

Approved Professional Information for Medicines for Human Use:

ZELARY 10

SCHEDULING STATUS

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1. NAME OF THE MEDICINE

ZELARY 10 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 10 mg cetirizine dihydrochloride.

Contains sugar: lactose monohydrate 105 mg.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets.

ZELARY 10 mg tablets:

White, circular biconvex film-coated tablets with a score line on one side.

The tablet can be divided into equal halves.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ZELARY 10 is indicated for the symptomatic relief of allergic conditions such as allergic rhinitis, and allergic skin conditions such as urticaria.

4.2 Posology and method of administration

Posology

Adults or children 12 years of age or older:

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One 10 mg tablet daily.

Children 6 to 12 years old:

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

Special populations

Elderly population

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.

Hepatic impairment

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

Paediatric population

ZELARY 10 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

ZELARY 10 is for oral administration.

4.3 Contraindications

- Hypersensitivity to cetirizine, hydroxyzine, any piperazine derivatives or to any of the excipients listed in 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.

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- Lactating women, since the active ingredient is excreted in breast milk.
- 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

- This medicine may lead to drowsiness and impaired concentration, which may be aggravated by the simultaneous intake of alcohol or other central nervous system depressant agents.
- Porphyria: Use with Caution.
- 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 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.
- ZELARY 10 lacks significant sedative effects. Patients should be warned, however, 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 alcohol or other central nervous system depressants (see section 4.5).

Paediatric population

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. It is recommended to use a paediatric formulation of cetirizine.

Excipient lactose

This medicine contains lactose:

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicines and other forms of interaction

Concomitant use of alcohol and other sedating agents should be avoided.

There is no evidence of an interaction between cetirizine and cimetidine, ketoconazole, erythromycin, azithromycin, diazepam, glipizide, theophylline (400 mg/day) and pseudoephedrine.

The extent of absorption of cetirizine is not reduced with food, although the rate of absorption is decreased (see section 5.2)

4.6 Fertility, pregnancy and lactation

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

Breastfeeding

Caution should be exercised when prescribing ZELARY 10 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

The patients ability to perform hazardous activities requiring mental alertness or physical coordination such as driving or operating machinery may be impaired.

4.8 Undesirable effects

a) Summary of the safety profile

Clinical studies have shown that cetirizine at the recommended dosage has minor undesirable effects on the CNS, including somnolence, fatigue, dizziness and headache. In some cases, paradoxical CNS stimulation has been reported.

Although cetirizine is a selective antagonist of peripheral H₁-receptors and is relatively free of anticholinergic activity, isolated 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 these resolves upon discontinuation of the treatment with cetirizine dihydrochloride.

b) Tabulated list of adverse reactions

The table below shows all adverse drug reactions (ADRs) observed during clinical trials and postmarket spontaneous reports with cetirizine dihydrochloride.

System Organ Class	Frequency		
	Frequent	Less Frequent	Not known
Blood and lymphatic system disorders		Thrombocytopenia	
Immune system		Hypersensitivity, anaphylactic shock	

disorders			
Metabolism and nutrition disorders			Increased appetite
Psychiatric disorders		Agitation, aggression, confusion, depression, hallucination, insomnia, tics, suicidal ideation, nightmare, somnolence	
Nervous system disorders		Paraesthesia, convulsions, dysgeusia, syncope, tremor, dystonia, dyskinesia, drowsiness, fatigue, dizziness, headache, anxiety, nervousness	Amnesia, memory impairment
Eye disorders		Accommodation disorder, blurred vision, oculogyric crisis	
Ear and labyrinth disorders			Vertigo
Cardiac disorders		Tachycardia	
Respiratory, thoracic and mediastinal disorders		Thickening of mucous, pharyngitis, rhinitis	
Gastrointestinal disorders		Nausea, gastrointestinal discomfort, increased appetite, dry mouth, diarrhoea	
Hepatobiliary		Hepatic function abnormal (increased transaminases,	Hepatitis

disorders		alkaline phosphatase, γ -GT and bilirubin)	
Skin and subcutaneous tissue disorders		Urticaria, skin rash, pruritus, angioneurotic oedema, fixed drug eruption	Acute generalized exanthematous pustulosis
Musculoskeletal and connective tissue disorders			Arthralgia, myalgia
Renal and urinary disorders		Dysuria, enuresis	Urinary retention
General disorders and administration site conditions		Malaise, asthenia, oedema	
Investigations		Weight increased	

c. Description of selected adverse reactions

After discontinuation of cetirizine, pruritus (intense itching) and/or urticaria have been reported.

Reporting of suspected adverse reactions

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Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Suspected adverse reactions can also be reported directly to the HCR via medsafety@ustell.co.za.

4.9 Overdose

Symptoms

Drowsiness is an expected symptom of overdosage.

Adverse events reported after an intake of at least 5 times the recommended daily dose is: somnolence, confusion, diarrhoea, dizziness, fatigue, headache, malaise, mydriasis, pruritus, rash, restlessness or agitation, sedation, somnolence, stupor, tachycardia, tremor, and urinary retention.

Treatment

To date 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

Mechanism of action

ZELARY 10 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 gastro-intestinal 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 ($93 \pm 0,3 \%$). 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 children aged 6 to 12 years is 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 core

Maize starch

Lactose monohydrate

Povidone polyvinyl pyrrolidone (Kollidon K30)

Magnesium stearate

Tablet coat

Hypromellose (Hydroxypropyl methylcellulose)

Propylene glycol

Titanium dioxide (C.I. No. 77891) (Anatase)

Talc

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at or below 25 °C. Protect from light.

Keep blisters in carton until required for use.

6.5 Nature and contents of container

ZELARY 10 tablets are packed in PVC/PVDC Aluminium Blister.

The tablets are packed in blisters of 10 's.

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The pack sizes are 1 x 10 and 3 x 10's in a unit carton.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

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8. REGISTRATION NUMBER

37/5.7.1/0428

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

02 July 2004

10. DATE OF REVISION OF THE TEXT

18 October 2024