PROFESSIONAL INFORMATION

SCHEDULING STATUS

S1

1. NAME OF THE MEDICINE

CETICIT 10mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each **CETICIT** film-coated tablets contains:

Cetirizine dihydrochloride 10 mg

Contains sugar:

Lactose monohydrate 0,0605 g

For the full list of excipients see section 6.1

3. PHARMACEUTICAL FORM

Film-coated tablets

White, capsule shaped, film-coated tablets with break line on one side and "M+" embossed on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Allergic processes responding to a histamine H_1 receptor antagonist.

Respiratory: Allergic rhinitis, hay fever.

Cutaneous: Allergic skin conditions associated with prurtis, e.g. urticaria

4.2 Posology and method of administration

Posology

Adults or children 12 years of age or older:

One 10 mg tablet daily once daily.

Children 6 to 12 years old:

10 mg (one tablet) once daily or 5 mg (half a tablet) twice daily.

Special populations

Elderly

No dose adjustment is necessary in healthy elderly patients with normal renal function (see section 4.4 and 5.2).

Pregnancy

CETICIT is contraindicated in pregnancy as the safety has not been established (see section 4.6).

Lactation

CETICIT is contraindicated in lactating women since the active ingredient is excreted in breast milk (see section 4.6).

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 (see section 4.2 & 4.3 & 4.8).

Hepatic impairment

In moderate to severe hepatic impairment, half the recommended daily dose should be used (see section 4.2 & 4.3 & 4.8).

Paediatric population

CETICIT 10mg film-coated tablets are 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.

Missed dose

Doctors should advise patients who forget to take **CETICIT** 10 mg film-coated tablets to take a dose as soon as possible and then continue with the normal dose. Patients should not take a double dose to compensate for the missed dose.

4.3 Contraindications

- History of hypersensitivity to cetirizine, hydroxyzine, any piperazine derivatives or to any of the ingredients of the formulation of **CETICIT**.
- **CETICIT** is contraindicated in lactating women since the active ingredient is excreted in breast milk (see section 4.6).

- **CETICIT** is contraindicated in pregnancy as the safety has not been established (see section 4.6).
- Patients with severe renal impairment at less than 30 mL/min creatinine clearance (see section 4.2 & 4.3 & 4.8).
- Asthma, as it may cause airway obstruction in patients who have previously experienced adverse reactions to antihistamines.
- Children under the age of two years, as safety and efficacy have not been demonstrated (see section 4.2 & 4.3 & 4.4).

4.4 Special warnings and precautions for use

Refer to “CONTRAINDICATIONS” (see section 4.3).

CETICIT lacks significant sedative effects. Patients should, however, be warned that a small number of individuals may experience sedation. It is therefore advisable to determine individual response before driving or performing complicated tasks (see section 4.7).

This effect may be compounded by the simultaneous intake of other central nervous system depressants.

At therapeutic doses, no clinically significant interactions have been demonstrated with alcohol (for a blood alcohol level of $\leq$0,5 g/L). Nevertheless, precaution is recommended if alcohol is taken concomitantly (see section 4.5).

Caution should be taken in patients with predisposition factors of urinary retention (e.g. spinal cord lesion, prostatic hyperplasia) as **CETICIT** may increase the risk of urinary retention (see section 4.3 & 4.4).

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

The use of the film-coated tablet formulation is not recommended in children aged less than 6 years since this formulation does not allow for appropriate dose adaptation.

Allergy skin tests are inhibited by **CETICIT** and a wash-out period (of 3 days) is required before performing them.

Pruritus and/or urticaria may occur when **CETICIT** 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.

CETICIT contains lactose. Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia, Lapp lactase deficiency, glucose-galactose malabsorption or fructose intolerance should not take **CETICIT** tablets.

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

Special Populations

Porphyria

Safety has not been established.

Pregnancy

CETICIT is contraindicated in pregnancy as the safety has not been established (see section 4.6).

Lactation

CETICIT is contraindicated in lactating women since the active ingredient is excreted in breast milk (see section 4.6).

4.5 Interaction with other medicines and other forms of interaction

To date there are no known interactions with other drugs, notably with pseudoephedrine or theophylline (400 mg/day). Studies with diazepam, glipizide, pseudoephedrine, ketoconazole, azithromycin, erythromycin and cimetidine have revealed no evidence of pharmacokinetic interactions. As with other antihistamines it is advisable to avoid excessive alcohol consumption and other sedating medicines (see section 4.3 & 4.4).

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

Alcohol and other Central Nervous System (CNS) depressants

In sensitive patients, the concurrent use of alcohol or other CNS depressants may cause additional reductions in alertness and impairment of performance, although cetirizine, as in **CETICIT**, does not potentiate the effect of alcohol (see section 4.3 & 4.4).

4.6 Fertility, pregnancy and lactation

Refer to "**CONTRAINDICATIONS**" (see section 4.3).

Safety and efficacy in pregnancy and lactation have not been established.

Breastfeeding

Caution should be exercised when prescribing **CETICIT** to lactating women. Cetirizine is excreted in human breast milk at concentrations representing 25 % to 90 % of those measured in plasma, depending on sampling time after administration.

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

CETICIT lacks significant sedative effects. Patients should, however, be warned that a small number of individuals may experience sedation. It is therefore advisable to determine individual response before driving or performing complicated and/or hazardous tasks and/or operating hazardous machinery. This effect may be compounded by the simultaneous intake of alcohol or other central nervous system depressants (see section 4.4).

4.8 Undesirable effects

Tabulated summary of adverse reactions

System Organ Class	Frequency	Side-effects
Blood and lymphatic system disorders	Less frequent	Thrombocytopenia, leucopoenia, haemolytic anaemia, agranulocytosis
Immune system disorders	Less frequent	Urticaria, skin rash, pruritus, angioedema, hypersensitivity reactions, anaphylaxis
Metabolism and nutrition disorders	Frequency unknown	Increased appetite
Psychiatric disorders	Less frequent Frequency unknown	Somnolence, depression, confusion, agitation, aggression, hallucinations, insomnia, Suicidal ideation, nightmares
Nervous system disorders	Less frequent Frequency unknown	Drowsiness, fatigue, malaise asthenia, tics Headaches, dizziness, anxiety, nervousness, paraesthesia, convulsions, movement disorders, dysgeusia, syncope, tremor, dystonia, dyskinesia, amnesia, memory impairment

Eye disorders	Less frequent	Accommodation disorder, blurred vision oculogyration
Ear and labyrinth disorders	Less frequent	Tinnitus, vertigo
Cardiac disorders	Less frequent	Palpitations, dysrhythmias, tachycardia
Vascular disorders	Frequent Less frequent	Hypotension
Respiratory, thoracic and mediastinal disorders	Frequent Less frequent	Pharyngitis, rhinitis Thickening of mucous, bronchospasm
Gastrointestinal disorders	Less frequent	Nausea, gastrointestinal discomfort, diarrhoea, constipation, dry mouth
Hepatobiliary disorders	Less frequent Frequency unknown	Hepatic function abnormal (increased transaminase, alkaline phosphatase, γ-GT and bilirubin), jaundice Hepatitis
Skin and subcutaneous tissue disorders	Less frequent Frequency unknown	Pruritus, rash, urticaria, fixed drug eruption, photosensitivity, hair loss, sweating Acute generalised exanthematous pustulosis
Musculoskeletal, connective tissue and bone disorders	Less frequent Frequency unknown	Myalgia Arthralgia
Renal and urinary disorders	Less frequent	Dysuria, enuresis, urinary retention
General disorders and administration site conditions	Less frequent	Asthenia, malaise, oedema
Investigations	Less frequent	Weight increased

Description of selected adverse reactions

Skin reactions occurring after discontinuation of **CETICIT**:

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

Post-marketing data

Not applicable

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

Signs and symptoms

Symptoms observed after an overdose of cetirizine, as in **CETICIT**, 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

Pharmacotherapeutic group: Piperazine derivatives

ATC code: R06A E07

Pharmacological classification: A 5.7.1 Antihistaminics.

Mechanism of action

CETICIT, a metabolite of hydroxyzine, is an anti-allergic agent, with a histamine H_1 receptor antagonism devoid of any significant anticholinergic and antiserotonin effects as demonstrated in experimental and clinical pharmacology. At the present stage of research into the mode of action of **CETICIT**, the anti-allergic activity seems to be exerted mainly via its effects on the release of certain mediators, such as histamine, together with a selective action on the H_1 receptors.

CETICIT also reduces eosinophil recruitment induced 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 (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

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 (see section 4.2).

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 (see section 4.2).

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 (see section 4.2).

In infants and toddlers aged 6 to 24 months, it is reduced to 3,1 hours (see section 4.2).

5.3 Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

calcium hydrogen phosphate anhydrous

colloidal anhydrous silica

hypromellose (E-5)

maize starch

magnesium stearate

povidone (K-30)

propylene glycol

purified talc

sodium starch glycolate (type-A)

titanium dioxide

lactose monohydrate (see section 4.3 & 4.4)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 25 °C.

Keep tablets in dry place. Protect from light.

Do not remove the blisters from the carton until required for use.

KEEP OUT OF REACH AND SIGHT OF CHILDREN.

6.5 Nature and contents of container

Packaged in blisters strips of 10's. Available in cartons of 10’s, 20’s or 30’s.

Not all pack sizes maybe marketed at the same time.

6.6 Special precautions for disposal and other handling

Any unused medicine should be disposed of in accordance with local requirements.

No special precautions.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited

1 New Road, Erand Gardens, Midrand, 1685

Customer care: 0860 ADCOCK / 232625

8. REGISTRATION NUMBER(S)

42/5.7.1/0821

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

20/06/2013

10. DATE OF REVISION OF THE TEXT

20 February 2024