DESLOR 5 mg
Desloratadine

1. NAME OF THE PHARMACEUTICAL PRODUCT

DESLOR 5 mg, film-coated tablet, box of 15

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 5 mg of Desloratadine.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet

4. CLINICAL DATA

4.1- Therapeutic indications

Deslor 5 mg is indicated for the symptomatic treatment of:
- allergic rhinitis
- chronic idiopathic urticaria

Desloratadine relieves symptoms associated with allergic rhinitis (nasal inflammation that may be caused by hay fever or dust mite allergy). These symptoms include sneezing, runny or itchy nose, itchy palate, itchy, red or watery eyes. It is also used to relieve the symptoms associated with urticaria (skin damage caused by an allergy), itchy urticaria and rash. The relief of these symptoms lasts all day and helps you to continue your normal daily activities and preserve your sleep.

4.2- Dosage and Administration

Adults and adolescents (12 years and older): One tablet once daily, with or between meals for the relief of symptoms associated with allergic rhinitis (including intermittent and persistent allergic rhinitis) and urticaria.
In adolescents aged 12 to 17, the experience of using desloratadine in clinical efficacy studies is limited.

Intermittent allergic rhinitis (presence of symptoms for less than 4 days per week or less than 4 weeks) should be managed based on the history of the patient's disease; the treatment can be interrupted after the disappearance of symptoms and restored at their reappearance.
In persistent allergic rhinitis (presence of symptoms over a period of 4 days or more per week and for more than 4 weeks), continuous treatment may be offered to patients during periods of allergen exposure.

4.3- Contraindications

Hypersensitivity to the active substance, to any of the excipients, or to loratadine.

4.4- Special warnings and precautions for use

The efficacy and safety of Deslor have not been established in children under 12 years of age.
Deslor should be used with caution in severe renal impairment (see section 5.2).

4.5- Drug interactions:

In clinical trials with Desloratadine tablets during which patients received erythromycin or ketoconazole in combination, no clinically significant interactions were observed (see section 5.1).
In a clinical pharmacology trial, there was no evidence of potentiation of the deleterious effects of alcohol in performance tests involving combinations with Deslor (see section 5.1).

4.6- Pregnancy and lactation:

Desloratadine did not show teratogenic effects in animal studies. The safety of use of the product during pregnancy has not been established. As a result, the use of Deslor during pregnancy is not recommended.
The Desloratadine is excreted into breast milk, therefore the use of Deslor is not recommended in breastfeeding women.

4.7 Effects on ability to drive and use machines

In clinical studies assessing the ability to drive, no effects have been reported in patients receiving Desloratadine. However, patients should be informed that very rare cases of drowsiness have been reported; cases in which their ability to drive or use machines may be affected.

4.8- Side effects:

In adults, side effects are nearly the same as those observed with placebo tablets.

In clinical trials conducted in allergic rhinitis and chronic idiopathic urticaria, at the recommended daily dose of 5 mg, adverse events were reported in 3% more patients than in those treated with placebo. The most commonly reported adverse events with an incidence greater than placebo were: asthenia (1.2%), dry mouth (0.8%) and headache (0.6%). In a clinical study in 578 adolescent patients aged 12 to 17, the most common adverse event was headache; it occurred in 5.9% of patients treated with Desloratadine and in 6.9% of patients receiving placebo. Other adverse effects have very rarely been reported since Deslor's marketing are listed below:

Psychiatric disorders Hallucinations
Nervous system disorders
Dizziness, drowsiness, insomnia, psychomotor hyperactivity, convulsions
Cardiac disorders Tachycardia, palpitations
Gastrointestinal disorders
Abdominal pain, nausea, vomiting, dyspepsia, diarrhea
Hepatobiliary disorders
Increase in liver enzymes, increased bilirubin, hepatitis
Musculoskeletal and systemic disorders: Myalgia
General disorders Hypersensitivity reactions (such as anaphylaxis, angioedema, dyspnea, pruritus, rash, and urticaria)

4.9- Overdosage

In case of overdose, tell your doctor or pharmacist. Elimination of the unabsorbed active substance by the usual methods should be considered. Symptomatic treatment and appropriate therapeutic measures are recommended.
In a repeat dose clinical trial, no clinically significant effect was observed when Desloratadine was administered at a dose of up to 45 mg (nine times the therapeutic dose).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties:

Pharmacotherapeutic group: antihistamines anti-H1, ATC code: R06A X27
Desloratadine is a non-sedating, long-acting antihistamine that exerts a selective antagonistic effect on peripheral H1 receptors. After oral administration, Desloratadine selectively blocks peripheral histamine H1 receptors because it does not spread in the central nervous system.

The antiallergic properties of Desloratadine have been demonstrated by in vitro studies. An inhibition of the release of pro-inflammatory cytokines such as IL-4, IL-6, IL-8, and IL-13 by human mast cells / basophils has been demonstrated, as well as an inhibition of the expression of the P-selectin adhesion molecule on endothelial cells. The clinical significance of these observations remains to be confirmed.
In a repeat dose clinical trial in which up to 20 mg daily of Desloratadine was administered for 14 days, no statistically or clinically significant cardiovascular effects were observed. In a clinical pharmacology trial, in which Desloratadine was administered at a dose of 45 mg per day (nine times the therapeutic dose) for ten days, no QT prolongation was observed.

Repeated dose interaction studies with ketoconazole and erythromycin did not show clinically significant changes in Desloratadine plasma concentrations.

Desloratadine does not spread easily into the central nervous system. In controlled clinical studies, at the recommended dose of 5 mg daily, there was no increase in the incidence of drowsiness compared with placebo. When administered once a day at a single dose of 7.5 mg, Deslor did not impair psychomotor performance in clinical trials. In a single dose study in adults, Desloratadine 5 mg did not change air flight performance parameters, including subjective sleep exacerbation or flight related tasks.

In clinical pharmacology trials, concomitant administration with alcohol did not increase drowsiness or impaired alcohol-induced performance. There was no significant difference between the Desloratadine and the placebo groups in psychomotility tests, whether administered alone or in combination with alcohol.
In patients with allergic rhinitis, Deslor relieved symptoms such as sneezing, runny nose and pruritus, ocular itching, tearing and redness, as well as itching of the palate.

Deslor correctly controlled the symptoms throughout a nycthemeron. The efficacy of Deslor tablets has not been clearly demonstrated in studies in adolescent patients aged 12 to 17 years.

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

Deslor decreased the disabling character of seasonal allergic rhinitis, as shown by the total score of the rhino-conjunctivitis quality of life questionnaire. The most significant improvement was observed in the area of practical problems and daily activities which are limited by symptoms.

Chronic idiopathic urticaria has been studied as a clinical model of urticarial manifestations because the underlying pathophysiology is similar (regardless of etiology), and also because chronic patients can be easily recruited prospectively. Since histamine release is a responsible factor for all urticarial pathologies, Desloratadine is expected to be effective in relief of other

urticarial manifestations' symptoms , in addition to chronic idiopathic urticaria, as it is recommended in the clinical guidelines.

In two controlled six-week trials versus placebo in patients with chronic idiopathic urticaria, Deslor was effective in relieving pruritus and decreasing the number and size of urticaria by the end of the first dose.

In each trial, the effects were maintained throughout a nycthemeron. As in other trials of antihistamines in chronic idiopathic urticaria, the few patients identified as non-respondent to antihistamines have been excluded. A decrease in pruritus of more than 50% was observed in 55% of patients treated with Desloratadine compared to 19% of patients treated with placebo. Deslor treatment has also significantly reduced nocturnal awakenings and interference with daytime activity according to parameters evaluated on a four-point scale.

5.2 Pharmacokinetic properties:

Plasma levels of Desloratadine can be detected within 30 minutes of after administration. Desloratadine is well absorbed with a peak concentration reached after approximately 3 hours; the half-life of the terminal phase is around 27 hours.

The accumulation factor of Desloratadine is related to its half-life (about 27 hours) and to its rate of administration in one dose per day. The bioavailability of Desloratadine is dose-dependent over a range of 5 mg to 20 mg.

In a pharmacokinetic trial in which patient demographics were comparable to those of the general population with potential for seasonal allergic rhinitis, 4% of subjects experienced a higher concentration of Desloratadine. This percentage may vary according to ethnicity. The maximum concentration of Desloratadine observed around the 7th hour was approximately 3 times higher and the half-life of the terminal phase was approximately 89 hours. The safety profile of the product observed in these subjects was not different from that of the general population.

Desloratadine binds moderately (83% - 87%) to plasma proteins. After a daily administration of Desloratadine once a day (5 mg to 20 mg) for 14 days, there was no clinical evidence of product accumulation.

The enzyme involved in the metabolism of Desloratadine has not been identified yet and, therefore, the risk of interaction with other drugs can not be totally excluded. In vivo, Desloratadine does not inhibit cytochrome P3A4 and in vitro studies have shown that the active substance does not inhibit cytochrome P2D6 and is neither a substrate nor an inhibitor of P-glycoprotein.

In a clinical trial with a single dose of 7.5 mg Desloratadine, Desloratadine was not affected by diet (high-calorie, high-fat breakfast).
In another trial, grapefruit juice has not changed the fate of Desloratadine.

5.3 Preclinical safety data

Desloratadine is the major active metabolite of loratadine. Nonclinical studies with Desloratadine and Loratadine demonstrated that there was no qualitative or quantitative difference in the toxicity profile of Desloratadine and Loratadine for comparable levels of exposure to Desloratadine.

Non-clinical which are data based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, and of reproductive functions reveal no special hazard for humans. The absence of carcinogenic potential has been demonstrated in studies conducted with Desloratadine and loratadine.

6. PHARMACEUTICAL PROPERTIES

6.1- List of excipients:

Calcium dihydrogen phosphate
Cellulose microcristalline
Amidon prégélatinisé
Stéarate de magnésium
Opadry II blue

6.2 – Incompatibility

Not applicable.

6.3- Shelf life

36 months.

6.4- Special precautions for storage:

Keep at temperature not exceeding 30 ° C
Store in the original package

6.5- Nature and content of the outer packaging:

15 tablets are packaged in a clear PVC / ALU blister bearing lot details. 1 blister is packed in a cardboard case with a leaflet.

6.6- Instructions for use and handling

No special requirements

7- HOLDER OF THE MARKETING AUTHORIZATION:

MédiS laboratories
Tunis Road - Km 7 - BP 206 - 8000 Nabeul - Tunisia

8. MARKETING AUTHORIZATION NUMBER (S)

923 336 2

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF AUTHORIZATION

Date of first authorization: 30/11/2005
Date of first renewal 30/11/2010
Second renewal date 30/11/2015

10. CONDITIONS OF PRESCRIPTION AND DISPENSING
List II.