SCHEDULING STATUS: S1

1. NAME OF THE MEDICINE

LEVOGEX 5 mg film coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each film-coated tablet contains: Levocetirizine dihydrochloride 5 mg.

Contains sugar: Lactose monohydrate 64 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM:

Film-coated tablets

White to off-white, oval, biconvex tablets debossed with “L9CZ” on one side and “5” on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications:

LEVOGEX film coated tablets are indicated for the relief of symptoms associated with the following allergic conditions in adults:

- Seasonal allergic rhinitis
- Perennial allergic rhinitis
- Chronic idiopathic urticaria

Safety and efficacy have not been demonstrated beyond six weeks.

4.2 Posology and 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.

Adults or children 6 years of age and older:

The daily recommended dose is one 5 mg tablet.

Patients with hepatic impairment:

No dosage adjustment is needed in patients with hepatic impairment.

Patients with renal impairment:

The total body clearance of levocetirizine is progressively reduced based on the severity of renal impairment. The dosing intervals must be individualised according to renal function. Use the table below to adjust the dose as indicated.

The patient's creatinine clearance can be estimated from the serum creatinine determination using the modified formula of Cockroft and Gault:

$$\mathbf{CL}_{cr}\ (\text{ml/min}) = \frac{(140 - \text{age in years}) \times \text{Wt in kg}}{\text{Serum creatinine } (\mu\text{mol}/\ell)}$$

For females multiply the answer by 0,85

Dosages in patients with renal impairment		
Renal status	**Creatinine clearance (CLcr)**	**Dose**
Moderate impairment	30 to 49 ml/min	5 mg every second day
Severe impairment	< 30 ml/min	5 mg every third day
End stage renal disease or receiving dialysis	< 10 ml/min	Contraindicated

4.3 Contraindications:

- Known hypersensitivity to Levocetirizine, piperazine derivative or to any of the excipients of LEVOGEX (See section 6.1).
- Safety and efficacy have not been established in children and therefore LEVOGEX is contraindicated in children under the age of 6 years (see Section 4.2).
- LEVOGEX is contraindicated in pregnancy and lactation (see Section 4.6).
- Patients with severe renal impairment with creatinine clearance of less than 10 ml/min (see Section 4.2).

4.4 Special warnings and precautions for use:

- **Risk of urinary retention:**

  Caution should be taken in patients with predisposing factors of urinary retention (e.g. spinal cord lesion, prostatic hyperplasia) as LEVOGEX may increase the risk of urinary retention.

- **Risk of seizure aggravation:**

  Caution should be taken in patients with epilepsy and patients at risk of convulsion as LEVOGEX 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.

- **Withdrawal syndrome:**

  Pruritus may occur when LEVOGEX is stopped even if those symptoms were not present before treatment initiation (see section 4.8). 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.

- **Lactose Intolerance:**

  LEVOGEX contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency, or glucose-galactose malabsorption should not take LEVOGEX.

4.5 Interaction with other medicines and other forms of interaction:

- Patients must be advised to avoid excessive alcohol consumption, as the simultaneous intake of LEVOGEX and alcohol or other CNS depressants, may increase the CNS depressant effects. (See Section 4.7)

- Interactions with other medicines have not been recorded. Studies with ketoconazole, erythromycin, azithromycin, cimetidine and pseudoephedrine have not demonstrated any clinically relevant interactions

4.6 Fertility, pregnancy and lactation:

Pregnancy:

The safety of levocetirizine has not been established in pregnancy and therefore LEVOGEX is contraindicated in pregnancy (see Section 4.3).

Lactation:

Levocetirizine is excreted in breast milk and therefore LEVOGEX is contraindicated in breastfeeding women (see Section 4.3).

Fertility:

No fertility data available.

4.7 Effects on ability to drive and use machines:

LEVOGEX lacks significant sedative effects. However, patients should be advised that certain individuals may experience sedation, somnolence, fatigue and therefore,

patients must be cautious when taking LEVOGEX while driving or performing hazardous tasks as they need to establish their individual reaction to the medication. The sedative effect may be aggravated by the simultaneous intake of alcohol or other central nervous system depressants (see Section 4.5).

4.8 Undesirable effects:

The undesirable effects listed are based on the MedDRA system organ classes (SOC) classification system. The frequency groupings listed conform to the following convention: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1 000 to <1/100); rare (≥1/10 000 to <1/1 000); very rare (<1/10 000) and unknown (cannot be estimated from the available data)

System organ class	Frequency	Undesirable effect
Immune system disorders	unknown	Hypersensitivity reactions together with skin reactions, angioedema and anaphylaxis.
Nervous system disorders	common	Headache, somnolence.
	unknown	Convulsions
Eye system disorders	unknown	Visual disturbances
Cardiac disorders	unknown	Palpitations, tachycardia.
Respiratory, thoracic and mediastinal disorders	unknown	Dyspnoea
Gastrointestinal disorders	common	Dry mouth, nausea.
	uncommon	Nausea and gastro-intestinal discomfort
Hepato-biliary disorders	unknown	Hepatitis, abnormal liver function.
Skin and subcutaneous tissue disorders	unknown	Urticaria, pruritus, rash, fixed drug eruption.
General disorders and administrative site conditions	common	Fatigue, myalgia.
	uncommon	Asthenia, malaise.
Investigations	unknown	Weight increase

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. Healthcare 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 Adverse Drug Reactions may also report to Adcock Ingram Limited using the following email: Adcock.AEReports@adcock.com

4.9 Overdose

Levocetirizine dihydrochloride

Symptoms:

The most likely symptom of overdosage is drowsiness. In children an overdosage may cause agitation and restlessness followed by drowsiness.

Treatment:

No specific antidote is known for levocetirizine. Treatment is symptomatic and supportive. Gastric lavage should be considered following short-term ingestion. Haemodialysis is not an effective means of removing levocetirizine from the body.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: 5.7.1 Antihistaminics

ATC code: R06AE07

Mechanism of action

Levocetirizine is the (R) enantiomer of cetirizine, and is a histamine H1 receptor antagonist.

5.2. Pharmacokinetic properties

Absorption:

Absorption of levocetirizine occurs after oral administration. Peak blood levels are obtained 0,9 hours after oral administration. Plasma levels are linearly related between 2,5 mg and 20 mg. In adults the plasma half- life is about 8 hours.

Metabolism:

Less than 14 % of the dose is metabolised by the body.

Elimination:

Levocetirizine is mainly excreted in the urine whereby almost 85 % of the dose is accounted for. Approximately 13 % is excreted in the faeces.

Plasma protein binding:

Levocetirizine is 90 % bound to plasma proteins.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Lactose monohydrate
- Microcrystalline cellulose
- Magnesium stearate
- Hypromellose
- Titanium dioxide
- Macrogol 400

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store at or below 25 ˚C.

Protect from moisture.

Store in blisters in outer carton until required for use.

6.5 Nature and contents of container

The tablets are available in transparent white opaque, PVC/PVDC or oPA/AI/PVC with aluminium lidding foil blister packs with 10 tablets per blister strip. Blister strips are stored in a unit carton in packs of 10 or 30 tablets.

6.6 Special precautions for disposal

Not applicable.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited

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Midrand, 1685

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8. REGISTRATION NUMBER

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9. DATE OF FIRST AUTHORISATION

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