Professional information for ZYNCET

SCHEDULING STATUS

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1. NAME OF THE MEDICINE

ZYNCET film coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains 10 mg cetirizine hydrochloride.

Excipients with known effect:

Contains sugar: Each film coated tablet contians 65,3 mg lactose monohydrate.

For the full list of excipients, see section 6 .1.

3. PHARMACEUTICAL FORM

Film coated tablets.

Oblong, biconvex, white, film coated tablet with score on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ZYNCET is indicated for symptomatic relief of allergic conditions such as allergic rhinitis, hay fever and allergic skin conditions associated with pruritus, such as urticaria.

4.2 Posology and method of administration

Tablets:

Adults or children 12 years of age or older: one 10 mg tablet once daily.

Children 6 to 12 years old: one 10 mg 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.

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.

Dosage in hepatic impairment:

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

Method of administration:

Oral administration.

Missed dose:

Doctors should advice patients who forget to take ZYNCET to take a dose as soon as possible and then to continue with the normal dose. Patients should not take a double dose to compensate for the missed dose.

4.3 Contraindications

- Hypersensitivity to cetirizine hydrochloride, hydroxyzine, any piperazine derivatives or any of the other ingredients in ZYNCET (see section 6.1).
- Patients with severe renal impairment at less than 30 mL/min creatinine clearance.
- Asthma, as it may cause airway obstruction in patients who have previously experienced adverse reactions to antihistamines.
- Lactating women, since the active ingredient is excreted in breastmilk.

- Pregnancy, as safety has not been established.
- Children under the age of two years, as safety and efficacy have not been demonstrated.

4.4 Special warnings and precautions for use

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

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.

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

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

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

Pruritus and/or urticaria may occur when cetirizine, as in ZYNCET, 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.
Porphyria: Use with caution.

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

Paediatric Population:

The use of ZYNCET is not recommended in children aged less than 6 years since this formulation does not allow for appropriate dose adaptation. It is recommended to use a paediatric formulation of cetirizine.

4.5 Interaction with other medicines and other forms of interaction

Concomitant use of alcohol and other sedating medicines should be avoided.
In sensitive patients, the concurrent use of alcohol or other CNS depressants may cause additional reductions in alertness and impairment of performance, although cetirizine does not potentiate the effect of alcohol (0,5 g/L blood levels) (see section 4.4).

Due to the pharmacokinetic, pharmacodynamic and tolerance profile of cetirizine, no interactions are expected with this antihistamine. Actually, neither pharmacodynamic nor significant pharmacokinetic interaction was reported in medicine-interaction studies performed, notably with pseudoephedrine or theophylline (400 mg/day).

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.

4.6 Fertility, pregnancy and lactation

Safety in pregnancy and lactation has not been established (see section 4.3).

Fertility:

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

4.7 Effects on ability to drive and use machines

ZYNCET lacks significant sedative effects. However, patients should be warned that a small number of individuals may experience sedation, drowsiness or impaired concentration. The patient's ability to perform hazardous activities requiring mental alertness or physical coordination such as driving or operating machinery may be impaired. It is therefore advisable to determine individual response before driving or performing complicated tasks.

This effect may be aggravated by simultaneous intake of alcohol or other central nervous system depressants (see section 4.5).

4.8 Undesirable effects

System organ class	Frequency	Side effects
Blood and lymphatic system disorders	*Less frequent*	thrombocytopenia, leucopoenia, haemolytic anaemia, agranulocytosis
Immune system disorders	*Less frequent*	angioedema, hypersensitivty reactions, anaphylaxis
Metabolism and nutrition disorders	*Frequency unknown*	increased appetite
Psychiatric disorders	*Less frequent*	drowsiness, depression, confusion, agitation, aggression, hallucinations, insomnia
	Frequency unknown	suicidal ideation, nightmares
Nervous system disorders	*Less frequent*	tics
	Frequency unknown	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	*Less frequent*	hypotension
Respiratory, thoracic and mediastinal disorders	*Frequent*	pharyngitis, rhinitis
	Less frequent	thickening of mucous, bronchospasm
Gastrointestinal disorders	*Less frequent*	nausea, gastrointestinal discomfort, dry mouth, constipation, diarrhoea
Hepatobiliary disorders	*Less frequent*	abnormal hepatic function (increased transaminases, alkaline phosphatase, y-GT and bilirubin), jaundice
	Frequency unknown	hepatitis
Skin and subcutaneous tissue disorders	*Less frequent*	pruritus, rash, urticaria, fixed drug eruption, photosensitivity, hair loss, sweating
	Frequency unknown	acute generalised exanthematous pustulosis (AGEP)
Musculoskeletal, connective tissue and bone disorders	*Less frequent*	myalgia
	Frequency unknown	arthralgia
Renal and urinary disorders	*Less frequent*	dysuria, enuresis, urinary retention
General disorders and administration site conditions	*Less frequent*	fatigue, malaise, asthenia, oedema
Investigations	*Less frequent*	increased weight

Description of selected adverse reactions:

Skin reactions occurring after discontinuation of ZYNCET:

After discontinuation of ZYNCET, 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

Symptoms:

Symptoms observed after an overdose of cetirizine, as in ZYNCET, 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:

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

Category and class: A 5.7.1 Antihistaminics

Pharmacotherapeutic group: Antihistamine for systemic use, Piperazine derivatives.

ATC code: R06AE07.

Cetirizine is a metabolite of hydroxyzine. It is a second-generation reversible, competitive inhibitor of histamine at the histamine-1 (H1) receptor. Cetirizine competes with histamine for the H1-receptor site. Cetirizine prevents, but does not reverse, pharmacological responses mediated by histamine, at the H1 receptor.

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.

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 – 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 impairment:

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).

Hepatic impairment:

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Eudragit E-100,

lactose monohydrate,

macrogol,

magnesium stearate,

maize starch,

povidone,

talcum, and

titanium dioxide.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

Store at or below 25 °C.

6.4 Special precautions for storage

Store in a cool dry place.

Protect from light.

6.5 Nature and contents of container

PVC/aluminium foil blister strips containing 10 tablets per strip. Each carton contains 10 or 30 tablets.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Unichem SA (Pty) Ltd

San Domenico

Ground Floor, Unit G4

10 Church Street

Durbanville 7551

8. REGISTRATION NUMBER

37/5.7.1/0651

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

11/02/2005

10. DATE OF REVISION OF THE TEXT

31/05/2024