Summary of Product Characteristics

1. NAME OF THE PRODUCT:

PIRICET tablets (Cetirizine Hydrochloride 10mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each film coated tablet contains

Cetirizine hydrochloride

Eq. to Cetirizine…….10mg

Excipients with known effect: Each tablet contains: Lactose [15.36mg]

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM:

Film Coated Tablet.
Round (5.5mm- 2.8mm), flat-faced, bevel edged, white coloured tablet, scored on one side and plain on the other.

The score-line is not for dividing the tablet into two equal parts.

Distribution category: Over The Counter Medicine (OTC).

CLINICAL PARTICULARS:

3.1 Therapeutic indications:

In adults and pediatric patients 6 years and above;
Piricet is indicated for:

- the relief of nasal and ocular symptoms of seasonal and perennial allergic rhinitis,
- the relief of symptoms of chronic idiopathic urticaria.

3.2 Posology and method of administration:

Posology

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

Adults and adolescents over 12 years of age: 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.

Patients with moderate to severe 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 (see section 5.2), 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. To use this dosing table, an estimate of the patient's creatinine clearance (CL_{CR}) in ml/min is needed. The CL_{CR} (ml/min) may be estimated from serum creatinine (mg/dl) determination using the following formula:

$$CL_{cr} = \frac{[140 - age(years)] \times weight\ (kg)}{72 \times serum\ creatinine\ (mg/dl)} (\times 0.85\ for\ women)$$

Dosing adjustments for adult patients with impaired renal function

Group	Creatinine clearance (ml/min)	Dosage and frequency
Normal	≥ 80	10 mg once daily
Mild	50 – 79	10 mg once daily
Moderate	30 – 49	5 mg once daily
Severe	< 30	5 mg once every 2 days
End-stage renal disease – Patients undergoing dialysis	< 10	Contra-indicated

In pediatric patients suffering from renal impairment, the dose will have to be adjusted on an individual basis considering the renal clearance of the patient, his age and his 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 tosevererenal impairment above).

Method of administration

For oral administration

The tablet needs to be swallowed with a glass of liquid

3.3 Contraindications:

Hypersensitivity to the active substance, to any of the excipients, to hydroxyzine or to any piperazine derivatives.
Patients with severe renal impairment at less than 10 ml/min creatinine clearance. Cetirizine is reported to be excreted in breast milk thus it is contraindicated in lactating women.

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

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. See section Adverse reactions.)

The use of the product is not recommended in children aged less than 2 years. Dosage adjustment is necessary in patients with moderate or severe renal impairment.
Pruritus and/or urticaria may occur when cetirizine is stopped, even if those symptoms were not present before treatment initiation (see section 4.8). In some cases, the symptoms may be intense and may require treatment to be restarted. The symptoms should resolve when the treatment is restarted.

Piricet be discontinued several days (usually 3 days) before allergic skin testing as antihistamines may suppress the cutaneous histamine response to allergen extracts. *Excipients*
Lactose: This product contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

3.5 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 have been 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 common with other antihistamines, it is recommended that excessive alcohol consumption be avoided.

Concurrent use of Cetirizine with other CNS depressants should also be avoided as reduction in alertness and impairment of performance may occur.

3.6 Pregnancy and Lactation:

For cetirizine, very rare clinical data on exposed pregnancies are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/fetal development, parturition or postnatal development. Caution should be exercised when prescribing to pregnant or breast feeding women because cetirizine is usually excreted in breast milk.

3.7 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.

Patients intending to drive, engaging in potentially hazardous activities or operating

machinery should not exceed the recommended dose and should take their response to the medicinal product into account. In these sensitive patients, concurrent use with alcohol or other CNS depressants may cause additional reductions in alertness and impairment of performance.

3.8 Undesirable effects:

Clinical studies have shown that cetirizine at the recommended dosage has minor undesirable effects on the CNS, including somnolence, fatigue, dizziness and headache, nausea, palpitations and gastro-intestinal discomfort. 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 this resolves upon discontinuation of the treatment with cetirizine dihydrochloride.

Clinical trials

Double blind controlled clinical or pharmacoclinical trials comparing cetirizine to placebo or other antihistamines at the recommended dosage, 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 10 mg in the placebo-controlled trials at rates of 1.0 % or greater:

Adverse event (WHO-ART)	**Cetirizine 10 mg (n= 3260)**	**Placebo (n = 3061)**
Body as a whole – general disorders Fatigue	1.63 %	0.95 %
Central and peripheral nervous system disorders Dizziness Headache	 1.10 % 7.42 %	 0.98 % 8.07 %
Gastro-intestinal system disorders Abdominal pain Dry mouth Nausea	 0.98 % 2.09 % 1.07 %	 1.08 % 0.82 % 1.14 %
Psychiatric disorders Somnolence	 9.63 %	 5.00 %
Respiratory system 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 usual daily activities are unaffected at the recommended daily dose in healthy young

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

Adverse drug reactions (WHO-ART)	**Cetirizine (n=1656)**	**Placebo (n =1294)**
Gastro-intestinal system disorders Diarrhoea	1.0 %	0.6 %
Psychiatric disorders Somnolence	1.8 %	1. 4 %
Respiratory system disorders Rhinitis	1.4 %	1.1 %
Body as a whole – general disorders Fatigue	1.0 %	0.3 %

Post-marketing experience:
In addition to the adverse effects reported during clinical studies and listed above, isolated cases of the following adverse drug reactions have been reported in post-marketing experience. For these less frequently reported undesirable effects, the estimated frequencies (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) are made based on post-marketing experience.

System organ class	**Frequency**	**Adverse reactions**
Blood and lymphatic disorders	Very rare	thrombocytopenia
Immune system disorders	rare	hypersensitivity
	Very rare	Anaphylactic shock
Psychiatric disorders	uncommon	Agitation
		Aggression, confusion, depression, hallucination, insomnia
	Very rare	tics
Metabolism and nutrition disorders	Not known	Increased appetite
Nervous system disorders:	Uncommon:	Paraesthesia
	rare	convulsions, movement disorders
	Very rare	Dysgeusia, syncope, tremor, dystonia, and dyskinesia
Eye disorders	Very rare	Accommodation disorder, blurred vision, oculogyration

Cardiac disorders	rare	Tachycardia
Hepatobiliary disorders	rare	Abnormal hepatic function (increased
		transaminases, alkaline, phosphatase, γ-GT and bilirubin).
Skin and subcutaneous tissue disorders	uncommon	pruritus, rash
	rare	urticaria
	Very rare	Angioneurotic oedema, erythema multiforme.
Renal and urinary disorders	Very rare	Dysuria, enuresis, micturition difficulties.
General disorders and administration site conditions	uncommon	Asthenia, malaise.
	Rare	oedema
Investigation	Rare	Weight increase

Reporting of suspected adverse reactions

Healthcare professional are requested to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Reporting System (PvERS) https://pv.pharmacyboardkenya.org.

Overdose:

Symptoms

Symptoms observed after an overdose of cetirizine are mainlyassociated 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 following ingestion of a short occurrence.
Cetirizine is not effectively removed by dialysis.

4. PHARMACOLOGICAL PROPERTIES:

4.1 Pharmacodynamic properties:

Pharmacotherapeutic group: Antihistamine (H1 receptor antagonist), Piperazine derivative.

ATC code: R06AE07

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.

In addition to its anti-H1 effect, cetirizine displays anti-allergic activities. At a dose of 10mg 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 10mg 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 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.

4.2 Pharmacokinetic properties:

Absorption

The steady - state peak plasma concentrations is approximately 300 ng/ml and is achieved within 1.0 ± 0.5 h. No accumulation is observed for cetirizine following daily doses for 10 days. 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, tablets or syrup.

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. It is metabolised to a small extent with a known inactive main metabolite.

Elimination

The terminal half-life is approximately 10 hours in adults and 6 hours in children between the ages of 6-12 years. About two third (60%) of the dose are excreted unchanged in urine within 96 hours.

Repeated administration does not lead to any accumulation, nor is the absorption or elimination affected.
Cetirizine exhibits linear kinetics over the range of 5 to 60 mg.

Special populations:
Elderly: Following a single 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.

Children, infants and toddlers: 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

Renally impaired patients: 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 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).

Hepatically impaired patients: 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 hepatically impaired patients if concomitant renal impairment is present.

4.3 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.

5. PHARMACEUTICAL PARTICULARS:

5.1 List of excipients:

- Lactose BP
- Dicalcium phosphate (D.C.P) BP
- Microcrystalline cellulose BP
- Polyvinylpyrollidone (PVP) K-30 BP
- Sodium starch Glycolate BP

- Aerosil BP
- Talc BP
- Magnesium stearate BP
- Maize starch BP

5.2 Incompatibilities:
Not applicable

5.3 Shelf life:
3 years

5.4 Special precautions for storage:
Do not store above 30°C. Store in a cool dry place, protected from direct sunlight.

5.5 Nature and contents of the container:
Blister pack: 1 x 10's & 10 x 10's in blisters made of PVC / Aluminum foils in a unit Cardboard carton with literature insert.

5.6 Special precautions for disposal:
No special requirements.

7.MARKETING AUTHORIZATION HOLDER & MANUFACTURING SITE ADDRESS
Biodeal Laboratories Limited,
Lunga Lunga Road,
Industrial Area,
P.O. Box 32040 – 00600,
Nairobi, Kenya.

8. MARKETING AUTHORIZATION NUMBER
H2020/CTD063/843ER

9. DATE OF FIRST REGISTRATION /RENEWAL
Date of first registration: Kenya: 15TH JUNE 2020

10. DATE OF REVISION OF TEXT
November 2023