PROFESSIONAL INFORMATION FOR ALLESOOTHE

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

ALLESOOTHE film coated tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains 10 mg cetirizine dihydrochloride.

Contains sugar (lactose monohydrate, 63,70 mg per film coated tablet).

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Film coated tablets

White, slightly biconvex, round, film coated tablet, plain on both sides.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ALLESOOTHE is indicated for the management of allergic processes which respond to histamine H1 receptor antagonists, including:

- hay fever,
- allergic rhinitis and
- allergic skin conditions that are associated with pruritus, e.g. urticaria.

4.2 Posology and method of administration

Posology

Adults and children 12 years of age or older:

Take 1 (one) tablet daily.

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Children 6 to 12 years of age:

Take 1 (one) tablet daily.

Special populations

Elderly:

No dose adjustment is necessary in healthy elderly patients with normal renal function.

Dosage in renal impairment:

In patients with renal impairment, where the creatinine clearance is less than 40 mL/min, the recommended daily dose of cetirizine should be halved.

In children with renal impairment, the dosing adjustment is to be done on an individual basis taking into account the renal clearance of the patient, their age and body weight (see section 5.2).

Dosage in hepatic impairment:

Half of the recommended daily dose should be used in patients with moderate to severe hepatic impairment.

For patients with renal insufficiency and moderate to severe hepatic impairment, an alternative dosage form is to be utilised, as ALLESOOTHE cannot be halved.

Method of administration:

Oral administration.

4.3 Contraindications

- Hypersensitivity to cetirizine hydrochloride, hydroxyzine, any piperazine derivatives or any of the other ingredients in ALLESOOTHE (see section 6.1).

- Patients with severe renal impairment where the creatinine clearance is less than 30 mL/min.
- Asthma, as it may cause airway obstruction in patients who have previously experienced adverse reactions to antihistamines.
- ALLESOOTHE is contraindicated in lactating women as the active ingredient is excreted in breast milk (see section 4.6).
- ALLESOOTHE is contraindicated in pregnancy; safety has not been established (see section 4.6).

4.4 Special warnings and precautions for use

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

ALLESOOTHE lacks significant sedative effects. Patients should be warned, however, that a small number of individuals may experience sedation.

The daily dose should be reduced in patients with renal insufficiency and patients with moderate to severe hepatic impairment (see section 4.2).

Life-threatening hepatitis may develop in long-term use of ALLESOOTHE.

For patients with renal insufficiency and moderate to severe hepatic impairment, an alternative dosage form is to be utilised as this film coated tablet cannot be halved.

It is recommended to take caution in epileptic patients and patients at risk of convulsions.

Allergy skin tests are inhibited by antihistamines and a wash-out period (of three days) is required before performing the tests.

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At therapeutic doses, there are no clinically significant interactions 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).

Elderly patients are more susceptible to many of the adverse effects of ALLESOOTHE.

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

Excipient warning:

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

4.5 Interaction with other medicines and other forms of interaction

Raised international normalised ratio (INR) and severe epistaxis have been reported in a patient after the addition of ALLESOOTHE to long-term anticoagulant therapy.

Due to the pharmacokinetic, pharmacodynamic and tolerance profile of cetirizine, no interactions are expected with ALLESOOTHE.

There is no evidence of an interaction between cetirizine and cimetidine, ketoconazole, erythromycin, azithromycin, diazepam, glipizide and pseudoephedrine.

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

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Alcohol and other Central Nervous System (CNS) depressants:

In sensitive patients, the concurrent use of alcohol or other central nervous system (CNS) depressants may cause additional reductions in alertness and impairment of performance, although cetirizine, as in ALLESOOTHE, does not potentiate the effect of alcohol (see section 4.4).

Alcohol, consumed in excess, should be avoided while taking ALLESOOTHE.

Antihistamines may suppress the cutaneous histamine response to allergen extracts and should be stopped several days before skin testing (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

ALLESOOTHE is contraindicated in pregnancy; safety has not been established (see section 4.3).

Breastfeeding

ALLESOOTHE is contraindicated in lactating women as the active ingredient 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

ALLESOOTHE does not produce significant sedative effects. However, patients should be warned that a small number of individuals may experience sedation. It is advisable to determine an individual's response before driving a vehicle or using machines. Sedation

may be enhanced by the simultaneous intake of alcohol or other central nervous system depressants, which may cause additional decrease in alertness and impaired performance in patients who are sensitive to the sedative effect of ALLESOOTHE.

4.8 Undesirable effects

Although ALLESOOTHE is relatively free of anticholinergic activity, cases of micturition difficulty, eye accommodation disorders and dry mouth have been reported.

Instances of abnormal hepatic function with elevated hepatic enzymes accompanied by elevated bilirubin have been reported.

Mostly this resolves upon discontinuation of the treatment with ALLESOOTHE.

System Organ Class	Frequency	Side effects
Blood and lymphatic system disorders	Less frequent	Agranulocytosis, leucopenia, haemolytic anaemia and thrombocytopenia.
Immune system disorders	Less frequent	Anaphylactic shock, angioedema and hypersensitivity (including angioedema and bronchospasm).
Metabolism and nutrition disorders	Frequent unknown	Increased appetite.
Psychiatric disorders	Frequent Less frequent Frequency unknown	Somnolence Agitation, aggression, confusion, depression, hallucinations, insomnia and tic. Suicidal ideation, nightmare.
Nervous system disorders	Frequent Less frequent	Dizziness and headache. Convulsions, dysgeusia,

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		dyskinesia, dystonia, movement disorders, paraesthesia, syncope, tremor, drowsiness, tics.
	Frequency unknown	Amnesia, memory impairment, anxiety, nervousness.
Eye disorder	Less frequent	Accommodation disorder, blurred vision and oculogyration.
Ear and labyrinth disorders	Less frequent	Tinnitus, vertigo.
Cardiac disorders	Less frequent	Dysrhythmias, palpitations and tachycardia.
Vascular disorders	Less frequent	Hypotension.
Respiratory, thoracic and mediastinal disorders	Frequent Less frequent	Pharyngitis, rhinitis. Thickening of mucous, bronchospasm
Gastrointestinal disorders	Frequent Less frequent	Abdominal pain, dry mouth and nausea. Diarrhoea (may be frequent in children aged 6 to 12 years), gastrointestinal discomfort, constipation.
Hepato-biliary disorders	Less frequent Frequency unknown	Abnormal hepatic function (increased transaminases, alkaline phosphatase, γ-GT and bilirubin), jaundice. Hepatitis.

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Skin and subcutaneous tissue disorders	Less frequent Frequency unknown	Fixed drug eruption pruritus, hair loss, rash, sweating, urticaria, pruritis Acute generalised exanthematous pustulosis.
Musculoskeletal, connective tissue and bone disorders	Less frequent Frequency unknown	Extrapyramidal effects and myalgia. Arthralgia.
Renal and urinary disorders	Less frequent	Dysuria, enuresis, urinary retention.
General disorders and administration site conditions	Frequent Less frequent	Fatigue Asthenia, malaise and oedema.
Investigations	Less frequent	Weight increased

Description of selected adverse reactions

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

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 requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

Signs and symptoms:

Symptoms observed after an overdose of cetirizine, as in ALLESOOTHE, 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.

Management of overdose:

There is no specific antidote. Cetirizine is not effectively removed by dialysis. Further treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties:

A 5.7.1 Antihistaminics

Pharmacotherapeutic group: Piperazine derivatives, ATC code: R06A E07.

Mechanism of action:

Cetirizine is an anti-allergic medicine with histamine H1 receptor antagonism. The anti-allergic activity is exerted mainly via its effect on the release of mediators (such as histamine) with its combined selective H1 receptor-blocking action. Cetirizine reduces eosinophil recruitment caused by an antigen-antibody reaction.

5.2 Pharmacokinetic Properties

Absorption:

Cetirizine is well absorbed from the gastrointestinal tract and peak plasma concentrations of 300 ng/mL are reached within 1 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.
No accumulation is observed for cetirizine following daily doses of 10 mg for 10 days.
The distribution of pharmacokinetic parameters such as peak plasma concentration (C_{max}) and area under curve (AUC), is unimodal.

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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:

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. Cetirizine is eliminated faster in children, and slower in patients with hepatic or renal impairment (creatinine clearance < 40 mL/min), with a resultant increase in half-life and decrease in clearance. The cumulative urinary excretion represents about two thirds of the dose given in both adults and children.

Linearity/non-linearity

Pharmacokinetics are linear over the range of 5 to 60 mg, with plasma concentrations increasing proportionately with increasing doses.

Pharmacokinetics in special 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 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

Children, infants and toddlers:

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.

5.3 Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

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Colloidal anhydrous silica

Croscarmellose sodium

Magnesium stearate

Microcrystalline cellulose.

Film coating

Hypromellose, polyethylene glycol, purified talc and titanium dioxide.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

48 months.

6.4 Special precautions for storage

Store at or below 30 °C.

Protect from light and moisture.

Do not remove blister strips from the outer carton until required for use.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

PVC-Alu blister strips of 10 tablets.

The blister strips will be placed in an outer carton

ALLESOOTHE is supplied in pack sizes of 10, 30 and 100 tablets.

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be returned to the pharmacist for safe disposal in accordance with local requirements.

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7. HOLDER OF CERTIFICATE OF REGISTRATION

Forrester Pharma (Pty) Ltd

2 Waterford Mews

Waterford Place

Century City

7441

Cape Town

8. REGISTRATION NUMBERS

48/5.7.1/1197

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

Registration date: 15 May 2019

10. DATE OF REVISION OF THE TEXT

27 February 2025