

SUMMARY OF PRODUCT CHARACTERISTIC (SPC)

1. NAME OF THE MEDICINAL PRODUCT

NEOLOR (Desloratadine) 5mg Film Coated Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains 5mg desloratadine

Colours: Titanium Dioxide, FD & C Blue No. 2 Aluminium Lake

For full list excipient, see section 6.1

3. PHARMACEUTICAL FORM

Film-coated tablet

Light blue colored, round shaped, biconvex, film coated tablets, plain on both sides. The tablet should be free of all physical defects.

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS:

Desloratadine is indicated in adults and adolescents aged 12 years and older for the relief of symptoms associated with:

- allergic rhinitis (see section Pharmacokinetic Properties)
- urticaria (see section Pharmacokinetic Properties)

4.2 POSOLOGY AND METHOD OF ADMINISTRATION:

Posology:

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

The recommended dose of desloratadine is one tablet once a day.

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.

Paediatric population:

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

The safety and efficacy of desloratadine tablets in children below the age of 12 years have not been established.

Method of administration:

Oral use.

The dose can be taken with or without food.

4.3 CONTRAINDICATIONS:

Hypersensitivity to the active substance or to any of the excipients listed in section Excipients or to loratadine.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE:

General:

Renal function impairment

In the case of severe renal insufficiency, desloratadine should be used with caution (see section Pharmacodynamic Properties).

Seizures

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

Desloratadine tablet contains lactose

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption 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 Pharmacokinetic Properties).

Paediatric population

Interaction studies have only been performed in adults.

In a clinical pharmacology trial desloratadine taken concomitantly with alcohol did not potentiate the performance impairing effects of alcohol (see section Pharmacokinetic Properties).

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:

A large amount of data on pregnant women (more than 1,000 pregnancy outcomes) indicate no malformative nor foeto/neonatal toxicity of Desloratadine. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section Preclinical Safety Data). As a precautionary measure, it is preferable to avoid the use of desloratadine during pregnancy.

Breast-feeding:

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 desloratadine therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman.

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 on clinical 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 UNDESIRABLE 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 with desloratadine were reported in 3 % of patients in excess of those treated with placebo. The most frequent of adverse reactions reported in excess of placebo were fatigue (1.2 %), dry mouth (0.8 %) and headache (0.6 %).

Paediatric population

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.

Tabulated list of adverse reactions

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 ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1,000$ to $< 1/100$), rare ($\geq 1/10,000$ to $< 1/1,000$), very rare ($< 1/10,000$) and not known (cannot be estimated from the available data).

System Organ Class	Frequency	Adverse reactions seen with Desloratadine
Metabolism and nutrition disorders	Not known	Increased appetite
Psychiatric disorders	Very rare	Hallucinations
	Not known	Abnormal behaviour, aggression, depressed mood

Nervous system disorders	Common	Headache
	Very rare	Dizziness, somnolence, insomnia, psychomotor hyperactivity, seizure
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	Not known	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
Investigations	Not known	Weight increased
Eye disorder	Not known	Eye dryness

Paediatric population

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

A retrospective observational safety study indicated an increased incidence of new-onset seizure in patients 0 to 19 years of age when receiving desloratadine compared with periods not receiving desloratadine. Among children 0-4 years old, the adjusted absolute increase was 37.5 (95% Confidence Interval (CI) 10.5-64.5) per 100,000 person years (PY) with a background rate of new onset seizure of 80.3 per 100,000 PY. Among patients 5-19 years of age, the adjusted absolute increase was 11.3 (95% CI 2.3-20.2) per 100,000 PY with a background rate of 36.4 per 100,000 PY. (See section Special Warning and Precautions for Use)

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. To report adverse events, email us at drugsafety@zyduslife.com or visit www.zyduslife.com.

4.9 OVERDOSE

The adverse event profile associated with overdosage, as seen during post-marketing use, is similar to that seen with therapeutic doses, but the magnitude of the effects can be higher.

Treatment

In the event of overdose, consider standard measures to remove unabsorbed active substance. Symptomatic and supportive treatment is recommended.

Desloratadine is not eliminated by haemodialysis; it is not known if it is eliminated by peritoneal dialysis.

Symptoms

Based on a multiple dose clinical trial, in which up to 45 mg of desloratadine was administered (nine times the clinical dose), no clinically relevant effects were observed.

Paediatric population

The adverse event profile associated with overdosage, as seen during post-marketing use, is similar to that seen with therapeutic doses, but the magnitude of the effects can be higher.

5. PHARMACOLOGICAL PROPERTIES:

5.1 Pharmacodynamic properties:

Pharmacodynamic properties:

Pharmacotherapeutic group: H1 antagonist

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.

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.

Pharmacodynamic effects

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, whether administered alone or with alcohol.

In patients with allergic rhinitis, desloratadine was effective in relieving symptoms such as sneezing, nasal discharge and itching, as well as ocular itching, tearing and redness, and itching of palate. Desloratadine effectively controlled symptoms for 24 hours.

Paediatric population

The efficacy of desloratadine tablets has not been clearly demonstrated in trials with adolescent patients 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 was 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:

Absorption:

Desloratadine plasma concentrations can be detected within 30 minutes of administration. 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.

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. This percentage may vary according to ethnic background. Maximum desloratadine concentration was about 3-fold higher at approximately 7 hours with a terminal phase half-life of approximately 89 hours. The safety profile of these subjects was not different from that of the general population.

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 can not be fully excluded. Desloratadine does not inhibit CYP3A4 *in vivo*, and *in vitro* studies have shown that the medicinal product does not inhibit 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.

Renally impaired patients:

The pharmacokinetics of desloratadine in patients with chronic renal insufficiency (CRI) was compared with that of healthy subjects in one single-dose study and one multiple dose study. In the single-dose study, the exposure to desloratadine was approximately 2 and 2.5-fold greater in subjects with mild to moderate and severe CRI, respectively, than in healthy subjects. In the multiple-dose study, steady state was reached after Day 11, and compared to healthy subjects the exposure to desloratadine was ~1.5-fold greater in subjects with mild to moderate CRI and ~2.5-fold greater in subjects with severe CRI. In both studies, changes in

exposure (AUC and Cmax) of desloratadine and 3-hydroxydesloratadine were not clinically relevant.

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 PARTICULARS

6.1 LIST OF EXCIPIENTS

Polacrillin Potassium

Citric Acid Anhydrous

Gelatin

Microcrystalline Cellulose

Crospovidone

Silica Colloidal Anhydrous

Mannitol

Lactose Monohydrate

Magnesium Stearate

Sodium Stearyl Fumarate

Instacoat Universal ICG-U-10272 Blue

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store upto 30°C. Protect from moisture, Keep out of reach of children.

6.5 Nature and contents of container

OPA COATED PVC - ALU BLISTER,

Pack size: Blister pack of 10x10 tablets

6.6 Special precautions for disposal and other handling

No special requirement

7. MARKETING AUTHORIZATION HOLDER

Name : Zydus Lifesciences Limited
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8. MARKETING AUTHORISATION NUMBER(S)

07321/07984/REN/2021

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 26/05/2017

Date of latest renewal: 13/04/2022

10. DATE OF REVISION OF THE TEXT

November 2023

11. REFERENCE