PROFESSIONAL INFORMATION

SCHEDULING STATUS

S2

1 NAME OF MEDICINE

ALERNOVA 0,5 mg/ml (Oral Solution)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml oral solution contains 0,5 mg levocetirizine dihydrochloride.

Excipient with known effect:

Each 1 ml of oral solution contains 400 mg liquid maltitol (sugar) and 4 mg sodium benzoate (preservative).

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral Solution.

Clear and colourless oral solution with wild strawberry-like smell and flavour.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

ALERNOVA is indicated for the relief of symptoms associated with the following allergic conditions in adults and children:

- 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 5 mg (10 ml) once daily.

Children aged 6 - 12 years of age

The daily recommended dose is 5 mg (10 ml) once daily.

Children aged 2 - 6 years of age

The daily recommended dose is 2,5 mg to be administered in 2 intakes of 1,25 mg (2,5 ml of oral solution twice daily).

Children aged less than 2 years of age

The administration of **ALERNOVA** to infants and toddlers aged less than 2 years is not recommended (see section 4.4).

Special populations

Elderly

Adjustment of the dose is recommended in elderly patients with moderate to severe renal impairment.

Renal impairment

Adults:

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:

$$Cl_{cr} = \frac{[140 - age\ (years)] \times weight\ (kg)}{serum\ creatinine\ (\mu mol/l)} (\times 0{,}85\ for\ women)$$

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 suffering from 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.

<u>Hepatic impairment</u>

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

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. Clinical experience with

ALERNOVA is currently available for a 6-month treatment period.

Method of administration

For oral use.

4.3 Contraindications

ALERNOVA is contraindicated in:

- Hypersensitivity to levocetirizine dihydrochloride, to any piperazine derivative or to any of the excipients listed in section 6.1.
- Infants and toddlers aged less than two years, as safety and efficacy have not been demonstrated.
- Pregnancy and lactation (see section 4.6).
- 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 intake of alcohol (see section 4.5). **ALERNOVA** 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.)

Patients with epilepsy

Caution should be taken in patients with epilepsy and patients at risk of convulsion as levocetirizine may cause seizure aggravation.

Risk of urinary retention

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

Skin allergy tests

Response to allergy skin tests is inhibited by antihistamines and a wash-out period (of 3 days) is required before performing them.

Discontinuation of treatment

Pruritus may occur when **ALERNOVA** 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.

Infants and children under 2 years of age

Data are not sufficient to support administration of **ALERNOVA** to infants and toddlers aged less than 2 years of age. Therefore, administration of **ALERNOVA** to infants and toddlers aged less than 2 years of age is not recommended.

Children aged less than 6 years

ALERNOVA is recommended for use in children aged less than 6 years.

Excipients

Maltitol

ALERNOVA contains maltitol. Patients with the rare hereditary condition of fructose intolerance should not take **ALERNOVA**.

Sodium benzoate

The presence of the preservative, sodium benzoate, may cause allergic reactions (see section 4.3).

4.5 Interaction with other medicines and other forms of interaction

No interaction studies have been performed with **ALERNOVA** (including CYP3A4 inducers). Studies with the racemate compound cetirizine demonstrated that there were no clinically relevant adverse interactions (with ketoconazole, erythromycin, azithromycin, cimetidine, pseudoephedrine, glipizide and diazepam).

Theophylline

A 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.

Ritonavir

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 approximately 40 % while the disposition of ritonavir was decreased by (-11 %).

Food

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

Alcohol

In sensitive patients the simultaneous administration of **ALERNOVA** and alcohol or other central nervous system (CNS) depressants may have effects on the central nervous system. It is advisable to avoid excessive alcohol consumption while using **ALERNOVA**.

4.6 Fertility, pregnancy and lactation

Pregnancy

ALERNOVA is contraindicated during pregnancy.

Breastfeeding

ALERNOVA is contraindicated in women who are breastfeeding their babies.

Fertility

No fertility data is available for ALERNOVA.

4.7 Effects on ability to drive and use machines

Some patients could experience somnolence, fatigue and asthenia during therapy with **ALERNOVA**. Therefore, patients intending to drive, engage in potentially hazardous activities or operate machinery should take their response to **ALERNOVA** into account.

4.8 Undesirable effects

a. Tabulated summary of adverse reactions

System Organ Class	**Frequency**	**Undesirable effect**
Immune system disorders	*Frequency unknown*	Angioedema, hypersensitivity including anaphylaxis
Nervous system disorders	*Frequent*	Headache, somnolence
	Frequency unknown	Convulsions, paraesthesia, dizziness, syncope, tremor, dysgeusia
Gastrointestinal disorders	*Frequent*	Dry mouth, diarrhoea, constipation
	Less frequent	Nausea, gastrointestinal discomfort, abdominal pain, vomiting
General disorders and administrative site conditions	*Frequent*	Fatigue
	Less frequent	Asthenia, malaise
	Frequency unknown	Oedema
Skin and subcutaneous tissue disorders	*Frequency unknown*	Hypersensitivity reactions including skin reactions, urticaria and pruritus, angioedema, fixed drug eruption, rash
Psychiatric disorders	*Frequent*	Sleep disorders

	Frequency unknown	Aggression, agitation, hallucination, depression, insomnia, suicidal ideation
Metabolism and nutrition disorders	*Frequency unknown*	Increased weight, increased appetite
Eye disorders	*Frequency unknown*	Visual disturbance, blurred vision
Ear and labyrinth disorders	*Frequency unknown*	Vertigo
Cardiac disorders	*Frequency unknown*	Palpitations, tachycardia
Respiratory, thoracic and mediastinal disorders	*Frequency unknown*	Dyspnoea
Hepatobiliary disorders	*Frequency unknown*	Hepatitis, abnormal liver function test
Musculoskeletal, connective tissues, and bone disorders	*Frequency unknown*	Myalgia, arthralgia
Renal and urinary disorders	*Frequency unknown*	Dysuria, urinary retention
Investigations	*Frequency unknown*	Abnormal liver function

b. 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 Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 5.7.1 Antihistaminics

Pharmacotherapeutic group: Antihistamines 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

No tissue distribution data are available in humans, neither concerning the passage of levocetirizine through the blood–brain barrier. Levocetirizine is 90 % bound to human

plasma proteins. The distribution of levocetirizine is restrictive, as the volume of distribution is 0,4 l/kg.

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

Maltitol, liquid (E965)

Glycerol (E 422)

Saccharin sodium

Sodium acetate trihydrate

Acetic acid, glacial

Sodium benzoate (E 211)

Wild strawberry aroma: flavouring substances, natural flavouring substances, propylene glycol (E1520)

Water, purified

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

3 months after first opening.

6.4 Special precautions for storage

Store at or below 25 ºC.

Keep the bottle tightly closed.

Store in the original package in order to protect from light.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

Type III amber glass bottle closed with a white or colourless polyethylene screw cap with a child-resistant closure with tamper evident security ring. A labelled bottle together with a package insert and a 10 ml oral syringe graduated at 0,5 ml (barrel and piston is made from colourless polyethylene LDPE and plunger is made from white polystyrene) is packed into a unit cardboard box.

Pack size: 200 ml.

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 HOLDERS OF CERTIFICATE OF REGISTRATION

Trinity Pharma (Pty) Ltd.

106 16th Road

Midrand

South Africa

1686

8 REGISTRATION NUMBER(S)

55/5.7.1/0310.309

9 DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

27 February 2023

10 DATE OF REVISION OF THE TEXT

14 February 2023