CET-Z-10

(Cetirizine Hydrochloride Tablets 10mg)

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. NAME OF THE MEDICINAL PRODUCT

Cet-Z-10 mg, Film Coated Oral Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Qualitative declaration
Cetirizine Hydrochloride

Quantitative declaration
Each film coated tablets contains:
Cetirizine Hydrochloride BP 5 mg
For full list of Excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film Coated Oral Tablets
Distribution Category: Over the Counter (OTC)
White coloured, caplet shaped, biconvex, film coated tablets, break line on one side and plain on other side.
The tablet can be divided into equal halves.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

It is indicated in adults and paediatric patients 6 years and above:
For the relief of nasal and ocular symptoms of seasonal and perennial allergic rhinitis.
For the relief of symptoms of chronic idiopathic urticaria.

4.2 Posology and method of administration

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

Posology
10 mg once daily (1 tablet).

Special population
Elderly
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 in patients with renal impairment. Since cetirizine is mainly eliminated via renal route, in cases 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 adjustments for adult patients with impaired renal function.

Group	Estimated Glomerular Filtration Rate (eGFR) (ml/min)	Dosage and frequency

Normal renal function	≥ 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	5 mg once every 2 days
End-stage renal disease	<15 requiring dialysis treatment	Contraindicated

Hepatic impairment
No dose adjustment is needed in patients with solely hepatic impairment. In patients with hepatic impairment and renal impairment, adjustment of the dose is recommended (see 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.

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

Adolescents over 12 years of age: 10 mg once daily (1 tablet).

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

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Alcohol interaction
No significant interaction with alcohol at therapeutic doses (up to 0.5 g/L), but caution is advised if taken together.

Urinary retention risk
Use cautiously in patients with conditions like spinal cord lesions or prostatic hyperplasia, as cetirizine may increase urinary retention risk.

Convulsion risks
Caution is advised in epileptic patients or those at risk of seizures.

Allergic skin tests
Cetirizine inhibits allergy skin test responses; a 3-day wash-out period is recommended before testing.

Withdrawal symptoms
Stopping cetirizine may cause intense pruritus or urticaria, even if not present before treatment.

	Restarting the treatment can alleviate these symptoms. Excipients with known effects: Propylene Glycol: Co-administration with any substrate for alcohol dehydrogenase such as ethanol may induce adverse effects in children less than 5 years old. Sucrose: This medicine contains 2000 mg of sucrose in each 5ml. This should be taken into account in patients with diabetes mellitus. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine. May be harmful to the teeth. Methyl Hydroxybenzoate: It may cause allergic reactions. Propyl Hydroxybenzoate: It may cause allergic reactions Sunset yellow supra: May cause allergic reactions. Sodium content: This medicine contains less than 1 mmol sodium (23 mg) per 5ml, that is to say essentially 'sodium-free'.
4.5	**Interaction with other medicinal products and other forms of interaction**
	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 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**
	Fertility Limited data is available on human fertility but no safety concern has been identified. Animal data show no safety concern for human reproduction. 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/fetal development, parturition or postnatal development. Caution should nevertheless be exercised when prescribing to pregnant women. Lactation and Breastfeeding

	Cetirizine is excreted in human breast milk at concentrations representing 25% to 90% of those measured in plasma, depending on sampling time after administration A risk of side effects in breastfed infants cannot be excluded. Therefore, caution should be exercised when prescribing cetirizine to lactating women.
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**
	The undesirable effects of cetirizine are categorized by frequency based on post-marketing data, as follows: Frequencies are defined as follows: Very common (≥ 1/10); common (≥ 1/100 to <1/10); uncommon (≥ 1/1,000 to <1/100); rare (≥ 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, hallucination, 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, γ -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 Rare: weight increased.

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 may 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 H1-receptors. In vitro receptor binding studies have shown no measurable affinity for other than H1-receptors. Pharmacodynamics effects In addition to its anti-H1 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 Cetirizine effectively inhibits wheal and flare reactions to high histamine concentrations at doses of 5 and 10 mg, though its efficacy correlation is unclear. A six-week study showed that a daily dose of 10 mg improved rhinitis symptoms in patients with allergic rhinitis and mild to moderate asthma, without affecting pulmonary function. Additionally, a high dose of 60 mg did not significantly prolong the QT interval, indicating cardiovascular safety. Overall, cetirizine enhances the quality of life for patients with allergic rhinitis. Paediatric population In a 35-day study in children aged 5 to 12, no tolerance to the antihistaminic 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 ± 0.5 h. The distribution of pharmacokinetic parameters such as peak plasma concentration (Cmax) 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 ± 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 third of the dose are excreted unchanged in urine. Linearity/Non-linearity Cetirizine exhibits linear kinetics over the range of 5 to 60 mg. Renal impairment Cetirizine's pharmacokinetics are similar in patients with mild renal impairment (creatinine clearance > 40 ml/min) and healthy individuals. In patients with moderate renal impairment, the half-life increases threefold and clearance decreases by 70%. For those on hemodialysis (creatinine clearance < 7 ml/min), the same changes occur, and cetirizine is poorly cleared by hemodialysis. Thus, dosing adjustments are needed for 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 had a 50 % increase in half-life along with a 40 % decrease in clearance compared to healthy subjects. Dosing adjustment is only necessary in patients with hepatic impairment if concomitant renal impairment is present. 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 the normal 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.
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**
	Core: Microcrystalline Cellulose (PH 102) Purified Talc

	Croscarmellose sodium Magnesium stearate Purified water **Coat:** Colour White SC-SP 3180 (Spraycel) Hydroxy Propyl Methyl Cellulose Polyethylene Glycol Talcum Titanium Dioxide
6.2	**Incompatibilities**
	This medicinal product must not be mixed with other medicinal products.
6.3	**Shelf life**
	36 Months
6.4	**Special precautions for storage**
	Store below 30°C. Protect from light.
6.5	**Nature and contents of container**
	3 x 10 Tablets in Alu-PVC Blister Pack 10 x 10 Tablets in Alu-PVC Blister Pack
6.6	**Special precautions for disposal and other handling**
	No special requirements. Any unused product or waste material should be disposed of in accordance with local requirements.
7.	**MARKETING AUTHORIZATION HOLDER AND MANUFACTURING SITE ADDRESSES**
7.1	**Name and address of marketing authorization holder**
	Generics And Specialities Ltd. 31, Awoniyi Elemo Street, Off Lateef Salami Street. Ajao Estate, Lagos, Nigeria. E-mail: info@zolonhealthcare.com
7.2	**Name and address of manufacturing site(s)**
	Lincoln Pharmaceuticals Limited Trimul Estate, Khatraj, Tal. -Kalol, Dist. - Gandhinagar, Gujarat State, India. Telephone no.: +91-079-41078096 Email: hiren@lincolnpharma.com Website: www.lincolnpharma.com
8.	**MARKETING AUTHORIZATION NUMBER**
	B4-0942

9.	**DATE OF FIRST <PREQUALIFICATION> / RENEWAL OF THE <PREQUALIFICATION >**
	Date of first authorization: 26 September 2013 Date of latest renewal : --
10.	**DATE OF REVISION OF THE TEXT**
	December 24