PROFESSIONAL INFORMATION

SCHEDULING STATUS S2

1. NAME OF THE MEDICINE

Clarex ODT 2,5, orodispersible tablet

Clarex ODT 5, orodispersible tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Clarex ODT 2,5

Each orodispersible tablet contains 2,5 mg desloratadine.

Clarex ODT 5

Each orodispersible tablet contains 5 mg desloratadine.

Excipients with known effect:

Clarex ODT 2,5

Each Clarex ODT 2,5 orodispersible tablet contains:

Sugar: mannitol (66,7 mg/tablet).

Sweetener: aspartame (1,5 mg/tablet).

Clarex ODT 5

Each orodispersible tablet contains:

Sugar: mannitol (133,5 mg/tablet).

Sweetener: aspartame (3 mg/tablet).

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Orodispersible tablets.

Clarex ODT 2,5: Red-brick, round, flat tablets with bevelled edges and '2.5' embossed on one side.

Clarex ODT 5: Red-brick, round, flat tablets with bevelled edges and '5' embossed on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Clarex ODT is indicated for the relief of symptoms associated with allergic rhinitis.

Clarex ODT is also indicated for the short-term relief of symptoms associated with chronic idiopathic urticaria.

4.2 Posology and method of administration

Paediatric population (6 to 11 years of age):

One Clarex ODT 2,5 orodispersible tablet placed in the mouth once a day.

Adolescents and adults (≥ 12 years of age):

One Clarex ODT 5 orodispersible tablet placed in the mouth once a day, regardless of mealtime for relief of symptoms associated with allergic rhinitis (during intermitted and persistent rhinitis) and chronic idiopathic urticaria.

Intermittent allergic rhinitis (presence of symptoms for less than 4 days per week of for less than 4 weeks) should be managed in accordance with the evaluation of the patient's disease history. Treatment can be discontinued after symptoms are resolved and re-initiated upon their reappearance.

In persistent allergic rhinitis (presence of symptoms for more than 4 days or more per week or for more than 4 weeks), continued treatment may be proposed to patients during allergen exposure periods.

Improvement of symptoms associated with seasonal allergic rhinitis, usually becomes noticeable within 1 to 2 hours after administration of Clarex ODT.

Method of administration

For oral use with or without food.

Immediately before use, the blister must be carefully peeled open and the dose of orodispersible tablet removed without crushing it. The dose of orodispersible tablet is placed in the mouth where it will disperse immediately. Water or other liquid is not needed to swallow the dose. The dose must be taken as soon as the blister has been opened.

4.3 Contraindications

Hypersensitivity to desloratadine or to any of the inactive ingredients (see section 6.1).

4.4 Special warnings and precautions for use

In the case of severe renal insufficiency, Clarex ODT should be taken with caution (see section 5.2).

Clarex ODT should be taken 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, as in Clarex ODT treatment. Health care providers may consider discontinuing desloratadine in patients who experience a seizure while on treatment.

Special Precautions

Clarex ODT 2,5

Safety and efficacy of CLAREX ODT 2,5 in children under 6 years of age has not been established.

Clarex ODT 5

Safety and efficacy of CLAREX ODT 5 in children under 12 years of age has not been established.

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

Aspartame

This medicine contains 1,5 mg mg aspartame in each Clarex ODT 2,5 orodispersible tablet and 3 mg in each Clarex ODT 5 orodispersible tablet.

Aspartame is hydrolysed in the gastrointestinal tract when orally ingested. One of the major hydrolysis products is phenylalanine.

4.5 Interaction with other medicines and other forms of interaction

Co-administration of desloratadine, as contained in Clarex ODT, 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 desloratadine with erythromycin increased the C_{max} of desloratadine by 24 % and the AUC by 14 %. Co-administration of desloratadine, as contained in Clarex ODT, with azithromycin resulted in an increase of both C_{max} (31 %) and AUC (12 %) of azithromycin. The increase in C_{max} and AUC of desloratadine, as contained in Clarex ODT, when co-administered with either ketoconazole or erythromycin did not cause any clinically relevant adverse events in populations studied.

Co-administration of cimetidine with desloratadine, as contained in Clarex ODT, did not significantly affect the pharmacokinetics of desloratadine. Co-administration of fluoxetine with

desloratadine, as contained in Clarex ODT, caused an increase in the C_{max} of desloratadine by 15 % and an increase of 13 % in AUC and 17 % in 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 desloratadine, as contained in Clarex ODT, and fluoxetine. No clinically relevant changes in desloratadine plasma concentrations were observed in multiple-dose ketoconazole, and cimetidine interaction trials.

In a clinical pharmacology trial, desloratadine tablets 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.

Paediatric population

Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation

Pregnancy

Desloratadine, as in Clarex ODT, were not found to be teratogenic in animal studies. The safe use of Clarex ODT tablets during pregnancy has not been established and is therefore not recommended.

Breastfeeding

Desloratadine is excreted into breast milk, therefore the use of Clarex ODT is not recommended in beastfeeding women.

Fertility

There are no data available on male and female fertility.

4.7 Effects on ability to drive and use machines

Desloratadine, as in Clarex ODT can cause dizziness and somnolence. It is recommended that patients be advised not to engage in activities requiring mental alertness, such as driving a vehicle or using machines, until they have established their own response to Clarex ODT.

4.8 Undesirable effects

System organ class	Frequency	Adverse reactions
Immune system disorders	Less frequent	Hypersensitivity reactions (such as anaphylaxis, angioedema, dyspnoea, pruritus, rash and urticaria)
Metabolism and nutrition disorders	Frequency unknown	Increased appetite
Psychiatric disorders	Less frequent Frequency unknown	Hallucinations Abnormal behaviour, aggression
Nervous system disorders	Frequent Less frequent	Headache Dizziness, somnolence, insomnia, psychomotor hyperactivity, seizures
Cardiac disorders	Less frequent Frequency unknown	Tachycardia, palpitations QT prolongation
Gastrointestinal disorders	Frequent Less frequent	Dry mouth 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 Frequency unknown	Fatigue Asthenia
Investigations	Frequency unknown	Increase in body mass

Paediatric population

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 ODT is important. It allows continued monitoring of the benefit/risk balance of Clarex ODT. 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

Side effects must also be reported to Unicorn Pharmaceuticals (Pty) Ltd to vigilance@unicornpharma.co.za. By reporting side effects, you can help provide more information on the safety of Clarex ODT.

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.

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.

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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 5.7.1 Antihistaminics

Pharmacotherapeutic group: antihistamines – H_1 antagonist, ATC code: R06A X27

Desloratadine 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. After oral administration, desloratadine selectively blocks peripheral histamine H_1-receptors. It does not readily penetrate into the central nervous system.

In addition to antihistaminic activity, desloratadine has demonstrated 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.

5.2 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 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 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 yet been identified, and therefore some interactions with other medicines cannot be fully excluded. *In vivo* studies with specific inhibitors of CYP3A4 and CYP2D6 have shown that these enzymes are not important in the metabolism of desloratadine. Desloratadine does not inhibit CYP3A4 or 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.

Special patient 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 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Aspartame

Citric acid monohydrate

Croscarmellose sodium

Iron oxide red E172

Magnesium stearate

Mannitol

Microcrystalline cellulose

Polacrilin potassium

Potassium hydroxide (for pH-adjustment)

Purified water

Tutti-frutti flavour

Tutti-frutti flavour contains:

Flavouring

Modified starch E1450

Maltodextrin

Propylene glycol E1520

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store below 30 °C.

Protect from moisture.

Keep blisters in outer carton until required for use.

Do not use tablets after the expiry date printed on the container.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6.5 Nature and contents of container

Clarex ODT is packed in Aluminium / peelable Aluminium blisters. The blisters are subsequently packed into cartons.

Pack sizes

Clarex ODT 2,5 pack sizes: 10, 30, 50, 60, 90, 100 and 150

Clarex ODT 5 pack sizes: 10, 20, 30, 50, 60, 90 and 100

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Unicorn Pharmaceuticals (Pty) Ltd

Cnr. Searle & Pontac Streets,

Cape Town,

South Africa, 8001

8. REGISTRATION NUMBERS

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

To be allocated by SAHPRA upon registration.