

## Summary of Product Characteristics

### 1. Name of the medicinal product.

Cetripinn 10 (Cetirizine Hydrochloride)

### 2. Qualitative and quantitative composition

Each tablet contains Cetirizine hydrochloride 10mg.

Excipients with known effects: one film-coated tablet contains 32.63 mg lactose

For the full list of excipients, see section 6.1.

### 3. Pharmaceutical form

Film-coated tablet.

Yellow colour, Round, Biconvex film coated tablet.

### 4. Clinical particulars

#### 4.1 Therapeutic indications In adults and paediatric patients 6 years and above:

Cetirizine is indicated for the relief of nasal and ocular symptoms of seasonal and perennial allergic rhinitis.

Cetirizine is indicated for the relief of symptoms of chronic idiopathic urticaria.

#### 4.2 Posology and method of administration

**Children aged from 6 to 12 years:** 5mg twice daily (a half tablet twice daily).

**Adults and adolescents over 12 years of age:** 10mg once daily (1 tablet)

The tablets need to be swallowed with a glass of liquid.

**Elderly subjects:** data do not suggest that the dose needs to be reduced in elderly subjects provided that the renal function is normal.

**Renal impairment:** there are no data to document the efficacy/safety ratio patients with renal impairment. Since cetirizine is mainly excreted via renal route (see section 5.2), in cases where no alternative treatment can be used, the dosing intervals must be individualized according to renal function. Refer to the following table and adjust the dose as indicated.

Dosing adjustment for adult patients with impaired renal function

Group	GFR (ml/min)	Dosage and frequency
Normal renal function	$\geq 90$	10 mg once daily
Mildly decreased renal function	60 - < 90	10 mg once daily
Moderately decreased renal function	30 - < 60	5 mg once daily
Severely decreased renal function	15 - < 30 not requiring dialysis treatment	5 mg once every 2 days
End-stage renal disease	< 15 not requiring dialysis treatment	Contra-indicated

In paediatric patients suffering from renal impairment, the dose will have to be adjusted on an individual basis taking into account the renal clearance of the patient, their age and body weight.

**Patients with hepatic impairment:** no dose adjustment is needed in patients with solely hepatic impairment.

**Patients with hepatic impairment and renal impairment:** dose adjustment is recommended (see Patients with moderate to severe renal impairment above).

***Paediatric Population***

The tablet formulation should not be used in children under 6 years of age as it does not allow the necessary dose adjustments.

**4.3 Contraindications**

Hypersensitivity to cetirizine hydrochloride, to any of the excipients listed in section 6.1, to hydroxyzine or to any piperazine derivatives. Patients with end-stage renal disease with GFR (Glomerular Filtration Rate) below 15 ml/min.

**4.4 Special warnings and precautions for use**

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 in epileptic patients and patients who are at risk of convulsions is recommended.

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

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

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.

**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.

**4.5 Interaction with other medicinal products and other forms of interaction**

Due to pharmacokinetic, pharmacodynamic and tolerance profile of cetirizine, no interactions are expected with this antihistamine. Actually, neither pharmacodynamic nor significant

pharmacokinetic interaction was reported in drug-drug interactions studies performed, notably with pseudoephedrine or theophylline (400 mg/day). The extent of absorption of cetirizine is not reduced with food, although the rate of absorption is decreased.

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).

#### **4.6 Fertility, pregnancy and lactation**

##### **Pregnancy**

For cetirizine prospectively collected data on pregnancy outcomes do not suggest potential for maternal or foetal/embryonic toxicity above background rates.

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or post natal development. Caution should be exercised when prescribing to pregnant women.

##### **Breast-feeding**

Cetirizine passes into breast milk. A risk of side effects in breastfed infants cannot be excluded. Cetirizine is excreted in human milk at concentrations representing 25% to 90% those measured in plasma, depending on sampling time after administration. Therefore, caution should be exercised when prescribing cetirizine to lactating women.

##### **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**

Objective measurements of driving ability, sleep latency and assembly line performance have not demonstrated any clinically relevant effects at the recommended dose of 10 mg.

However patients who experience somnolence should refrain from driving, engaging in potentially hazardous activities or operating machinery. They should not exceed the recommended dose and should take their response to the medicinal product into account.

#### **4.8 Undesirable effects**

Clinical studies

- Overview

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 H<sub>1</sub>-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 this resolves upon discontinuation of the treatment with cetirizine hydrochloride.

• Listing of ADRs

Double blind controlled clinical trials comparing cetirizine to placebo or other antihistamines at the recommended dosage (10 mg daily for cetirizine), of which quantified safety data are available, included more than 3200 subjects exposed to cetirizine.

From this pooling, the following adverse events were reported for cetirizine 10mg in the placebo-controlled trials at rates of 1.0% or greater.

<b>Adverse event (WHO-ART)</b>	<b>Cetirizine 10mg (n = 3260)</b>	<b>Placebo (n = 3061)</b>
General disorders and administration site conditions		
Fatigue	1.63%	0.95%
Nervous system disorders		
Dizziness	1.10%	0.98%
Headache	7.42%	8.07%
Gastro-intestinal disorders		
Abdominal pain	0.98%	1.08%
Dry mouth	2.09%	0.82%
Nausea	1.07%	1.14%
Psychiatric disorders		
Somnolence	9.63%	5.00%
Respiratory thoracic and mediastinal disorders		
Pharyngitis	1.29%	1.34%

Although statistically more common than under placebo, somnolence was mild to moderate in the majority of cases. Objective tests as demonstrated by other studies have demonstrated that usually daily activities are unaffected at the recommended daily dose in healthy young volunteers.

**Paediatric population**

Adverse drug reactions at rates of 1% or greater in children aged from 6 months to 12 years, included in placebo-controlled clinical trials are:

<b>Adverse event (WHO-ART)</b>	<b>Cetirizine (n = 1656)</b>	<b>Placebo (n = 1294)</b>
Gastro-intestinal system disorders		
Diarrhoea	1.0%	0.6%
Psychiatric disorders		
Somnolence	1.8%	1.4%

Respiratory thoracic and mediastinal disorders		
Rhinitis	1.4%	1.1%
General disorders and administration site conditions		
Fatigue	1.0%	0.3%

### **Post marketing experience**

In addition to the adverse effects reported during clinical studies and listed above, the following undesirable effects have been reported in post-marketing experience.

Undesirable effects are described according to MedDRA System Organ Class and by estimated frequency based on post-marketing experience.

Frequencies are defined as follows: Very common ( $\geq 1/10$ ); common ( $\geq 1/100$  to  $<1/10$ ); uncommon ( $\geq 1/1,000$  to  $<1/100$ ); rare ( $\geq 1/10,000$  to  $<1/1,000$ ); very rare ( $<1/10,000$ ), not known (cannot be estimated from the available data)

#### *Blood and lymphatic disorders:*

Very rare: thrombocytopenia

#### *Immune system disorders:*

Rare: hypersensitivity

Very rare: anaphylactic shock

#### *Metabolism and nutrition disorders:*

Not known: increased appetite

#### *Psychiatric disorders:*

Uncommon: agitation

Rare: aggression, confusion, depression, hallucinations, insomnia

Very rare: tics

Not known: suicidal ideation, nightmare

#### *Nervous system disorders:*

Uncommon: paraesthesia

Rare: convulsions

Very rare: dysgeusia, syncope, tremor, dystonia, dyskinesia

Not known: amnesia, memory impairment

#### *Eye disorders:*

Very rare: accommodation disorder, blurred vision, oculogyric Crisis

#### *Ear and labyrinth disorders:*

Not known: vertigo

#### *Cardiac disorders:*

Rare: tachycardia

#### *Gastro-intestinal disorders:*

Uncommon: diarrhoea

#### *Hepatobiliary disorders:*

Rare: hepatic function abnormal (increased transaminases, alkaline phosphatase,  $\gamma$ -GT and bilirubin)

Not known: hepatitis

#### *Skin and subcutaneous tissue disorders:*

Uncommon: pruritus, rash

Rare: urticaria

Very rare: angioneurotic oedema, fixed drug eruption  
Not known: acute generalized exanthematous pustulosis  
*Musculoskeletal and connective tissue disorders*

Not known: arthralgia, myalgia

*Renal and urinary disorders:*

Very rare: dysuria, enuresis

Not known: urinary retention

*General disorders and administration site conditions:*

Uncommon: asthenia, malaise

Rare: oedema

*Investigations:*

Rare: weight increased

### **Description of selected adverse reactions**

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

### **Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) <https://pv.pharmacyboardkenya.org>.

## **4.9 Overdose**

### **Symptoms**

Symptoms observed after an overdose of cetirizine are mainly associated with CNS effects or with effects that could suggest an anticholinergic effect. Adverse events reported after an intake of at least 5 times the recommended daily dose are: confusion, diarrhoea, dizziness, fatigue, headache, malaise, mydriasis, pruritus, restlessness, sedation, somnolence, stupor, tachycardia, tremor, and urinary retention.

### **Management**

There is no known specific antidote to cetirizine. Should overdose occur symptomatic or supportive treatment is recommended. Gastric lavage should be considered shortly after ingestion of the drug.

Cetirizine is not effectively removed by haemodialysis.

## **5. Pharmacological properties**

### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: antihistamine for systemic use, piperazine derivatives.

ATC code: R06A E07

### **Mechanism of action**

Cetirizine, a human metabolite of hydroxyzine, is a potent and selective antagonist of peripheral H<sub>1</sub>-receptors. *In vitro* receptor

binding studies have shown no measurable affinity for other than H<sub>1</sub>-receptors.

#### **Pharmacodynamics effects**

In addition to its anti-H<sub>1</sub> effect, cetirizine was shown to display anti-allergic activities: at a dose of 10 mg once or twice daily, it inhibits the late phase recruitment of eosinophils, in the skin and conjunctiva of atopic subjects submitted to allergen challenge.

#### **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 10mg 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 antihistamine 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**The steady-state peak plasma concentrations is approximately 300 ng/ml and is achieved within  $1.0 \pm 0.5$  h. The distribution of pharmacokinetic parameters such as peak plasma concentration ( $C_{max}$ ) and area under curve (AUC), is unimodal.

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, capsules or tablets.

#### **Distribution**

The apparent volume of distribution is 0.50 l/kg. Plasma protein binding of cetirizine is  $93 \pm 0.3\%$ . Cetirizine does not modify the protein binding of warfarin.

#### **Biotransformation**

Cetirizine does not undergo extensive first pass metabolism.

#### **Elimination**

The terminal half-life is approximately 10 hours and no accumulation is observed for cetirizine following daily doses

of 10 mg for 10 days. About two thirds of the dose are excreted unchanged in urine.

#### **Linearity/Non-linearity**

Cetirizine exhibits linear kinetics over the range of 5 to 60 mg.

#### **Special populations**

*Elderly:* Following a single 10 mg oral dose, half life increased by about 50% and clearance decreased by 40% in 16 elderly subjects compared to younger subjects. The decrease in cetirizine clearance in these elderly volunteers appeared to be related to their decreased renal function.

*Paediatric population:* The half-life of cetirizine was about 6 hours in children of 6 – 12 years and 5 hours in children 2 – 6 years. In infants and toddlers aged 6 to 24 months, it is reduced to 3.1 hours.

*Renal impairment:* The pharmacokinetics of the drug were similar in patients with mild impairment (creatinine clearance higher than 40 ml/min) and healthy volunteers. Patients with moderate renal impairment had a 3-fold increase in half-life and 70% decrease in clearance compared to healthy volunteers.

Patients on hemodialysis (creatinine clearance less than 7 ml/min) given a single oral 10 mg dose of cetirizine had a 3-fold increase in half-life and a 70% decrease in clearance compared to normal. Cetirizine was 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 disease (hepatocellular, cholestatic, and biliary cirrhosis) given 10 or 20 mg of cetirizine as a single dose had a 50 % increase in half life along with a 40 % decrease in clearance compared to healthy subjects.

Dosing adjustment is only necessary in hepatically impaired patients if concomitant renal impairment is present.

### **5.3 Preclinical safety data**

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.

## **6. Pharmaceutical particulars**

### **6.1 List of excipients**

Colloidal Anhydrous silica  
Lactose\*  
Maize Starch  
Purified water  
Talc  
Magnesium Stearate  
Sodium Starch Glycolate  
Sheffcoat PVA Yellow



Purified water

**6.2 Incompatibilities**

Not applicable.

**6.3 Shelf life**

24 months.

**6.4 Special precautions for storage**

No special precautions for storage.

**6.5 Nature and contents of container**

**7. Marketing authorisation holder**

Pinnacle Life Science Pvt. Ltd. Mahendra Industrial Estate, Ground Floor Plot no .109-D, Rd no 29 Sion (East), Mumbai 400 022, India

**Manufacturing address.**

Pinnacle Life Science Pvt. Ltd. Mahendra Industrial Estate, Ground Floor Plot no .109-D, Rd no 29 Sion (East), Mumbai 400 022, India.

**8. Marketing authorisation number(s)**

H2022/CTD7225/14197

**9. Date of first authorisation/renewal of the authorisation**

October 2022

**10. Date of revision of the text**

October 2022