SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

ESLOTIN 5 mg Film Coated Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance: Each film coated tablet contains 5 mg Desloratadine.

Excipient(s):

For excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film coated tablet

ESLOTIN is a blue colored, round, one side scored, biconvex film coated tablet.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ESLOTIN is indicated for the relief of symptoms associated with allergic rhinitis, such as sneezing, runny nose and itching, congestion/nasal congestion, as well as itching of the eyes, tearing and redness, itching of the palate and coughing.

ESLOTIN is also indicated for the relief of symptoms that occur with urticaria, such as itching, swelling and redness of the skin.

4.2 Posology and method of administration

Posology/frequency and time of administration

Adolescents aged 12 and over and adults:

The recommended dose of ESLOTIN Film Coated Tablets is one tablet once a day.

Intermittent allergic rhinitis with symptoms lasting 4 days a week or less than 4 weeks should be treated according to the evaluation of patient's disease history and the treatment should be discontinued after symptoms are resolved and reinitiated in case of recurrence of symptoms.

In persistent allergic rhinitis with symptoms seen for 4 days or more a week and for more than 4 weeks, continuous treatment of the patient should be recommended if allergy occurs.

Pediatric population

There is limited clinical study experience regarding the efficacy of Desloratadine use in adolescents aged 12-17 years (see sections 4.8 and 5.1).

The safety and efficacy of ESLOTIN Film Coated Tablets in children younger than 12 years of age have not been established. There is no data.

Method of administration:

It is used orally.

The dose can be taken with or without food.

Additional information about specific populations:

Hepatic impairment:

No data are available in patients with hepatic impairment.

Renal impairment:

ESLOTIN should be used carefully in severe renal impairment.

Pediatric population:

The efficacy and safety of Desloratadine tablet form in pediatric population below the age of 12 years have not yet been established. There is no data.

There is limited clinical study experience regarding the efficacy of Desloratadine use in adolescents aged 12-17 years (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 or any of the excipients listed in section 6.1 or to loratadine.

4.4 Special warnings and precautions for use

ESLOTIN should be used with caution in severe renal impairment (see section 5.2).

The efficacy and safety of Desloratadine tablet form in children below the age of 12 years have not yet been established.

4.5 Interaction with other medicinal products and other forms of interaction

No clinical interactions were observed in clinical studies performed with Desloratadine tablets in which erythromycin or ketoconazole were co-administered (see section 5.1).

In clinical pharmacology studies where Desloratadine was taken concomitantly with alcohol, Desloratadine did not increase the performance-impairing effect of alcohol..

4.6 Pregnancy and lactation

General advice

Its pregnancy category is C.

Women of childbearing potential/birth control (Contraception)

No data are available on the effects on reproductive ability in women of childbearing potential.

Pregnancy period

There are limited or no data available on the use of Desloratadine in pregnant women (results of less than 300 pregnancies). Researches performed on animals do not show direct or indirect harmful effects in terms of reproductive toxicity (see section 5.3).

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

Lactation period

Desloratadine has been detected in neonates/infants breastfed by treated women. The effect of Desloratadine on neonates/infants is unknown. Considering 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 ESLOTIN treatment or discontinuing breastfeeding.

Reproductive ability/fertility

There are no data on male and female fertility.

4.7 Effects on ability to drive and use machines

According to clinical studies, Desloratadine has no or negligible effect on the ability to drive and use machines. Patients should be informed that most people do not experience somnolence. However, as the response to all medicinal products differs between 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 the safety profile

In clinical studies covering indications including allergic rhinitis and chronic idiopathic urticaria, at the recommended doses of 5 mg daily, 3% of patients using Desloratidine experienced more side effects than placebo. Undesirable reactions which are seen more than placebo and reported most commonly are fatigue (1.2%), dry mouth (0.8%) and headache (0.6%).

In a clinical study of 578 adolescent patients aged 12-17 years, the most common undesirable event was headache, which was observed in 5.9% of patients using Desloratadine and 6.9% of patients taking placebo.

Other undesirable effects that were reported more than placebo in clinical trials and that were reported in the post-marketing period are listed below. The frequencies are defined as:

In different organ sytems,
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 can not be estimated from the available data).

Psychiatric disorders:
Very rare: Hallucinations.

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

Cardiac disorders:
Very rare: Tachycardia, palpitations
Unknown: QT prolongation

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

Hepato-biliary disorders:
Very rare: Elevations of liver enzymes, increased hepatitis-bilirubin
Unknown: Jaundice

Skin and subcutaneous disorders:

Unknown: Photosensitivity

Musculoskeletal, connective tissue and bone disorders:

Very rare: Myalgia

General disorders and disorders related to the administration site:

Common: Fatigue

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

Unknown: Asthenia

Pediatric population

Other undesirable side effects of unknown frequency obtained from post-marketing data in pediatric patients have been reported to include QT prolongation, arrhythmia and bradycardia.

4.9 Overdose and treatment

In case overdose, standard precautions should be taken to remove unabsorbed active substance. Symptomatic and supportive treatment is recommended.

In a multiple dose clinical research in adults and adolescents, in which up to 45 mg (9 times the clinical dose) Desloratadine was administered, no clinically significant 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 antagonist

ATC code: R06A X27

Mechanism of action

Desloratadine is a non-sedating, long-acting, potent, selective peripheral histamine H1-receptor antagonist. Desloratadine selectively blocks peripheral histamine H1-receptors, due to its inability to enter the central nervous system after oral administration.

Desloratadine has demonstrated antiallergic properties in *in vitro* studies. These include inhibition of the release of proinflammatory cytokines such as IL-4, IL-6, IL-8 and IL-13 from human mast cells/basophils and inhibition of the expression of the adhesion molecule P-selectin in endothelial cells. The clinical significance of these observations has yet to be confirmed.

Clinical efficacy and safety

In a multiple dose clinical research, in which up to 20 mg Desloratadine was administered daily for 14 days, no statistically or clinically significant cardiovascular effect was observed. In a clinical pharmacology research, in which Desloratadine was given at a dose of 45 mg daily (9 times the clinical dose) for ten days, no prolongation of QTc (the time between Q wave and T wave in ECG) interval was observed.

In interaction studies performed with multiple doses of ketoconazole and erythromycin, no changes in the plasma concentration of Desloratadine were observed.

Desloratadine does not readily penetrate the central nervous system. In controlled clinical studies, there was no increase in the incidence of somnolence at the recommended daily dose of 5 mg compared to placebo. Desloratadine given at a daily dose of 7.5 mg did not affect psychomotor performance in clinical studies. In a single dose study in adults, Desloratadine 5 mg does not affect standard measures of flight performance, including exacerbation of subjective somnolence or flight-related activities.

In clinical pharmacology studies, co-administration with alcohol did not result in alcohol-induced impairment of performance or increased insomnia.

No significant difference was found in the psychomotor test results between Desloratadine and placebo groups, whether taken alone or with alcohol.

In patients with allergic rhinitis, Desloratadine were effective in relieving symptoms such as sneezing, runny nose and itching, congestion/nasal congestion, as well as itching of the eyes, tearing and redness and itching of palate. Desloratadine effectively controlled symptoms for 24 hours. The efficacy of Desloratadine has not been clearly demonstrated in clinical studies in adolescents aged 12–17 years.
Allergic rhinitis can be classified as seasonal and perennial allergic rhinitis, as well as intermittent and persistent allergic rhinitis according to the frequency of symptoms. Intermittent allergic rhinitis can be defined as the occurrence of symptoms less than 4 days a week or less than 4 weeks. Persistent allergic rhinitis can be defined as the occurrence of symptoms 4 days or more in a week and for more than 4 weeks.
The efficacy of Desloratadine in alleviating the complaints related to seasonal allergic rhinitis was shown by the total score in the rhino-conjunctivitis quality of life questionnaire. The greatest amelioration was seen in the domains of daily activities and practical problems limited by symptoms.

Chronic idiopathic urticaria has been studied as a clinical model for urticaria, regardless of its etiology, because the background physiopathology is similar and chronic patients who will participate in prospective studies can be found more easily. Since histamine release is a causative factor in all urticarial diseases, Desloratadine is expected to be effective in relieving symptoms in other urticarial diseases in addition to chronic idiopathic urticaria, as recommended in clinical guidelines.

In two 6-week placebo-controlled studies in patients with chronic idiopathic urticaria, Desloratadine was effective in relieving itching and reducing the size and number of swellings and rednesses on the skin from the first day of treatment. In both studies, the effect remained unchanged during the 24-hour dosing interval. In other antihistamine studies in chronic idiopathic urticaria, a proportion of patients who did not respond to antihistamines were excluded from the

study. An amelioration in pyuria was observed in 50% of patients treated with Desloratadine in 55% compared to 19% treated with placebo. Treatment with Desloratadine also resulted in amelioration in sleep and daily function, measured on a four-point scale, with reduced interference with sleep and daily routine activities.

5.2 Pharmacokinetic properties

General properties

Absorption:

Desloratadine plasma concentrations become detectable within 30 minutes after administration. Desloratadine is well absorbed and the maximum concentration is reached 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 once-daily dose dosing frequency. The bioavailability of Desloratadine is dose-proportional between 5 and 20 mg.

Distribution:

Desloratadine is moderately (83%–87%) bound to plasma proteins. There were no clinically relevant signs of drug accumulation following once daily dose (5 mg to 20 mg) of Desloratadine administration for 14 days.

Biotransformation:

Since the enzyme responsible for Desloratadine metabolism has not yet been identified, some interactions that may occur with other drugs cannot be completely ruled out.

Desloratadine does not inhibit CYP3A4 in in vivo conditions and in vitro studies have shown that the medicinal product does not inhibit CYP2D6. It is not a substrate or inhibitor of P-glycoprotein.

In a multiple dose pharmacokinetic study conducted with the tablet formulation in healthy adult cases, four cases were found to metabolize Desloratadine slowly, which would change as four percent. In these cases, the Cmax concentration around 7 hours is approximately 3 times higher and the half-life in the terminal phase is around 89 hours.

In a series of pharmacological and clinical researches, plasma concentrations of Desloratadine were found higher in 6% of cases. The prevalence of this slow metabolizer phenotype is comparable in adult (6%) and pediatric (6%) cases aged 2-11 years and is higher in blacks (adults 18%, pediatric cases 16%) than in whites (adults 2%, pediatric cases 3%); however, the safety profile in these cases is not different from that in the general population.

Elimination:

In a single dose research where Desloratadine is used at a dose of 7.5 mg, it was shown that food (high-fat, high caloric breakfast) had no effect on the disposition of Desloratadine. In another study, it was found that grapefruit juice had no effect on the disposition of Desloratadine.

Linearity/Non-linear Situation:

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. There are no comparable clinical studies performed with Desloratadine and loratadine that show qualitative or quantitative differences of Desloratadine exposure to the toxicity profile of Desloratadine and loratadine.

Non-clinical data reveal no special hazard for humans based on conventional studies examining safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential, reproductive toxicity and development. Absence of carcinogenic potential has been shown in clinical studies performed with Desloratadine and loratadine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Dibasic Calcium Phosphate Anhydrous

Maize Starch

Microcrystalline cellulose

Talc

Magnesium stearate

Opadry blue 85F20400:

– Polyvinyl alcohol

– Macrogol

– Titanium dioxide (E171)

– Talc

– Indigo carmine aluminum lake (E132)

6.2 Incompatibilities

Not applicable for this product.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at room temperature below 30ºC by protecting from moisture.

6.5 Nature and contents of container

It is blistered as to be 10, 20 and 30 tablets in Alu-PVC/Aclar foil blisters.

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

World Medicine İlaç San ve Tic A.Ş.

Bağcılar, İstanbul/TURKEY

8. MARKETING AUTHORISATION NUMBER(S)