PROFESSIONAL INFORMATION FOR CLAREX

ORAL SOLUTION

SCHEDULING STATUS S2

1. NAME OF THE MEDICINE

CLAREX ORAL SOLUTION oral solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 mL of oral solution contains 2,5 mg desloratadine.

Contains sugar: Sorbitol (150 mg/mL) (a sugar alcohol).

Contains sweetener: Sucralose (2 mg/mL).

Solvent: Propylene glycol (150 mg/mL).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral solution

CLAREX ORAL SOLUTION is a clear, colourless solution with a pleasant fruity odour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

CLAREX ORAL SOLUTION is indicated for the relief of symptoms associated with allergic rhinitis (AR).

CLAREX ORAL SOLUTION is also indicated for the short-term relief of symptoms associated with chronic idiopathic urticaria (CIU).

4.2 Posology and method of administration

Posology

Children 2 to 5 years of age:

2,5 mL (1,25 mg) CLAREX ORAL SOLUTION once a day.

Children 6 to 11 years of age:

5 mL (2,5 mg) CLAREX ORAL SOLUTION once a day.

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

10 mL (5 mg) CLAREX ORAL SOLUTION once a day.

Method of administration

Oral use.

The dose can be taken with or without food.

4.3 Contraindications

Hypersensitivity to desloratadine or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

CLAREX ORAL SOLUTION 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 with desloratadine treatment. Health care providers may consider discontinuing desloratadine in patients who experience a seizure while on treatment.

Paediatric population

In children below 2 years of age, the diagnosis of allergic rhinitis is particularly difficult to distinguish from other forms of rhinitis. The absence of upper respiratory tract infection or structural abnormalities, as well as patient history, physical examinations, and appropriate laboratory and skin tests should be considered.

Approximately 6 % of adults and children 2 to 11 years old are phenotypic poor metabolisers of desloratadine and exhibit a higher exposure (see section 5.2). The safety of desloratadine, as in CLAREX ORAL SOLUTION in children 2 to 11 years of age who are poor metabolisers, is the same as in children who are normal metabolisers. The effects of desloratadine in poor metabolisers < 2 years of age have not been studied.

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

CLAREX ORAL SOLUTION contains 150 mg sorbitol per mL.
The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account.
The content of sorbitol in medicines for oral use may affect the bioavailability of other medicines for oral use administered concomitantly.

4.5 Interaction with other medicines and other forms of interaction

No clinically relevant interactions were observed in clinical trials with desloratadine in which

erythromycin or ketoconazole were co-administered (see section 5.1).

There was no effect of food or grapefruit juice on the disposition of desloratadine.

Co-administration of desloratadine with azithromycin resulted in an increase of both Cmax (31 %) and AUC (12 %) of azithromycin.

Co-administration of fluoxetine with desloratadine caused an increase in the Cmax of desloratadine by 15 % and an increase of 13 % in AUC and 17 % in Cmax of 3-OH desloratadine respectively.
The Cmax 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 desloratadine and fluoxetine.

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 5.1). 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 Fertility, pregnancy and lactation

Pregnancy

The safe use of CLAREX ORAL SOLUTION during pregnancy has not been established. The use of CLAREX ORAL SOLUTION during pregnancy is therefore not recommended.
Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

Breastfeeding

Desloratadine is excreted into breast milk, therefore the use of CLAREX ORAL SOLUTION is not recommended in mothers who are breastfeeding their infants.

The effect of desloratadine on newborns/infants is unknown.

4.7 Effects on ability to drive and use machines

CLAREX ORAL SOLUTION has no or negligible influence on the ability to drive a vehicle or operate machines. However, a small number of individuals may experience dizziness or sedation (see section 4.8). Patients should be advised to take special care when performing tasks requiring their attention, until they are reasonably certain that their performance is not affected by CLAREX ORAL SOLUTION.

4.8 Undesirable effects

Paediatric population

The most frequently occurring adverse event reported was headache.

Adults and adolescents

The most frequently occurring adverse events reported were fatigue, dry mouth and headache.

System organ class	Frequency	Adverse reactions
Metabolism and nutrition disorders	Frequency unknown	Increased appetite
Psychiatric disorders	Less frequent Frequency unknown	Hallucinations Abnormal behaviour, aggression
Nervous system disorders	Frequent Frequent (children less than 2 years) Less frequent	Headache Insomnia Dizziness, somnolence, insomnia, psychomotor hyperactivity, seizures
Cardiac disorders	Less frequent Frequency unknown	Tachycardia, palpitations QT prolongation

Gastrointestinal disorders	Frequent Frequent (children less than 2 years) Less frequent	Dry mouth Diarrhoea Abdominal pain, nausea, vomiting, dyspepsia, diarrhoea
Hepatobiliary disorders	Less frequent Frequency unknown	Elevations of liver enzymes, increased bilirubin, hepatitis Jaundice
Skin and subcutaneous tissue disorders	Frequency unknown	Photosensitivity
Musculoskeletal and connective tissue disorders	Less frequent	Myalgia
General disorders and administration site conditions	Frequent Frequent (children less than 2 years) Less frequent Frequency unknown	Fatigue Fever Hypersensitivity reactions (such as anaphylaxis, angioedema, dyspnoea, pruritus, rash, and urticaria) Asthenia
Investigations	Frequency unknown	Increase in body mass

Post-marketing studies

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

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of CLAREX ORAL SOLUTION is important. It allows continued monitoring of the benefit/risk balance of CLAREX ORAL SOLUTION. Health care providers are asked to report any suspected adverse reactions via the **Adverse Drug Reaction Reporting Form**, found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

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.

5. PHARMACOLOGICAL PROPERTIES

Category and class: A 5.7.1 Antihistaminics

Pharmacotherapeutic group: Antihistamines – H_1 antagonist

ATC code: R06A X27

5.1 Pharmacodynamic properties

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

Desloratadine has demonstrated antiallergic, antihistaminic and anti-inflammatory properties from *in vitro* studies. These include inhibiting the release of pro-inflammatory 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.

5.2 Pharmacokinetic properties

Absorption

Desloratadine plasma concentrations can be detected within 30 minutes of desloratadine administration in adults and adolescents. 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.

Distribution

Desloratadine is moderately bound (83 % – 87 %) to plasma proteins. There is no evidence of clinically relevant active substance accumulation following once daily adult and adolescent 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.
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 energy breakfast) on the disposition of desloratadine. In another study, grapefruit juice had no effect on the disposition of desloratadine.
In separate single dose studies, at the recommended doses, paediatric patients had comparable AUC and C_{max} vaues of desloratadine to those in adults who received a 5 mg dose of desloratadine syrup.

Special populations

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 both studies, changes in exposure (AUC and C_{max}) of desloratadine and 3-hydroxydesloratadine were not clinically relevant.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hypromellose, sucralose, citric acid, sodium citrate, sorbitol, propylene glycol, tutti frutti flavourant

(propylene glycol, flavouring substances), purified water.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 30 ºC.

Keep the bottle tightly closed when not in use.

Keep the bottle in the outer carton until required for use.

Store in the original packaging.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

CLAREX ORAL SOLUTION is filled into amber type III glass bottles of 30 / 60 / 100 / 125 / 150 / 220/ 250 / 300 mL and closed with a white plastic child-resistant screw cap.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Unicorn Pharmaceuticals (Pty) Ltd

Corner of Searle & Pontac Streets

Cape Town

South Africa 8001

8. REGISTRATION NUMBER

To be allocated by SAHPRA upon registration.

9. DATE OF FIRST AUTHORISATION

To be allocated by SAHPRA upon registration.

10. DATE OF REVISION OF THE TEXT

Not applicable.

