PROFESSIONAL INFORMATION FOR

ALLECET

SCHEDULING STATUS

S1

1. NAME OF THE MEDICINE

ALLECET 10,0 mg, tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated ALLECET tablet contains 10 mg cetirizine dihydrochloride.

Contains sugar: 102 mg lactose monohydrate.

For the full list of excipients, see **section 6.1**.

3. PHARMACEUTICAL FORM

Film-coated tablets.

White, circular, biconvex, film-coated tablets with “A” debossed on one side and a deep score on the other.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ALLECET is indicated for the treatment of allergic conditions, which respond to histamine H_1- receptor antagonists:

- Respiratory: Allergic rhinitis (it effectively relieves sneezing, rhinorrhoea, nasal and ocular pruritis, and tearing), hay fever.
- Cutaneous: Allergic skin conditions associated with pruritus e.g. urticaria.

4.2 Posology and method of administration

Posology

Adults, and children 12 years and older: 10 mg (one tablet) daily.

Children 6 to 12 years old: 10 mg (one tablet) once daily, or, alternatively, 5 mg (half a tablet) twice daily, depending on symptom severity.

Special populations

Elderly*:* Currently there is no data available to suggest that dose reduction is required in this population.

Renal impairment*:* The dosage should be reduced to half the usual recommended dose in patients where the creatinine clearance is less than 40 mL/min. Where the creatinine clearance is less than 30mL/min, ALLECET is contraindicated (see **section 4.3**).

Hepatic impairment: In moderate to severe hepatic impairment, half the recommended daily dose should be used.

Paediatric population

ALLECET is contraindicated in children under the age of two years, as safety and efficacy have not been demonstrated (see **section 4.3**).

Method of administration

Oral administration.

4.3 Contraindications

ALLECET is contraindicated in:

- Known hypersensitivity to cetirizine, or any of the other components in the formulation, to hydroxyzine, or any piperazine derivatives (see **section 6.1**).
- Severe renal impairment with creatinine clearance of less than 30 mL/min.
- ALLECET is contraindicated in lactating woman, as cetirizine has been shown to be excreted in breast milk (see **section 4.6**).
- Pregnancy, as safety has not been established (see **section 4.6**).
- In children younger than 2 years of age.

4.4 Special warnings and precautions for use

ALLECET lacks significant sedative effects, however a small number of patients may experience sedation. The simultaneous intake of alcohol or other central nervous system depressants may exacerbate this effect.

Although ALLECET is relatively free of anticholinergic activity, being a selective antagonist of peripheral H_1-receptors, caution is advised in patients with urinary retention, prostatic hyperplasia, closed-angle glaucoma and pyloroduodenal obstruction. There have been reports of micturition difficulty, eye accommodation disorders and dry mouth (see **section 4.8**).

As cetirizine may increase the risk of urinary retention, caution is advised in patients with predisposition factors of urinary retention (e.g. spinal cord lesion, prostatic hyperplasia).

Caution in epileptic patients and patients at risk of convulsions is recommended.

ALLECET should be stopped several days (at least 3 days is recommended) before skin allergy tests as it may suppress positive skin test results.

ALLECET is not indicated for the treatment of asthma.

Elderly patients have been shown to be more susceptible to many adverse effects of antihistamines, especially when inappropriately used for postural dizziness or vertigo (see **section 4.8**).

Pruritus and/or urticaria may occur when ALLECET is stopped, even if those symptoms were not present before treatment initiation. The symptoms may be intense and may require treatment to be restarted. The symptoms should resolve when the treatment is restarted.

There is no information to indicate that abuse or dependency occurs with cetirizine.

Paediatric population

The use of ALLECET in tablet form is not recommended in children younger than 6 years of age as the suitable dose adjustments to be made are not possible.

Lactose

ALLECET contains lactose. Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia, total lactase deficiency, glucose-galactose malabsorption should not take ALLECET.

Lactose may have an effect on the glycaemic control of patients with diabetes mellitus.

4.5 Interaction with other medicines and other forms of interaction

ALLECET may enhance the sedative effects of central nervous system depressants including anxiolytics, neuroleptics, opioid analgesics, hypnotics, barbiturates and alcohol. Other antimuscarinic medicines, such as atropine and tricyclic antidepressants and MAOI's may enhance the antimuscarinic effects of ALLECET if used concomitantly.

Studies with diazepam, cimetidine, glipizide, pseudoephedrine ketoconazole, azithromycin and erythromycin have shown no evidence of pharmacokinetic interactions with ALLECET.

It has been suggested that antihistamines, such as ALLECET could possibly mask the warning signs of otic damage caused by ototoxic drugs such as aminoglycoside antibiotics.

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

4.6 Fertility, pregnancy and lactation

Pregnancy

Some antihistamines have been associated with foetal abnormalities when taken during pregnancy, but a number of large studies have failed to demonstrate any strong associations.

Since the safety of cetirizine dihydrochloride in pregnancy has not been established, ALLECET is contraindicated in pregnancy (see **section 4.3**).

Breastfeeding

ALLECET is contraindicated in lactating women since cetirizine is excreted in breast milk (see **section 4.3**).

Fertility

Limited data is available on human fertility, but no safety concern has been identified. Animal data show no safety concern for human reproduction.

4.7 Effects on ability to drive and use machines

ALLECET may lead to drowsiness and impaired concentration that may be aggravated by the simultaneous intake of alcohol or other nervous system depressants. Patients should be advised, particularly at the initiation of therapy, against taking charge of vehicles or machinery or performing potentially hazardous tasks where loss of concentration could lead to accidents.

4.8 Undesirable effects

a. Summary of the safety profile

Clinical studies have shown that at recommended doses cetirizine has minor CNS undesirable effects such as somnolence, fatigue, dizziness and headache.

Paradoxical CNS stimulation have been reported in some cases. There have been reports of isolated cases of micturition difficulty and eye accommodation disorders. Cases of abnormal hepatic function with elevated hepatic enzymes accompanied by elevated bilirubin have been reported. Cessation of the treatment with cetirizine dihydrochloride, mostly resolves this.

b. Tabulated summary of adverse reactions

MedDRA system organ class	**Frequency**	**Side effects**
Psychiatric disorders	Frequent	Somnolence.
Nervous system disorders	Frequent	Dizziness, headache.
Respiratory, thoracic and mediastinal disorders	Frequent	Pharyngitis.
	Less frequent	Thickening of mucous, bronchospasm.
Gastrointestinal disorders	Frequent	Dry mouth, nausea.
	Less frequent	Abdominal pain.
General disorders and administration site conditions	Frequent	Fatigue.
Vascular disorders	Less frequent	Hypotension.
Ear and labyrinth Disorders	Less frequent	Tinnitus, vertigo.
Gastrointestinal disorders	Less frequent	Gastrointestinal discomfort, diarrhoea, constipation.

Skin and subcutaneous tissue disorders	Less frequent	Photosensitivity, hair loss, sweating.
Blood and lymphatic system disorders	Less frequent	Leucopoenia, haemolytic anaemia, agranulocytosis.
Nervous system Disorders	Less frequent	Drowsiness, fatigue.
	Frequency unknown	Anxiety, nervousness.
Hepatobiliary Disorders	Less frequent	Jaundice.

c. Description of selected adverse reactions

Skin reactions occurring after discontinuation of ALLECET:

After discontinuation of ALLECET, pruritus (intense itching) and/or urticaria have been reported (see **section 4.4**).

d. Paediatric population

Children 6 to 12 years of age

MedDRA system organ class	**Frequency**	**Side effects**
Psychiatric disorders	Frequent	Somnolence.

Respiratory, thoracic and mediastinal disorders	Frequent	Rhinitis.
Gastrointestinal disorders	Frequent	Diarrhoea.
General disorders and administration site conditions	Frequent	Fatigue.

Post marketing

MedDRA system organ class	**Frequency**	**Side effects**
Blood and lymphatic disorders	Frequency unknown	Thrombocytopenia.
Immune system disorders	Frequency unknown	Hypersensitivity, anaphylactic shock.
Psychiatric disorders	Frequency unknown	Agitation, aggression, confusion, depression, hallucination, insomnia, tics, suicidal ideation, nightmare.
Metabolism and nutrition disorders	Frequency unknown	Increased appetite.
Nervous system disorders	Frequency unknown	Paraesthesia, convulsions, dysgeusia, dyskinesia, dystonia, syncope, tremor. Amnesia, memory impairment.
Eye disorders	Frequency unknown	Accommodation disorder, blurred vision, oculogyration.
Ear and labyrinth disorders	Frequency unknown	Vertigo.

Cardiac disorders	Frequency unknown	Tachycardia.
Gastrointestinal disorders	Frequency unknown	Diarrhoea.
Hepatobiliary disorders	Frequency unknown	Hepatic function abnormal (increased transaminases, alkaline phosphatase, γGT and bilirubin), hepatitis.
	Frequency unknown	Hepatitis.
Skin and subcutaneous tissue disorders	Frequency unknown	Pruritus, rash, urticaria, angioneurotic oedema, fixed drug eruption, acute generalised exanthematous pustulosis.
Musculoskeletal and connective tissue disorders	Frequency unknown	Arthralgia, myalgia.
Renal and urinary disorders	Frequency unknown	Dysuria, enuresis, urinary retention.
General disorders and administration site conditions	Frequency unknown	Asthenia, malaise, oedema.
Investigations	Frequency 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.

Health care providers are asked to report any suspected adverse reactions to SAHPRA via the “Adverse drug reaction and quality problem reporting form”, found online under SAHPRA’s publications: https://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/ or to Cipla Medpro (Pty) Ltd. by email: drugsafetysa@cipla.com or telephone: 080 222 6662 (toll free).

4.9 Overdose

Symptoms

Overdose of cetirizine are mainly associated with CNS effects or with effects that could suggest an anticholinergic effect.

Confusion, diarrhoea, dizziness, fatigue, headache, malaise, mydriasis, pruritus, restlessness, sedation, somnolence, stupor, tachycardia, tremor, and urinary retention have been reported as adverse effects after intake of at least 5 times the recommended daily dose.

Management

Treatment is symptomatic and supportive, should overdose occur.

There is no known specific antidote to cetirizine.

Haemodialysis doesn’t effectively remove cetirizine.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: A 5.7.1 Antihistaminics

Pharmacotherapeutic group: Antihistamines for systemic use, Piperazine derivatives

ATC code: R06AE07

Mechanism of action

Experimental and clinical pharmacology has shown cetirizine dihydrochloride, a metabolite of hydroxyzine, to be a potent and selective histamine H_1-receptor antagonist without any significant anticholinergic or antiserotonergic effects.

Pharmacodynamic effects

Cetirizine dihydrochloride is an anti-allergic medicine.

The anti-allergic activity of cetirizine is mainly due to its ability to inhibit the release of certain mediators (especially histamine), as well as its selective blocking of H_1-receptors. Furthermore, cetirizine reduces eosinophil recruitment induced by antigen-antibody reactions.

Clinical efficacy and safety

Studies in healthy volunteers show that cetirizine, at doses of 5 and 10 mg strongly inhibits the wheal and flare reactions induced by very high concentrations of histamine into the skin, but the correlation with efficacy is not established. In a reported six-week, placebo-controlled study of 186 patients with allergic rhinitis and concomitant mild to moderate asthma, cetirizine 10 mg once daily improved rhinitis symptoms and did not alter pulmonary function. This study supports the safety of administering cetirizine to allergic patients with mild to moderate asthma. In a placebo-controlled study, cetirizine given at the high daily dose of 60 mg for seven days did not cause statistically significant prolongation of QT interval.

At the recommended dosage, cetirizine has demonstrated that it improves the quality of life of patients with perennial and seasonal allergic rhinitis.

Paediatric population

In a reported 35-day study in children aged 5 to 12, no tolerance to the antihistaminic effect (suppression of wheal and flare) of cetirizine was found. When a treatment with cetirizine is stopped after repeated administration, the skin recovers its normal reactivity to histamine within 3 days.

5.2 Pharmacokinetic properties

Absorption

Cetirizine reaches peak blood levels of 300 ng/mL within one hour after administration of oral doses**.** Food delays the time to peak plasma concentrations but does not decrease the amount of cetirizine absorbed. The extent of bioavailability is similar when cetirizine is given as solutions or tablets.

The distribution of pharmacokinetic parameters such as peak plasma concentration (C_{max}) and area under curve (AUC), is unimodal.

Distribution

The apparent volume of distribution is 0,50 L/kg. Plasma protein binding of cetirizine is 93 ± 0,3 %. Cetirizine does not modify the protein binding of warfarin.

Biotransformation

Cetirizine does not undergo extensive first pass metabolism.

Elimination

In adults, the terminal half-life is approximately 10 hours, in children aged 6 to 12 years, 6 hours and in children aged 2 to 6 years, 5 hours, respectively. This data is consistent with the urinary excretion half-life of cetirizine. The cumulative urinary

excretion represents two thirds of the dose given in both adults and children. The apparent plasma clearance is higher in children compared to adults.

No accumulation is observed for cetirizine following daily doses of 10 mg for 10 days.

Linearity/ non-linearity

There is a linear relationship between the dosage given and the plasma levels reached by cetirizine, over the range of 5 to 60 mg.

Pharmacokinetics in specific patient groups

Elderly

Following a single 10 mg oral dose in elderly patients, half-life increases by about 50 % and clearance decreases by 40 % compared to younger patients. The decrease in cetirizine clearance in these elderly patients appears to be related to their decreased renal function.

Renally impaired patients

The pharmacokinetics of the drug are similar in patients with mild impairment (creatinine clearance higher than 40 mL/min) and patients with normal renal function. Patients with moderate renal impairment have a 3-fold increase in half-life and 70 % decrease in clearance compared to patients with normal renal function.

Patients on haemodialysis (creatinine clearance less than 7 mL/min) given a single oral 10 mg dose of cetirizine have a 3-fold increase in half-life and a 70 % decrease in clearance compared to patients with normal renal function. Cetirizine is poorly cleared by haemodialysis. Dosing adjustment is necessary in patients with moderate or severe renal impairment (see **section 4.2**).

Hepatically impaired patients

Patients with chronic liver diseases (hepatocellular, cholestatic and biliary cirrhosis) given 10 or 20 mg of cetirizine as a single dose have a 50 % increase in half-life along with a 40 % decrease in clearance compared to healthy patients.

Dosing adjustment is only necessary in hepatically impaired patients if concomitant renal impairment is present.

Paediatric population

The terminal half-life in adults is approximately 10 hours; in children aged 6 to 12 years, 6 hours; in children aged 2 to 6 years, 5 hours. This is consistent with the urinary excretion half-life of the medicine.

In infants and toddlers aged 6 to 24 months, it is reduced to 3,1 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet Cores

Colloidal anhydrous silica

Lactose monohydrate

Magnesium stearate

Maize starch

Microcrystalline cellulose

Purified talc

Opadry White

Hypromellose

Lactose monohydrate

Macrogol/PEG 4000

Sodium citrate dihydrate

Titanium dioxide

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at or below 25 º C in a dry place.

6.5 Nature and contents of container

Aluminium foil and colourless, transparent PVC film strips of 10 tablets, packed in 10’s or 30’s in an outer carton.

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

CIPLA MEDPRO (PTY) LTD.

Building 9

Parc du Cap

Mispel Street

Bellville

7530

Customer Care: 080 222 6662

8. REGISTRATION NUMBER(S)

37/5.7.1/0034

Namibia: NS1 06/5.7.1/0100

Botswana: S3 BOT1001640

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

First authorisation: 07 May 2004.

Latest renewal: Not applicable.

10.DATE OF REVISION OF THE TEXT

28 October 2024.