SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE HUMAN MEDICINAL PRODUCT
ALRINAST 2.5 mg/5 mL syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 1mL of syrup contains 0.5 mg desloratadine

Excipient(s):

Sucrose:	490 mg/mL
Sorbitol (70%):	150 mg/mL
Sodium benzoate:	1 mg/mL
Sodium citrate dihydrate:	1.26 mg/mL
Disodium edetate:	0.25 mg/mL
Sunset yellow FCF:	0.02 mg/mL
Propylene glycol:	100.00 mg/mL

See section 6.1 for the excipients.

3. PHARMACEUTICAL FORM
Syrup
Clear and light orange colour solution.

4. CLINICAL PROPERTIES

4.1. Therapeutic indications
ALRINAST is indicated in relieving symptoms associated with allergic rhinitis such as sneezing, nasal discharge and itching, congestion/nasal obstruction, as well as ocular itching, tearing and redness, itching of palate, and coughing.

ALRINAST is also indicated to relieve the symptoms associated with urticaria, including itching, hives and rash.

4.2. Posology and mode of administration

Posology/frequency 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.

Mode of administration:
The drug is supplied with a 2-, 2.5- and 5-mL measuring spoon as within the box.

Children 6 to 11 months of age: ALRINAST may be taken alone or with meals at a dose of 2 mL (1 mg) once daily for the relief of symptoms associated with allergic rhinitis, including intermittent and persistent allergic rhinitis, and urticaria.
Use measuring spoon up to 2mL.

Children 1 to 5 years of age: ALRINAST may be taken alone or with meals at a dose of
2.5 mL (1.25 mg) once daily for the relief of symptoms associated with allergic rhinitis,including intermittent and persistent allergic rhinitis, and urticaria.

Use measuring spoon up to 2.5mL.

Children 6 to 11 years of age: ALRINAST may be taken alone or with meals at a dose of 5mL (2.5 mg) once daily for the relief of symptoms associated with allergic rhinitis, including intermittent and persistent allergic rhinitis, and urticaria.
Use measuring spoon up to 5mL.

Adults and children 12 years and over: ALRINAST may be taken alone or with meals at adose of 10 mL (5 mg) once daily for the relief of symptoms associated with allergic rhinitis, including intermittent and persistent allergic rhinitis, and urticaria.
Use measuring spoon up to 5mL twice.

Commented [EM1]: Please review the dose for adults and children 12 years and above. Note that, the dose of 5mg is regarded as under dosing

Additional information regarding special populations:

Renal failure:
Caution should be exercised in patients with severe renal failure.

Liver failure:
No data is available concerning its use in patients with liver failure.

Pediatric population:
The mode of administration for the pediatric population is given above.

Geriatric population:
Efficacy and safety have not been established in geriatric population.

Method of administration
For oral administration.

4.3. Contraindications

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

4.4. Special warnings and special precautions of use

Efficacy and safety of ALRINAST have not been established in children younger under 6months of age (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 orstructural abnormalities, as well as patient history, physical examinations, and appropriatelaboratory 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 desloratadine inchildren 2 to 11 years of age who are poor metabolizers is the same as in children who are normal metabolizers. The effects of ALRINAST in poor metabolizers < 2 years of age have not been studied.

ALRINAST should be used with caution in patients with severe renal failure (see section5.2).

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

Sunset Yellow FCF:
This medicinal product contains Sunset yellow FCF as the colorant which may causeallergic reactions.

Sodium:
This medicinal product contains less than 1 mmol (23 mg) sodium in each dose; no dose-related side effect is anticipated.

The medical product contains 100 mg/mL of propylene glycol. Side effects due topropylene glycol is not expected for this dose.

4.5. Interactions with other medical products and other forms of interaction

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

In clinical pharmacology trials, Desloratadine taken concomitantly with alcohol did notpotentiate the performance-impairing effects of alcohol (see section 5.1).

Desloratadine interacts with orally taken birth control drugs. Therefore, an alternative,efficient and safe contraception method should be applied throughout the treatment.

4.6. Pregnancy and lactation General recommendation

Pregnancy category is C.

Women with childbearing potential/Birth control (Contraception)
Desloratadine interacts with orally taken birth control drugs. Therefore, an alternative,efficient and safe contraception method should be applied throughout the treatment.

Pregnancy period
There is limited data regarding the use of ALRINAST in pregnancy. Animal investigations have not demonstrated reproductive toxicity. No potential risk for humans is known (see section 5.3). Therefore, the drug is not recommended during pregnancy.

Lactation period
Desloratadine is excreted in breast milk at an extent to cause an effect on the breastfed children if the therapeutic doses of ALRINAST are given to breastfeeding women. ALRINAST should not be used during lactation.

Reproductivity/Fertility
Animal investigations have not demonstrated reproductive toxicity. The potential risk onhumans is not known.

4.7. Effects on ability to drive and use machines

No effects on the ability to drive and use machines have been observed with the use of ALRINAST. 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 pediatric population, desloratadine was administered to a total of 246children aged 6 months through 11 years. The overall incidence of adverse events in children 2 through 11 years of age was similar for desloratadine and the placebo groups. Ininfants aged 6 to 23 months, the most frequent adverse events reported in excess of placebo were diarrhea (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 effectswith desloratadine were reported in 3% of patients 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 %).

Adverse events as per the system organ class are listed below. 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); unknown (cannot be estimated from the available data.

Nervous system disorders:
Common: Fatigue
Uncommon: Headache

Gastrointestinal disorders:
Uncommon: Dry mouth

Post marketing experience:
Other undesirable effects reported very rarely during the post-marketing period are listedbelow.

Psychiatric disorders:
Very rare: Hallucinations.

Nervous system disorders:
Very rare: Dizziness, drowsiness, insomnia, psychomotor hyperactivity, seizure.

Cardiac disorders:
Very rare: Tachycardia, palpitations.

Gastrointestinal disorders:
Very rare: Abdominal pain, nausea, vomiting, dyspepsia, diarrhea.

Hepatobiliary disorders:
Very rare: Increased liver enzymes, increased hepatitis and bilirubin.

Musculoskeletal system, connective tissue and bone disorders:
Very rare: Myalgia.

General disorders and administration site conditions:
Very rare: Hypersensitivity reactions (anaphylaxis, angioedema, dyspnea, pruritus,

pruritus and urticaria).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Health care providers are asked to report any suspected adverse reactions to the marketing authorization holder, or, if available, via the national reporting system (see details below);

Paper based reporting: TMDA yellow card
Online reporting: https://sqrt.tmda.go.tz/
*USSD reporting: send a simple short text message to report any suspected Adverse Drug Reaction by dialing *152*00# and follow the instructions*

4.9. Overdose and treatment

In the event of overdose, standard measures to remove unabsorbed active substance shouldbe considered.

Symptomatic and supportive treatment is recommended.

Based on a multiple dose clinical trial in adults and adolescents, in which up to 45 mg ofdesloratadine was administered (nine times the clinical dose), no clinically relevant effectswere observed.

Desloratadine is not eliminated by hemodialysis; 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 potent, selective peripheral H_1-receptor antagonist activity. After oral administration, desloratadine selectively blocks peripheral histamine H_1-receptors because the drug does not readily penetrate the central nervous system.

Desloratadine has demonstrated antiallergic activities from *in vitro* studies. These includeinhibiting 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 hasnot been confirmed yet.

Efficacy of ALRINAST syrup has not been investigated in separate pediatric trials. Safety of Desloratadine was demonstrated in three pediatric trials. Children, 6 months-11 years ofage, who were candidates for antihistamine therapy received a daily desloratadine dose of1 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 (Electrocardiography) data, including QTc (corrected QT). When given at the recommended doses, the plasma concentrations of desloratadine were comparable in the pediatric and adult populations. Thus, since the course of allergic rhinitis/chronic idiopathic urticaria and the profile of desloratadine are similar in adults and pediatric patients, desloratadine efficacy data in adults can be

extrapolated to the pediatric population.
In a multiple dose clinical trial, in adults and adolescents, 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 at a dose of 45 mg daily (nine times the clinical dose) forten days, no prolongation of QTc (the duration between Q and T waves in ECG) intervalwas seen.

Desloratadine does not readily penetrate the central nervous system. At the recommendeddose of 5 mg daily, there was no excess incidence of somnolence as 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 placebogroups.
Desloratadine, alone or co-administered with alcohol, did not increase the alcohol-inducedimpairment effects.

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 effectivein 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 canalternatively 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, regardless of its etiology, was studied as a clinical model for urticaria due to the similar background physiopathology and the availability of chronic patients to be enrolled in the prospective studies. Since histamine release is the cause of allurticarial diseases, desloratadine is expected to be effective in relieving the symptoms ofother urticarial diseases, in addition to chronic idiopathic urticaria, as recommended by 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 as of the first day of treatment. In each trial, the effects were sustained over the 24 hour dosing interval. As with other antihistamine trials in chronic idiopathic urticaria, theminority 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 patientstreated 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:

Plasma concentrations of desloratadine are detectable within 30 minutes of 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 is consistent with its half-life (approximately 27 hours) and a once daily dosing frequency. Desloratadine bioavailability is dose proportional within the range of 5mg to 20mg.

Distribution:

Higher desloratadine concentrations were obtained in 6% of subjects in a series of pharmacokinetic and clinical trials. The prevalence of desloratadine poor metabolizer phenotype is similar in the adult (6%) and pediatric (2-11 years old) subjects (6%), whereas higher in African Americans (18% of adults; 16% of children) as compared to Caucasians (2% of adults; 3% of children) in both populations.

A multi-dose pharmacokinetic study conducted with the tablet formulation in healthy adult subjects determined four subjects as poor metabolizers of desloratadine. Cmax concentration was 3 times higher in approximately 7 hours, with a terminal half-life of approximately 89 hours in that population.

Multi-dose pharmacokinetic studies performed with the syrup formulation in pediatric poor metabolizers (2-11 years old) diagnosed with allergic rhinitis also demonstrated similar pharmacokinetic parameters. 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 pediatric poor metabolizers when treated with age-appropriate doses. The overall safety profile of thesesubjects 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 ofclinically relevant drug accumulation following once daily dosing of desloratadine (5 mgto 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 Cmax 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 medicines can not be fully excluded. In vivo studies performed with the specific inhibitors of CYP3A4 and CYP2D6 have shown thatthese enzymes do not affect the metabolism of desloratadine. Desloratadine does not inhibit 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 trials conductedwith desloratadine and loratadine indicated that desloratadine, at the recommended doses,gave similar qualitative and quantitative toxicity profile to loratadine.

Data from non-clinical trials of desloratadine including safety pharmacology, repeated dose toxicity, genotoxicity and reproductive toxicity indicated no hazard to humans. In trials performed with loratadine, absence of carcinogenic potential was demonstrated.

6. PHARMACEUTICAL PROPERTIES

6.1. List of excipients

Sucrose
Propylene
glycolSorbitol
(70 %) Sodium
benzoate
Sodium citrate
dihydrateCitric acid
anhydrous Disodium
edetate
Sunset yellow FCF
Tutti frutti flavor
Deionized water

6.2. Incompatibilities

No incompatibility is known.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at room temperature below 30°C in its original package while closed.
Store at room temperature below 30°C after opening. Discard 28 days after opening.

6.5 Nature and contents of package

The box contains a 150 mL Type III amber glass bottle and measuring spoon as 2, 2.5 and 5 mL.

6.6 Special precautions

Unused products and waste materials should be disposed of in accordance with “Medicinal Products Waste Management Directive” and “Packaging and Packaging WasteManagement Directive".

7. Marketing Authorization Holder

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8. Date of review of text
October, 2023