PROFESSIONAL INFORMATION

SCHEDULING STATUS: S2

1. NAME OF THE MEDICINE
XYLEVE ODT 5 mg Orodispersible Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
XYLEVE ODT 5 mg orodispersible tablets:
Each orodispersible tablet contains 5 mg levocetirizine dihydrochloride.

Excipients with known effect:
Contains sugars.
Each XYLEVE ODT 5 mg orodispersible tablet contains 104,00 mg lactose monohydrate, 5,00 mg aspartame (E951), mannitol contained in Pharmaburst B2 (Mannitol (E421), Polyplasdone, Sorbitol (E420) and Syloid)) and 0,018 µg of sulphite ammonia caramel (E150d). Each XYLEVE ODT 5 mg contains 39 mg of potassium.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Orodispersible tablets.
White to off-white, round, flat, bevelled edged orodispersible tablets and plain on both the sides.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
XYLEVE ODT is indicated for the relief of symptoms associated with the following allergic conditions:
- seasonal allergic rhinitis
- perennial allergic rhinitis
- chronic idiopathic urticaria

4.2 Posology and method of administration
Posology
Adults and adolescents 12 years of age and older
The daily recommended dose is one 5 mg orodispersible tablet.
Children
For children aged 2 - 6 years no adjusted dosage is possible with the orodispersible tablet formulation.
Children aged 6 - 12 years:
The daily recommended dose is one 5 mg orodispersible tablet.

Special populations
Elderly
Adjustment of the dose is recommended in elderly patients with moderate to severe renal impairment (see "Renal impairment" below).

Renal impairment
Adults with renal impairment:
The dosing interval must be individualised according to renal function. Refer to the following table and adjust the dose as indicated. To use this dosing table, an estimate of the patient's creatinine clearance (Clcr) in mL/min is needed.
The Clcr (mL/min) may be estimated from serum creatinine (µmol/L) determination using the following formula:

$$CL_{cr} = \frac{[140 - \text{age (years)}] \times \text{weight (kg)}}{\text{serum creatinine (µmol/L)}} \quad (\times 0{,}85 \text{ for women})$$

Dosing adjustments for patients with impaired renal function:

Group	Creatinine Clearance (ml/min)	Dosage and Frequency
Normal	≥ 80	5 mg once daily
Mild	50 - 79	5 mg once daily
Moderate	30 - 49	5 mg once every 2 days
Severe	< 30	5 mg once every 3 days
End-stage renal disease - patient undergoing dialysis	< 10	Contraindicated

Paediatric patients with renal impairment:
The dose will have to be adjusted on an individual basis taking into account the renal clearance of the patient and his/her body weight. There are no specific data for children with renal impairment.

Hepatic impairment
No dose adjustment is needed in patients with solely hepatic impairment. In patients with hepatic impairment and renal impairment, adjustment of the dose is recommended (see "Renal impairment" above).

Duration of use
Intermittent allergic rhinitis (symptoms < 4 days/week or during less than 4 weeks) has to be treated according to the disease and its history; it can be stopped once the symptoms have disappeared and can be restarted again when symptoms reappear. In case of persistent allergic rhinitis (symptoms > 4 days. week or during more than 4 weeks), continuous therapy can be proposed to the patient during the period of exposure to allergens.

Method of administration
The orodispersible tablet should be placed on the tongue and should be sucked, not chewed, until completely disintegrated. The resulting suspension must be swallowed with saliva. The orodispersible tablet can be taken with or without water and may be taken with or without food. It is recommended to take the daily dose in one single intake.

4.3 Contraindications
XYLEVE ODT is contraindicated:
- in hypersensitivity to levocetirizine, to any piperazine derivative or to any of the excipients listed in section 6.1.
- in infants and toddlers aged less than two years, as safety and efficacy have not been demonstrated.
- during breastfeeding of infants and while pregnant (see section 4.6).
- in patients with end stage renal disease, at less than 10 ml/min creatinine clearance.

4.4 Special warnings and precautions for use
Alcohol
Precaution is recommended with concurrent intake of alcohol. XYLEVE ODT lacks significant sedative effects. Patients should, however, be warned that a small number of individuals may experience sedation. This effect may be compounded by the simultaneous intake of alcohol or other central nervous system depressants (see section 4.5).
Risk of urinary retention
Caution should be taken in patients with predisposing factors of urinary retention (e.g., spinal cord lesion, prostatic hyperplasia) as levocetirizine may increase the risk of urinary retention.
Epilepsy and convulsion risk patients
Caution should be taken in patients with epilepsy and patients at risk of convulsion as levocetirizine may cause seizure aggravation.
Allergy skin tests
Response to allergy skin tests is inhibited by antihistamines and a wash-out period (of 3 days) is required before performing them.
Pruritus
Pruritus may occur when levocetirizine is stopped even if those symptoms were not present before treatment initiation. The symptoms may resolve spontaneously. In some cases, the symptoms may be intense and may require treatment to be restarted. The symptoms should resolve when the treatment is restarted (see section 4.8).

Paediatric population
The use of the orodispersible tablet formulation is not recommended in children aged less than 6 years since this formulation does not allow for appropriate dose adaptation. It is recommended to use a paediatric formulation of levocetirizine.

Excipients
Lactose intolerance
This medicine contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.
Aspartame
Aspartame is a source of phenylalanine. Patients with phenylketonuria (PKU) should not take this medicine.
Sulphite ammonia caramel
This medicine contains "sulphite" and may rarely cause severe hypersensitivity reactions and bronchospasm. Patients with rare hereditary problems of sucrase-isomaltase insufficiency should not take XYLEVE ODT.
Sorbitol
Patients with rare hereditary problems of fructose intolerance should not take this medicine.
Potassium
This medicine contains potassium, less than 1 mmol (39 mg) per orodispersible tablet, i.e., essentially "potassium-free".

4.5 Interaction with other medicines and other forms of interaction
No interaction studies have been performed with levocetirizine (including no studies with CYP3A4 inducers); studies with the racemate compound cetirizine demonstrated that there were no clinically relevant adverse interactions (with antipyrine, azithromycin, cimetidine, diazepam, erythromycin, glipizide, ketoconazole and pseudoephedrine). A small decrease in the clearance of cetirizine (16 %) was observed in a multiple dose study with theophylline (400 mg once a day); while the disposition of theophylline was not altered by concomitant cetirizine administration.

In a multiple dose study of ritonavir (600 mg twice daily) and cetirizine (10 mg daily), the extent of exposure to cetirizine was increased by about 40 % while the disposition of ritonavir was slightly altered (-11%) further to concomitant cetirizine administration.

The extent of absorption of levocetirizine is not reduced with food, although the rate of absorption is decreased.

In sensitive patients, the concurrent administration of cetirizine or levocetirizine and alcohol or other CNS depressants may cause additional reductions in alertness and impairment of performance.

4.6 Fertility, pregnancy and lactation
Pregnancy
XYLEVE ODT is contraindicated in pregnancy as safety has not been demonstrated (see section 4.3).
Breastfeeding
XYLEVE ODT is contraindicated in breastfeeding (see section 4.3). Levocetirizine is excreted in human milk.
Fertility
No clinical data are available.

4.7 Effects on ability to drive and use machines
Comparative clinical trials have revealed no evidence that levocetirizine at the recommended dose impairs mental alertness, reactivity or the ability to drive. Nevertheless, some patients could experience somnolence, fatigue and asthenia under therapy with levocetirizine. Therefore, patients intending to drive, engage in potentially hazardous activities or operate machinery should take their response to the medicine into account.

4.8 Undesirable effects
a) Tabulated list of adverse reactions

The table below shows all adverse drug reactions (ADRs) observed during post-market spontaneous reports with levocetirizine dihydrochloride.

System Organ Class	Frequency		
	Frequent	**Less Frequent**	**Not Known**
Immune system disorders			hypersensitivity including anaphylaxis, angioedema
Metabolism and nutrition disorders			increased appetite, increased weight
Psychiatric disorders			aggression, agitation, hallucination, depression, insomnia, suicidal ideation, nightmare
Nervous system disorders	headache, somnolence		convulsion, paraesthesia, dizziness, syncope, tremor, dysgeusia
Eye disorders			visual disturbances, blurred vision, oculogyration
Ear and labyrinth disorders			vertigo
Cardiac disorders			palpitations, tachycardia
Respiratory, thoracic and mediastinal disorders			dyspnoea
Gastrointestinal disorders	dry mouth	gastrointestinal discomfort, abdominal pain	nausea, vomiting, diarrhoea
Hepatobiliary disorders			hepatitis
Skin and subcutaneous tissue disorders			fixed drug eruption, pruritus, rash, urticaria
Musculoskeletal and connective tissue disorders			myalgia, arthralgia
Renal and urinary disorders			dysuria, urinary retention
General disorders and administration site conditions			oedema
Investigations			abnormal liver function tests

b) Description of selected adverse reactions
After levocetirizine discontinuation, pruritus has been reported (see section 4.4 above).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose
Symptoms
Symptoms of overdose may include drowsiness in adults. In children, agitation and restlessness may initially occur, followed by drowsiness.
Management of overdoses
There is no known specific antidote to XYLEVE ODT. Should overdose occur, symptomatic or supportive treatment is recommended. Levocetirizine is not effectively removed by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacological Classification/ Category and Class: A 5.7.1 Antihistaminics
Pharmacotherapeutic group: Antihistamine for systemic use, piperazine derivatives.
ATC Code: R06A E09.

Levocetirizine, the (R) enantiomer of cetirizine, is a histamine H_1 receptor antagonist.

5.2 Pharmacokinetic properties
Absorption
Levocetirizine is absorbed after oral administration with peak blood levels reached 0,9 hours after oral administration. Plasma levels are linearly related between 2,5 mg and 20 mg.
Distribution
Levocetirizine is 90 % bound to human plasma proteins.
Biotransformation
The extent of metabolism is less than 14 % of the dose. The plasma half-life is approximately 8 hours in adults.
Elimination
The main route of excretion is via urine, accounting for approximately 85 % of the dose. Approximately 13 % is excreted in the faeces.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Polacrilin Potassium
Lactose monohydrate
Aspartame (E951)
Silica, colloidal anhydrous
Magnesium stearate
Blackcurrant flavour (contains flavouring substances, flavouring preparations, natural flavouring substances, Maize maltodextrin, E1518 Glyceryl triacetate, E1505 Triethyl citrate, E150d Sulphite ammonia caramel and moisture).
Pharmaburst B2 (contains Mannitol (E421), Polyplasdone, Sorbitol (E420) and Syloid).

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
3 years.

6.4 Special precautions for storage
Store at or below 25 ºC.
KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container
Alu-Alu blisters.
Pack sizes of 1, 2, 4, 5, 7, 10, 2 x 10, 10 x 10, 14, 15, 20, 21, 28, 30, 40, 50, 60, 70, 90 or 100 orodispersible tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling
No special requirements for disposal.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION
Trinity Pharma (Pty) Ltd.
106 16th Road
Midrand
South Africa
1686

8. REGISTRATION NUMBER
XYLEVE ODT: 52/5.7.1/0342.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
26 July 2022

10. DATE OF REVISION OF THE TEXT

TRINITY PHARMA

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