DR REDDY'S LABORATORIES (PTY) LTD.
DESODENE (TABLETS)
APPROVED PACKAGE INSERT
15.04.2020

SCHEDULING STATUS

S2

PROPRIETARY NAME AND DOSAGE FORM

DESODENE (tablet)

COMPOSITION

DESODENE: Each film-coated tablet contains desloratadine 5 mg.

Contains sugar (lactose anhydrous).

The other ingredients are colloidal silicon dioxide, hypromellose, indigo carmine, L-arginine, macrogol, opadry blue, polyethylene glycol, purified water, starch and titanium dioxide.

PHARMACOLOGICAL CLASSIFICATION

A 5.7.1 Antihistaminics

PHARMACOLOGICAL ACTION

Mechanism of action

Desloratadine is a major metabolite of loratadine, and is a non-sedating long-acting histamine antagonist with selective peripheral H_1- receptor antagonist activity.

Desloratadine has demonstrated anti-allergic, antihistaminic and anti-inflammatory activity.

Pharmacodynamic properties

After oral administration, desloratadine selectively blocks peripheral histamine H_1-receptors. It does not cross the blood-brain barrier to any great extent.

Desloratadine has demonstrated in addition to antihistaminic activity, anti-allergic and anti-inflammatory activity

from numerous *in vitro* (mainly conducted on cells of human origin) and *in vivo* studies. These studies have shown that desloratadine inhibits the broad cascade of events that initiate and propagate allergic inflammation.

Pharmacokinetic properties

Absorption

Desloratadine plasma concentrations can be detected within 30 minutes of desloratadine 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 is consistent with its half-life (approximately 27 hours) and a once daily dosing frequency. The bioavailability of desloratadine is dose proportional over the range of 5 mg to 20 mg.

Distribution

Desloratadine is moderately bound (83 % to 87 %) to plasma proteins. There is no evidence of clinically relevant drug 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 drugs cannot be fully excluded. *In vivo* studies show that desloratadine does not inhibit CYP3A4.

In vitro studies have shown that desloratadine does not inhibit CYP2D6 and is neither a substance 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 a different 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 C_{max}) of desloratadine and 3-hydroxydesloratadine were not clinically relevant.

INDICATIONS

DESODENE is indicated for the relief of symptoms associated with seasonal allergic rhinitis.

CONTRAINDICATIONS

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

WARNINGS AND SPECIAL PRECAUTIONS

In the case of severe renal insufficiency, **DESODENE** should be used with caution (see Pharmacokinetic properties).

DESODENE should be administered with caution in patients with medical or familial history of seizures, and mainly young children, being more susceptible to develop new seizures under **DESODENE** treatment. Healthcare providers may consider discontinuing **DESODENE** in patients who experience a seizure while on treatment.

DESODENE lacks significant sedative effects, however, some individuals may still experience the sedative effects. It is therefore advisable to determine individual response before driving or performing complicated tasks.

Safety and efficacy of **DESODENE** in children under 12 years of age have not been established.

Safety and efficacy of desloratadine have not been established for treatment periods in excess of 4 weeks.

DESODENE tablets should not be taken by patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption.

Effects on ability to drive and use machines

A few patients treated with non-sedating anti-histamines have experienced drowsiness. Therefore it is prudent to exercise caution before driving or operating machinery. The effect of a drug on a particular patient can be ascertained after the first few doses.

INTERACTIONS

DESODENE taken concomitantly with alcohol did not potentiate the performance impairing effects of alcohol.

Co-administration of **DESODENE** with ketoconazole increases the maximum desloratadine concentration (C_{max}) by 45 % and the area under the time concentration curve (AUC) by 37 %. Co-administration of **DESODENE** with erythromycin increased the C_{max} of desloratadine by 24 % and the AUC by 14 %.

Co-administration of **DESODENE** with azithromycin resulted in an increase of both C_{max} (31 %) and AUC (12 %) of azithromycin.

Co-administration of **DESODENE** with cimetidine did not significantly affect the pharmacokinetics of desloratadine.

Co-administration of **DESODENE** with fluoxetine caused an increased in the C_{max} of desloratadine by 15 %, and an increase of 13 % in AUC, and 17 % in the C_{max} of 3-OH desloratadine respectively. The C_{max} and AUC of fluoxetine were reduced by 9 % and 11 % respectively. The corresponding mean parameters of norfluoxetine increased by 23 % and 18 % respectively, with co-administration of **DESODENE** and fluoxetine.

There is no effect of food and grapefruit juice on **DESODENE**.

PREGNANCY AND LACTATION

Pregnancy

Safety in pregnancy and lactation has not been established.

The use of **DESODENE** during pregnancy is therefore not recommended.

Lactation

Desloratadine is excreted into breast milk, therefore the use of **DESODENE** is not recommended in breastfeeding women.

DOSAGE AND DIRECTIONS FOR USE

Adults and adolescents ($\geq$12 years of age): One tablet once a day regardless of mealtime,

Improvement of symptoms associated with seasonal allergic rhinitis usually becomes noticeable within 1 - 2 hours after administration of **DESODENE**.

SIDE EFFECTS

Metabolism and nutrition disorders

Frequency unknown: Increased appetite.

Psychiatric disorders

Less frequent: Hallucinations.

Frequency unknown: Abnormal behaviour, aggression.

Nervous system disorders

Frequent: Headache

Less frequent: Dizziness, fatigue, somnolence, insomnia, seizures, psychomotor hyperactivity.

Cardiac disorders

Less frequent: Tachycardia, palpitations.

Frequency unknown: QT prolongation.

Respiratory, thoracic and mediastinal disorders

Frequent: Pharyngitis.

Gastrointestinal disorders

Frequent: Dry mouth.

Less frequent: Abdominal pain, nausea, vomiting, dyspepsia, diarrhoea.

Hepatobiliary disorders

Less frequent: Elevations of liver enzymes, increased bilirubin, hepatitis.

Frequency unknown: Jaundice.

Skin and subcutaneous tissue disorders

Frequency unknown: Photosensitivity.

Musculoskeletal, connective tissue and bone disorders

Less frequent: Myalgia.

Reproductive system and breast disorders

Less frequent: Dysmenorrhoea.

General disorders and administration site conditions

Frequent: Fatigue.

Less frequent: Hypersensitivity reactions (such as anaphylaxis, angioedema, dyspnoea, pruritis, rash and urticaria).

Frequency unknown: Asthenia.

Investigations:

Frequency unknown: Weight increased.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS 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.

IDENTIFICATION

Dark blue coloured, round shaped, biconvex film-coated tablets, embossed "RDY" on one side and "227" on the other side.

PRESENTATION

30 film-coated tablets in white HDPE bottles and or 7's/10's film-coated tablets in Alu/Alu or PVC/Alu blisters

STORAGE INSTRUCTIONS

Store at or below 25 °C.

Protect from light.

Keep tablets in the original container.

Keep blisters in carton until required for use.

Keep out of reach of children.

REGISTRATION NUMBER

41/5.7.1/0779

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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