SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

ARIA-DES 2.5 mg/ 5 ml Syrup, 150 ml

2. QUALITIVE and QUANTITIVE COMPOSITION

Each 5 ml scale contains;

Active ingredient

Desloratadine	2.50 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Syrup

Clear, colorless solution.

4. CLINICAL PARTICULAR

4.1. Therapeutic indications

ARIA-DES is indicated for the relief of symptoms associated with allergic rhinitis such as sneezing, runny nose and itching, congestion / stuffiness, but also in the eyes itching, tearing and redness, palate itching and coughing.

ARIA-DES also is indicated for the relief of itching associated with urticaria, the elimination of symptoms such as swelling and redness in the skin.

4.2.Posology and method of administration

Posology /the frequancy and duration of administration:

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:

5 ml spoon with drugs is supplied in the box.

Children 6 through 11 months of age : ARIA-DES is used 2 ml once a day (1 mg) by alone or with food for the elimination of allergic rinitis including intermittent and persistent allergic rhinitis developing symptoms with urticaria.

Children 1 through 5 years of age: ARIA-DES is used 2.5 ml once a day (1.25 mg) by alone or with food for the elimination of allergic rinitis including intermittent and persistent allergic rhinitis developing symptoms with urticaria.

Children 6 through 11 years of age: ARIA-DES is used 5 ml once a day (2.5 mg) by alone or with food for the elimination of allergic rinitis including intermittent and persistent allergic rhinitis developing symptoms with urticaria.

Adults, 12 years of age and over: ARIA-DES is used 10 ml once a day (5 mg) by alone or with food for the elimination of allergic rinitis including intermittent and persistent allergic rhinitis developing symptoms with urticaria.

Additional information on special populations:

Renal insufficiency:
In the case of severe renal insufficiency, should be used with caution.

Hepatic insufficiency:
There are no data regarding the use in patients with hepatic impairment.

The pediatric population:
Method of administration for the pediatric population are given above.

The geriatric population:
Dose adjustment is not necessary in elderly patients.
However, caution should be exercised in dose selection in the elderly due to the generally higher incidence of decreased hepatic, renal and cardiac function and concomitant disease or other drug therapy.

4.3. Contraindications

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

4.4. Special warnings and precautions for use

Efficacy and safety of ARIA-DES tablets in children under 6 months of age have not been established (see selection 5.1).

In children below 2 years of age, the diagnosis of allergic rhinitis is particularly difficult to distinguish from other forms of rhinitis. In 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 too.

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 < 2 years of age have not been studied.

In the case of severe renal insufficiency, ARIA-DES should be used with caution (see selection 5.2).

Sucrose and sorbitol:
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.

4.5.Interaction with other medicinal products and other forms of interaction

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

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

Desloratadine interacts with birth control pills for oral administration. So alternative, effective and safe method of birth control should be applied during treatment.

4.6. Pregnancy and lactation

General advise

Pregnancy category C.

Women of childbearing potential / Birth control (Contraception)

ARIA-DES interacts with birth control pills for oral administration. So alternative, effective and safe method of birth control should be applied during treatment.

Pregnancy

There are no or limited amount of data from the use of ARIA-DES in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. The potential risk for humans is unknown (see section 5.3). As a precautionary measure, it is preferable to avoid the use of ARIA-DES during pregnancy.

Breast-feeding

When therapeutic doses of ARIA-DES are administered to breastfeeding women, are excreated in the breast that may cause effects on the child. ARIA-DES should not be used during breast-feeding.

Fertility

There are no fertility toxicity in studies conducted animals. The potential risk of desloratadine on humans is unknown.

4.7. Effects on ability to drive and use machines

ARIA-DES has no ifluence on the ability to drive and use machines. Patients should be informed that drowsiness may rarely occur in some patients and in this case affect the use of their vehicles and machines.

4.8. Undesirable effects

In clinical trials in a paediatric population, the desloratadine syrup formulation was administered 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 the desloratadine and the placebo groups. In infants and toddlers aged 6 to 23 months, the most frequent adverse reactions 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 was observed in %3 of patients who using desloratadine much more than plasebo The most frequent of adverse events reported in excess of placebo were fatigue (1.2 %), dry mouth (0.8 %) and headache (0.6 %).

Undesirable effects are listed in the following system organ class. Frequencies are defined as:

In different organ systems;
Very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000) not known (cannot be estimated from the available data).

Nervous system disorders:
Common: Fatigue
Uncommon: Headache

Gastrointestinal disorders:
Uncommon: Dry mouth

Post-marketing experience:
The following are very rare side effects reported in post-marketing experience.

Psychiatric disorders:
Very rare: Hallucinations.

Nervous system disorders:
Very rare:Dizziness, somnolence, insomnia, psychomotor hyperactivity, stroke

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 and connective tissue disorders:
Very rare: Myalgia.

General disorders and administration site conditions:
Very rare: Hypersensitivity reactions (such as anaphylaxis, angioedema, dyspnoea, pruritus, rash, and urticaria).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continuous monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to Turkish Pharmacovigilance Center (TÜFAM) (www.titck.gov.tr; e- mail: tufam@titck.gov.tr; Tel: 0 800 314 00 08; Fax: 0 312 218 35 99)

4.9. Overdose and treatment
In the event of overdose, consider standard measures 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 the clinical dose), no clinically relevant effects were observed.
Desloratadine is not eliminated by haemodialysis; it is not known if it is eliminated by peritoneal dialysis.

5. PHARMACOLOGICAL PROPERTIES
5.1. Pharmacodynamic properties
Pharmacotherapeutic group: Other antihistamines for systemic use
ATC code : R06A X27

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 H1-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.

Efficacy of Deslaratadine syrup has not been investigated in separate paediatric trials. However, the safety of Deslaratadine syrup, which contains the same concentration of desloratadine, was demonstrated in three paediatric trials. Children, 6 months through -11 years of age, who were candidates for antihistamine therapy received a daily desloratadine dose of 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 (Electrocardiography) interval data, including QTc(corrected QT). When given at the recommended doses, the plasma concentrations of desloratadine (see section 5.2) were comparable in the paediatric and adult populations. Thus, since the course of 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 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 adults and adolescents, in which desloratadine was administered to adults at a dose of 45 mg daily (nine times the clinical dose) for ten days, no prolongation of QTc interval was seen.

Desloratadine does not readily penetrate the central nervous system. In controlled clinical trials, at the recommended dose of 5 mg daily for adults and adolescents, there was no excess incidence of somnolence as compared to placebo. Neoclarityn tablets given at a single daily dose of 7.5 mg to adults and adolescents did not affect psychomotor performance in clinical trials. In a single dose study performed in adults, 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, whether administered alone or with alcohol.

Desloratadine has not increased performance distorting effects of alcohol when it is taken alone or with 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.

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 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 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 properties

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.

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 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 subjects were found to be poor metabolisers 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 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.

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, paediatric patients had comparable AUC and Cmax values of desloratadine to those in adults who received a 5 mg dose of desloratadine syrup.

Biotransformation:
Since the enzyme responsible for the metabolism of desloratadine has not yet been identified, some interactions with other drugs cannot be completely ruled out. In vivo studies with specific inhibitors of CYP3A4 and CYP2D6 have shown that these enzymes are not effective in desloratadine metabolism. Desloratadine does not inhibit CYP3A4 or CYP2D6 and is not a P-glycoprotein substrate or inhibitor.

In a multi-dose pharmacokinetic study of the tablet formulation in healthy adult subjects, four subjects were found to metabolize desloratadine slowly. In these subjects, the Cmax concentration at around 7 hours was approximately 3 times higher and the half-life in the terminal phase was around 89 hours.

In a series of pharmacological and clinical studies, plasma concentrations of desloratadine were higher in 6% of subjects. The prevalence of this slow metabolizing phenotype was comparable in adult (6%) and pediatric subjects aged 2-11 years (6%) and was higher in blacks (adults 18%, pediatric subjects 16%) than in whites (adults 2%, pediatric subjects 3%); however, the safety profile in these subjects did not differ from that in 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/Nonlinearity:
The bioavailability of desloratadine is dose proportional in the range 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 reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development. The lack of carcinogenic potential was demonstrated in studies conducted with desloratadine and loratadine.

6. PHARMACEUTICAL PROPERTIES

6.1 List of excipients

Sorbitol %70 (E420)
Propylene glycol
Citric acid monohydrate
Trisodium citrate dihydrate
Sodium benzoate
Disodium EDTA
Sucrose
Strawberry flavor (powder)
Deionized water

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

24 months.

6.4. Special precautions for storage

Store at room temperature below 30 ° C.

6.5. Nature and contents of container

150 ml Type III amber glass bottles with LDPE cap, 5 ml spoon

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

Humanis Saglik A.S.
Istanbul/Turkey

8. MARKETING AUTHORISATION NUMBER (S)

07602/09528/NMR/2022
09499/08812/VAR/2023

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: Aug 5, 2022
Date of latest renewal:

10. DATE OF REVISION OF THE TEXT

20.03.2020