SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

ALRINAST 5 mg film coated tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Desloratadine .....5 mg

Excipient(s):

Lactose monohydrate.....2.8 mg

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Film coated tablet

ALRINAST film coated tablet is light blue coloured**,** round shaped tablet.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

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

ALRINAST is also indicated for the elimination of symptoms such as ridges and redness of the skin, relief of itching associated with urticaria.

4.2. Posology and method of administration

Posology/administration frequency and duration:

Adults and adolescents (12 years of age and over):

The recommended dose is one tablet once a day.

Intermittent allergic rhinitis with presence of symptoms for 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 should be suspended in the event of removal and recurrence of symptoms.

In persistent allergic rhinitis with presence of symptoms for 4 days or more per week and for more than 4 weeks, continuous treatment should be recommended in the event of the emergence of the patient's allergies.

Paediatric population

There is limited clinical trial efficacy experience with the use of desloratadine in adolescent s12 through 17 years of age (see sections 4.8 and 5.1).

The safety and efficacy of desloratadine film-coated tablets in children below the age of 12 years have not been established. No data are available.

Method of administration:

Oral use.

The dose can be taken with or without food.

Additional information on special populations:

Hepatic impairment:

There is no data on the use in patients with hepatic insufficiency.

Renal impairment:

ALRINAST should be used cautiously in patients with severe renal insufficiency.

Pediatric population:

The safety and efficacy of ALRINAST in children below the age of 12 years have not yet been established. No data are available.

There is limited clinical trial efficacy experience with the use of desloratadine in adolescents 12 through 17 years of age (see sections 4.8 and 5.1).

Geriatric population:

There are no specific studies targeting the geriatric population.

4.3. Contraindications

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

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

Desloratadine should be administered with caution in patients with medical or familial history of seizures, and mainly young children (see section 4.8), 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.

This medicinal product contains 2.8 mg lactose monohydrate at each dose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactosemalabsorption 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 (see section 5.1).

In a clinical pharmacology trial, desloratadine taken concomitantly with alcohol, did not potentiate the performance impairing effects of alcohol. However, cases of alcohol intolerance and intoxication have been reported during post-marketing use. Therefore, caution is recommended if alcohol is taken concomitantly.

4.6. Pregnancy and lactation

Pregnancy category: C

Women with childbearing potential / Birth control (contraception)

There is no data on effects on fertility in woman with childbearing potential.

Pregnancy

There is limited (less than 300 pregnancy outcomes) or no data on the use of desloratadine in pregnant women. Animal studies do not indicate direct or indirect harmful effects withrespect to reproductive toxicity (see section 5.3).

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

Lactation

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 breast-feeding or to discontinue/abstain from ALRINAST therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Reproductivity / fertility

There are no data available on male and female fertility.

4.7. Effects on ability to drive and use machines

Desloratadine has no or negligible influence on the ability to drive and use machines based onclinical trials. Patients should be informed that most people do not experience drowsiness. Nevertheless, as there is individual variation in response to all medicinal products, it is recommended that patients are advised not to engage in activities requiring mental alertness, such as driving a car or using machines, until they have established their own response to the medicinal product.

4.8. Adverse effects

Summary of the safety profile

In clinical trials in a range of indications including allergic rhinitis and chronic idiopathic urticaria, at the recommended dose of 5 mg daily, undesirable effects were reported in 3 % of patients using desloratadine more than those treated with placebo. The most common adverse reactions reported and observed more than placebo was fatigue (1.2%), dry mouth (0.8%) and headache (0.6%).

In a clinical trial with 578 adolescent patients, 12 through 17 years of age, the most common adverse event was headache; this occurred in 5.9% of patients treated with desloratadine and 6.9% of patients receiving placebo.

The frequency of the clinical trial adverse reactions reported in excess of placebo and other undesirable effects reported during the post-marketing period are listed in the following table. Frequencies are defined as 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) and not known (cannot be estimated from the available data).

Psychiatric disorders
Very rare: Hallucinations

Nervous system disorders:
Common: Headache
Very rare: Dizziness, somnolence, insomnia, psychomotor hyperactivity, seizures

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

Gastrointestinal disorders:
Common: Dry mouth
Very rare: Abdominal pain, nausea, vomiting, dyspepsia, diarrhoea

Hepatobiliary disorders:
Very rare: Elevations of liver enzymes, increased bilirubin, hepatitis
Not known: Jaundice

Skin and subcutaneous tissue disorders:
Not known: Photosensitivity

Musculoskeletal and connective tissue disorders:
Very rare: Myalgia

General disorders and administration site conditions:

Common: Fatigue

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

Not known: Asthenia

Paediatric population

Other undesirable effects reported during the post-marketing period in paediatric patients with an unknown frequency included QT prolongation, arrhythmia, and bradycardia.

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 which up to 45 mg of desloratadine was administered (9 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: Antihistamines-H1 antagonistATC code: R06A X27

Mechanism of action

Desloratadine is a non-sedating, long-acting, potent, selective peripheral H_1-receptor antagonist. Desloratadine selectively blocks peripheral histamine H_1-receptors because the substance is excluded from entry to the central nervous system after oral administration.

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, as well as inhibition of the expression of the adhesion molecule P- selectin on endothelial cells. The clinical importance of these observations remains to be confirmed.

Clinical efficacy and safety

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 at a dose of 45 mg daily (nine times the clinical dose) for ten days, no prolongation of QTc interval was seen.

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

Desloratadine does not readily penetrate the central nervous system. In controlled clinical

trials, at the recommended dose of 5 mg daily, there was no excess incidence of somnolence as compared to placebo. Desloratadine given at a single daily dose of 7.5 mg 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, 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 alone or taken together with alcohol.

In patients with allergic rhinitis desloratadine, was effective in relieving symptoms such as sneezing, runny nose and itching, congestion / stiffness, as well as ocular itching, tearing and redness, and itching of palate. Desloratadine effectively controlled symptoms for 24 hours. The efficacy of desloratadine tablets has not been clearly demonstrated in trials with adolescents 12 through 17 years of age.

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 is effective in reducing complaints related to seasonal allergic rhinitis, in total scoring of rhino-conjunctivitis quality of life questionnaire. The greatest improvement was seen in the area of restricted daily activities by symptoms and practical problems.

Chronic idiopathic urticaria, was studied as a clinical model for urticaria due to be similar regardless of the etiology of the underlying pathophysiology and the patients to participate in a prospective study are more easily available. Since histamine release is a cause that leads to all urticarial diseases, desloratadine is also expected to be effective in relieving symptoms in other urticarial diseases, in addition to chronic idiopathic urticaria as recommended in clinicalguidelines.

In two placebo-controlled six-week trials in patients with chronic idiopathic urticaria, desloratadine tablet was effective in relieving pruritus and decreasing the size and number of ridges and redness of the skin 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.

Pharmacokinetic propertiesGeneral characteristics Absorption:
Desloratadine plasma concentrations become detectable levels within 30 minutes after administration. Absorption of desloratadine is good and maximum concentration is reached after about 3 hours. Terminal phase half-life of desloratadine is about 27 hours. The degree ofaccumulation of desloratadine is compatible with half-life (approximately 27 hours) and a single dose daily dosing frequency. The bioavailability of desloratadine is dose proportional between 5 and 20 mg.

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.

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.
in vivo studies with specific inhibitors of CYP3A4 and CYP2D6 have shown that these enzymes are not effective in metabolism of desloratadine. Desloratadine does not inhibit CYP3A4 and CYP2D6 and is neither a substrate nor an inhibitor of P-glycoprotein.

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. Maximum desloratadine concentration was about 3-fold higher at approximately 7 hours with a terminal phase half-life of approximately 89 hours.

In a series of pharmacological and clinical trials, 6% of the subjects achieved a higher plasma concentration of desloratadine. This slower metabolizing phenotype prevalence is comparable in adults (6%) and in pediatric (6%) cases aged 2-11 years and higher in blacks (adults 18%, pediatric cases 16%) than in whites (adults 2%, pediatric cases 3%); but the safety profile of these events 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 / Nonlinear Condition:
The bioavailability of desloratadine is proportional to the dose in the range of 5-20 mg.

5.3 Preclinical safety data

Desloratadine is the primary active metabolite of loratadine. There are no clinical studies conducted with Desloratadine and loratadine on comparable levels showing the qualitative or quantitative differences in the toxicity profile of loratadine and desloratadine with the exposure to desloratadine.

Based on the classical studies done on preclinical data, safety, pharmacology, repeat dose toxicity, genotoxicity and reproductive toxicity reveals that there is no specific danger for humans. Carcinogenic potential deprivation has been shown in clinical studies conducted with desloratadine and loratadine.

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients

Dibasic calcium phosphate
dihydrateLactose monohydrate
Hypromellose
Microcrystalline cellulose
Corn starch
Talc
Titanium dioxide
Polyethylene glycol
FD&C blue no.2

6.2. Incompatibilities

There are not any known incompatibilities.

6.3. Shelf life

24 months

6.4. Special precautions for storage

Store below 30°C at room temperature in order to protect from moisture.

6.5. Nature and contents of container

In the box, PVC / PVDC-Alu Blister packaging, available in 20 tablets.

6.6 Special precautions for disposal and other handling

Unused products or excess materials must be exterminated according to "Medical Waste Control Regulations" and "Package and packaging waste control regulations"

7. MARKETING AUTHORISATION HOLDER

İlko İlaç San. Tic. A.Ş.
Veysel Karani Mah. Çolakoğlu Sok. No: 10
34885 Sancaktepe / İstanbul-Turkey
Phone: +90 (216) 564 80 00
Fax: +90 (216) 564 80 99

8. MARKETING AUTHORISATION NUMBER

TAN 21 HM 0019

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

24/12/2020

10. DATE OF REVISION OF THE TEXT

March 2021