Austell Pharmaceuticals (Pty) Ltd, Lezlerg 5 mg, Lergilez 5 mg and Levocetirizine 5 mg Austell film-coated tablets

Approved Professional Information for Medicines for Human Use:

[PRODUCT NAME]

Please note: This variation application is submitted as a duplicate and hence [PRODUCT NAME] is used in 1.5.5 to indicate the proprietary names as approved and registration numbers as per registration certificates.

Master /Duplicate	**Approved proprietary name [PRODUCT NAME]**	**SAHPRA Registration number**
Master	LEZLERG 5 MG	48/5.7.1/1135
Duplicate 1	LERGILEZ 5 MG	48/5.7.1/1134
Duplicate 2	LEVOCETIRIZINE 5 MG AUSTELL	48/5.7.1/1132

SCHEDULING STATUS

S1

1. NAME OF THE MEDICINE

[PRODUCT NAME] 5 mg Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

[PRODUCT NAME] 5 mg tablets

Each film-coated tablet contains 5 mg levocetirizine dihydrochloride.

Contains sugar: lactose monohydrate

Each [PRODUCT NAME] 5 mg tablet contains 70,00 mg lactose monohydrate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets

Austell Pharmaceuticals (Pty) Ltd, Lezlerg 5 mg, Lergilez 5 mg and Levocetirizine 5 mg Austell film-coated tablets

[PRODUCT NAME] 5 mg Tablets

White to off-white, oval, biconvex film-coated tablets with '5' embossed on one side and plain on other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

[PRODUCT NAME] 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 tablet.

Children

For children aged 2 - 6 years no adjusted dosage is possible with the film-coated tablet formulation.

Children aged 6 - 12 years:

The daily recommended dose is one 5 mg 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 (Cl_{cr}) in mL/min is needed.

The Cl_{cr} (mL/min) may be estimated from serum creatinine (µmol/L) determination using the following formula:

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

Dosing adjustments for patients with impaired renal function:

Group	Creatine 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 – patients 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 film-coated tablet must be taken orally, swallowed with liquid and may be taken with or without food. It is recommended to take the daily dose in one single intake.

4.3 Contraindications

[PRODUCT NAME] 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. [PRODUCT NAME] 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 are 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 film-coated 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.

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

[PRODUCT NAME] is contraindicated in pregnancy as safety has not been demonstrated (see section 4.3).

Lactation

[PRODUCT NAME] 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 [PRODUCT NAME].

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 them 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

Tablet core

Cellulose microcrystalline

Colloidal anhydrous silica

Lactose monohydrate

Magnesium stearate

Film-coating

Hypromellose E464

Macrogols – 400 (Polyethylene glycol)

Purified talc

Titanium dioxide E171

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 25 °C and in the original packaging.

6.5 Nature and contents of container

[PRODUCT NAME] are packed in clear PVDC coated PVC/aluminium blisters 4's, 8's, 10's, 20's, 30's, 50's, and 100's.

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

Austell Pharmaceuticals (Pty) Ltd

1 Sherborne Road

Parktown

JOHANNESBURG

2193

South Africa

Tel: 0860287835

8. REGISTRATION NUMBERS

LEZLERG 5 mg: 48/5.7.1/1135

LERGILEZ 5 mg: 48/5.7.1/1134

LEVOCETIRIZINE 5 mg AUSTELL: 48/5.7.1/1132

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Austell Pharmaceuticals (Pty) Ltd, Lezlerg 5 mg, Lergilez 5 mg and Levocetirizine 5 mg Austell film-coated tablets

20 September 2022

10. DATE OF REVISION OF THE TEXT

29 September 2023