: Myalgia

General disorders and administration site conditions
Common: Fatigue, fever (children under 2 years)
Very rare: Hypersensitivity reactions (such as anaphylaxis, angioedema, dyspnea, pyuritis, rash, and urticaria).
Not known: Asthenia

4.9 Overdose and treatment
In case of overdose, standard measures should be taken to remove the unabsorbed active substance. Symptomatic and supportive treatment is recommended.

In a multi-dose clinical trial in adults and adolescents administered desloratadine up to 45 mg (9 times the clinical dose), no clinically significant effects were observed.

Desloratadine is not eliminated by hemodialysis. It is not known whether it is eliminated by peritoneal dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties
Pharmacotherapeutic group: Other antihistamines for systemic use.
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 the substance is excluded from entry to the central nervous system.

Desloratadine has demonstrated anti allergic properties in *in vitro* studies. These include inhibiting the release of pro inflammatory 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.

Clinical efficacy and safety
Efficacy of oral solution has not been investigated in separate pediatric trials. However, the safety of ALORES was demonstrated in three paediatric trials. Children aged 6 months to 11 years who are candidates for antihistamine treatment received a daily desloratadine dose of 1 mg (6 through 11 months of age), 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. When given at the recommended doses, the plasma concentrations of desloratadine were comparable in the paediatric and adult populations. Thus, since the course of seasonal allergic rhinitis/chronic idiopathic urticaria and the profile of desloratadine are similar in adults and paediatric patients, desloratadine efficacy data in adults can be extrapolated to the paediatric population.

In a multi-dose clinical trial administered desloratadine up to 20 mg per day for 14 days, no statistically or clinically relevant cardiovascular effect was observed. In a clinical pharmacological trial in which desloratadine was administered at a dose of 45 mg daily (nine times the clinical dose) for 10 days, no prolongation of QTc interval was seen.

Desloratadine does not readily penetrate the central nervous system. At the recommended daily dose of 5 mg, there was no increase in the incidence of somnolence compared to placebo. Desloratadine tablets given at a single 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, 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.

Desloratadine, alone or in combination with alcohol, did not increase the alcohol- induced impairment in performance.

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

The effectiveness of desloratadine syrup in children under 12 years of age has not been investigated in pediatric studies.

In adult and adolescent patients with allergic rhinitis, desloratadine tablets were effective in relieving symptoms such as sneezing, nasal discharge and itching, and congestion as well as ocular itching, tearing and redness, and itching of palate. Desloratadine tablets effectively controlled symptoms for 24 hours. The efficacy of desloratadine-containing tablets in adolescent patients aged 12-17 years has not been clearly demonstrated in the studies.

In addition to the established classifications of seasonal and perennial, allergic rhinitis can alternatively be classified as intermittent allergic rhinitis and persistent allergic rhinitis according to the duration of symptoms. Intermittent allergic rhinitis is defined as the presence of symptoms for less than 4 days per week or for less than 4 weeks. Persistent allergic rhinitis is defined as the presence of symptoms for 4 days or more per week and for more than 4 weeks.

Desloratadine tablets was 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 can 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 trial, 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 characteristics

Absorption:
Desloratadine plasma concentrations can 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 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.

Similar pharmacokinetic parameters have been observed in multiple dose pharmacokinetic studies 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 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 ageappropriate 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 Cmax values of desloratadine to those in adults who received a 5 mg dose of desloratadine syrup.

Distribution:
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 pediatric subjects 2- to 11-year old (6%), and greater among Blacks (18% adult, 16% pediatric) than Caucasians (2% adult, 3% pediatric) in both populations.

In a multiple-dose pharmacokinetic study conducted with the tablet formulation in healthy adult subjects, four subjects were found to be poor metabolizers of desloratadine. These subjects 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 of these subjects was not different from that of the general population. The effects of desloratadine in poor metabolisers < 2 years of age have not been studied.

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 of desloratadine, the tablet and the syrup formulations were found to be bioequivalent.

In separate single dose studies, at the recommended doses, pediatric 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, and therefore, some interactions with other medicinal products can not 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.

In a multi-dose pharmacokinetic study conducted tablet formulation in healthy adult subjects it has been found that four cases metabolized desloratadine slowly. In these cases, Cmax concentration at 7 hours is about 3 times higher. Terminal half-life is about 89 hours.

A series of pharmacological and clinical trials, desloratadine plasma concentrations were higher in 6% of cases. The prevalence of this poor metaboliser phenotype in adult (6%) and 2-11 years of age pediatric patients (6%) was comparable. The prevalence of this poor metaboliser phenotype in blacks (18% in adults, 16% in pediatric patients) was higher than whites (2% in adults, 3% in pediatric patients), but the safety profile of these cases is not different from the general population.

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.

Linearity / Non-Linearity:
The bioavailability of desloratadine is dose-proportional in the range of 5-20 mg.

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 desloratadine and loratadine.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Propylene glycol,
Sorbitol 70% (E420),
Citric acid monohydrate,
Sodium citrate
Sodium benzoate (E211)
Sodium edetate,
Sucrose
Strawberry aroma

FDC yellow no:6 (E110)
Sodium hydroxide
Deionized water

6.2 Incompatibilities
Not applicable

6.3 Shelf-life
60 months

6.4 Special precautions for storage
Store at under the 25 °C in room temperature.

6.5 Nature and contents of container
ALORES is marketed in amber colored glass bottles (Type III) containing 60 ml and 150 ml syrup closed with pilfer-proof high density polyethylene (HDPE) cap and low density polyethylene (LDPE) seal.
Each carton contains one bottle containing 60 ml or 150 ml syrup and one 5 ml spoon.

6.6. Special precautions for disposal and other handling
Unused product or waste materials should be disposed of according to the regulations on "Control of Medicinal Wastes" and "Control of Packaging and Packaging Wastes"

7. MARKETING AUTHORIZATION HOLDER

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8. MARKETING AUTHORIZATION NUMBER(S)

235/10

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORIZATION

Date of first authorization: 23.09.2011
Date of latest renewal: 13.04.2017

10. DATE OF REVISION OF THE TEXT