PROFESSIONAL INFORMATION FOR

ALLECET SYRUP

SCHEDULING STATUS

S1

1. NAME OF THE MEDICINE

ALLECET SYRUP (Syrup)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 mL of ALLECET SYRUP contains 1 mg cetirizine dihydrochloride.

Preservatives:

Methyl parahydroxybenzoate: 0,2 % *m/v*

Propyl parahydroxybenzoate: 0,02 % *m/v*

ALLECET SYRUP contains sugar (2,5 g sorbitol per 5 mL .)

ALLECET SYRUP contains sweetener (0,01 g monoammonium glycerrhizinate per 5 mL.)

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

3. PHARMACEUTICAL FORM

Syrup

A clear, colourless, pineapple and sweet orange flavoured syrup with a sweet taste.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ALLECET SYRUP is indicated for the treatment of allergic conditions responding to histamine H_1-receptor antagonist:

- Respiratory: Allergic rhinitis, 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 or older: 10 mg (10 mL) daily (two medicine measures) once daily.

Children 6 to 12 years: 10 mg (10 mL) daily, either as a single 10 mL dose (two medicine measures), or as two divided doses of 5 mL (one medicine measure) each in the morning and in the evening, respectively.

Children 2 to 6 years: 5 mg (one 5 mL medicine measure) daily, either as a single dose (5 mL), or as two divided doses of 2,5 mL (half a medicine measure) each in the morning and in the evening, respectively.

Special populations

Elderly: At present there are no data to suggest that the dose needs to be reduced in elderly patients with normal renal function.

Renal impairment: The dosage should be reduced to half the usual recommended dose in patients with renal impairment (creatinine clearance less than 40 mL/min) (see **section 4.3**).

Hepatic impairment: The dosage should be reduced to half the recommended daily dose in patients with moderate to severe hepatic impairment.

Paediatric population

ALLECET SYRUP 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 SYRUP is contraindicated in:

- History of hypersensitivity to cetirizine or to any of the excipients of ALLECET SYRUP, to hydroxyzine or to any piperazine derivatives.
- Patients with severe renal impairment at less than 30 mL/min creatinine clearance (see **section 5.2**).
- Since cetirizine is excreted in breast milk, ALLECET SYRUP is contraindicated in breastfeeding women (see **section 4.6**).
- ALLECET SYRUP is contraindicated during pregnancy as its 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 SYRUP lacks significant sedative effects, however a small number of individuals may experience sedation.

Antihistamines, including ALLECET SYRUP, should be used with care in patients with urinary retention, prostatic hyperplasia, closed-angle glaucoma and pyloroduodenal obstruction due to their antimuscarinic properties.

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).

ALLECET SYRUP should be used with caution in patients with epilepsy or at risk of convulsions and severe cardiovascular disorders based on its side effects (see **section 4.8**). ALLECET SYRUP is not indicated for the treatment of asthma. Elderly patients have been shown to be more susceptible to many adverse effects of ALLECET SYRUP, including sedation, antimuscarinic effects and hypotension (see **section 4.8**).

At therapeutic doses, no clinically significant interactions have been demonstrated with alcohol (for a blood alcohol level of 0.5 g/L). Nevertheless, precaution is recommended if alcohol is taken concomitantly (see **section 4.5**.) Excessive alcohol consumption should be avoided when taking ALLECET SYRUP.

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

Pruritus and/or urticaria may occur when ALLECET SYRUP 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.

Special warnings about the excipients

ALLECET SYRUP contains sorbitol. Patients with the rare hereditary condition of sorbitol intolerance should not take ALLECET SYRUP.

The preservatives methyl parahydroxybenzoate and propyl parahydroxybenzoate included in ALLECET SYRUP may cause allergic reactions (possibly delayed).

4.5 Interaction with other medicines and other forms of interaction

ALLECET SYRUP may enhance the sedative effects of central nervous system depressants including anxiolytics, neuroleptics, opioid analgesics, hypnotics, barbiturates and alcohol. ALLECET SYRUP has an additive antimuscarinic action when combined with other antimuscarinic medicines, such as atropine and tricyclic antidepressants. MAOI’s may enhance the antimuscarinic effects of ALLECET SYRUP.

It has been suggested that antihistamines, such as ALLECET SYRUP could possibly mask the warning signs of otic damage caused by ototoxic medicines such as aminoglycoside antibiotics. There is no reduction in the extent of absorption of ALLECET SYRUP when it is taken with food although a decrease in the rate of absorption has been reported.

4.6 Fertility, pregnancy and lactation

Pregnancy

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

Breastfeeding

ALLECET SYRUP is contraindicated in women breastfeeding their infants, 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 SYRUP 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

b. Tabulated summary of adverse reactions

MedDRA system organ class	**Frequency**	**Side effects**
Blood and lymphatic system disorders	Less frequent	Haemolytic anaemia, agranulocytosis,

		leucopenia, thrombocytopenia.
Psychiatric disorders	Frequent	Somnolence (may vary from slight drowsiness to deep sleep).
	Frequency unknown	Agitation.
Nervous system disorders	Frequent	Dizziness, headache.
	Frequency unknown	In-coordination, nervousness, paraesthesias.
Ear and labyrinth disorders	Frequency unknown	Tinnitus.
Vascular disorders	Frequency unknown	Hypotension.
Respiratory, thoracic and mediastinal disorders	Frequent	Pharyngitis, rhinitis.
	Less frequent	Thickening of mucous, bronchospasm.
Gastrointestinal disorders	Frequent	Dry mouth, nausea.
	Less frequent	Epigastric pain.
	Frequency unknown	Constipation, vomiting, increased appetite.
General disorders and administration site conditions	Frequent	Lassitude.

Skin and subcutaneous tissue disorders	Less frequent	Jaundice, hair loss, sweating, photosensitivity.
	Frequency unknown	Skin reactions (rash), angioedema (with cross sensitivity to related medicines).

c. Description of selected adverse reactions

Skin reactions occurring after discontinuation of ALLECET SYRUP:

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

d. Paediatric population

Children below 12 years of age

MedDRA system organ class	**Frequency**	**Side effects**
Gastro-intestinal disorders	Frequent	Diarrhoea
Psychiatric disorders	Frequent	Somnolence.
	Less frequent	Hallucinations, nightmares.
	Frequency unknown	Insomnia, euphoria, nervousness, irritability.
Nervous system disorders	Frequency unknown	Tremors, convulsions.

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

Post-marketing data

The following post-marketing adverse effects, have been reported:

MedDRA system organ class	**Frequency**	**Side effects**
Blood and lymphatic disorders	Less frequent	Thrombocytopenia.
Immune system disorders	Less frequent	Hypersensitivity, anaphylactic shock, angioedema.
Metabolism and nutrition disorders	Frequency unknown	Increased appetite.
Psychiatric disorders	Less frequent	Agitation, aggression, confusion, depression, hallucination, insomnia, tics.
	Frequency unknown	Suicidal ideation, nightmare.
Nervous system disorders	Less frequent	Paraesthesia, convulsions, dysgeusia, dyskinesia, dystonia, syncope, tremor.

	Frequency unknown	Amnesia, memory impairment.
Eye disorders	Less frequent	Accommodation disorder, blurred vision, oculogyration.
Ear and labyrinth disorders	Frequency unknown	Vertigo.
Cardiac disorders	Less frequent	Tachycardia.
Gastrointestinal disorders	Less frequent	Diarrhoea.
Hepatobiliary disorders	Less frequent	Abnormal hepatic function (increased transaminases, alkaline phosphatase, γ-GT and bilirubin).
	Frequency unknown	Hepatitis.
Skin and subcutaneous tissue disorders	Less frequent	Pruritus, rash, urticaria, fixed drug eruption.
	Frequency unknown	Acute generalized exanthematous pustulosis.
Musculoskeletal and connective tissue disorders	Frequency unknown	Myalgia, arthralgia.

Renal and urinary disorders	Less frequent	Dysuria, enuresis.
	Frequency unknown	Urinary retention.
General disorders and administration site conditions	Less frequent	Asthenia, malaise, oedema.
Investigations	Less frequent	Weight increased.

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 or to Cipla Medpro (Pty) Ltd. by email: drugsafetysa@cipla.com or telephone: 080 222 6662 (toll free).

4.9 Overdose

Symptoms

Symptoms observed after an overdose of cetirizine, as in ALLECET SYRUP, are mainly associated with CNS effects or with effects that could suggest an anticholinergic effect. Drowsiness is an expected symptom of overdosage. Overdosage may produce agitation, confusion, diarrhoea, dizziness, headache, malaise, mydriasis, restlessness, sedation, somnolence, stupor, pruritus, rash, urinary retention, fatigue, tremor and tachycardia.

Overdosage with ALLECET SYRUP may be fatal, especially in infants and children. In infants and children, central nervous system stimulation usually predominates over

central nervous system depression, leading to tremors, excitement, ataxia, psychoses, hallucinations and convulsions. Hyperpyrexia may also occur. This may be followed by deepening coma and cardiorespiratory collapse.

Alternatively in adults, central nervous system depression is more common presenting with drowsiness, convulsions and coma, which may progress to respiratory failure or possible cardiovascular collapse.

Management

Treatment is symptomatic and supportive. ALLECET SYRUP is not effectively removed by dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: A 5.7.1 Antihistaminics

Pharmacotherapeutic group: Antihistamine for systemic use, Piperazine derivatives

ATC code: R06A E07

Mechanism of action

Experimental and clinical pharmacology of cetirizine dihydrochloride, a metabolite of hydroxyzine, have demonstrated histamine H_1 receptor antagonism without any significant anticholinergic and antiserotonergic effects. Current research into the mode of action of cetirizine has shown that the anti-allergic activity seems to be exerted mainly via its effects on the release of certain mediators (mainly histamine) in association with a selective action on the H_1 receptors.

Pharmacodynamic effects

Cetirizine dihydrochloride is an anti-allergic medicine. Furthermore, cetirizine has been shown to reduce eosinophil recruitment induced by an antigen-antibody reaction.

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 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 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 oral administration. The extent of absorption of cetirizine is not reduced with food, although the rate of absorption is decreased. The extent of bioavailability is similar when cetirizine is given as solutions or tablets.

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

Distribution

The apparent volume of distribution is 0,50 L/kg. A high proportion of cetirizine is bound to human plasma proteins (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. This data is consistent with the urinary excretion half-life of the medicine. The cumulative urinary excretion represents two thirds of the dose given in both adults and children. In children, the apparent plasma clearance is higher than that measured in adults. There is an increase in the half-life and a decrease in total clearance in patients with impaired renal clearance (less than 40 mL/min) and hepatic insufficiency. 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 cetirizine 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 10mg 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

Liquid sorbitol

Methyl parahydroxybenzoate

Propyl parahydroxybenzoate

Glycerol

Pineapple Singapore

Sweet Orange No. 1

Monoammonium glycerrhizinate

Propylene glycol

Sodium citrate dihydrate

Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

PET bottle: 24 months

Glass bottle: 36 months

6.4 Special precautions for storage

Store in a cool dry place at or below 25 ºC. Protect from light.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

Packed in 50 mL or 150 mL amber glass bottles stoppered with a plastic or metal cap fitted with an expanded polyethylene (EPE) or low density polyethylene (LDPE) liner, or in amber PET bottles stoppered with a plastic or metal cap fitted with a low density polyethylene (LDPE) or expanded polyethylene (EPE) liner, packed in an outer carton, with a polypropylene measuring cup.

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

37/5.7.1/0153

Namibia: NS1 06/5.7.1/0093

Botswana: S2 BOT0801310

9. DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

Date of first authorisation: 07 May 2004

Date of latest renewal: Not applicable.

10. DATE OF REVISION OF THE TEXT

7 March 2024