

Size: 210 x 240 mm
Folding size: 30 x 60 mm
Carton size: 45 x 30 x 85 mm

Front

210 mm



CETIRIZINE Hydrochloride

ASKEY™

10 mg Tablet

ANTIHISTAMINE

PRODUCT NAME:

Cetirizine Hydrochloride Tablet

DOSAGE FORM AND STRENGTH:

Film-coated Tablet, 10mg

PHARMACOLOGIC CATEGORY:

ANTIHISTAMINE

PRODUCT DESCRIPTION:

White, small caplet shaped film coated tablets with score line on one surface and plain on the other surface.

FORMULATION/COMPOSITION:

Each film-coated tablet contains:
Cetirizine Hydrochloride BP.....10 mg

PHARMACODYNAMICS/PHARMACOKINETICS:

Pharmacodynamics:

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 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.

Pharmacokinetics:

Absorption: Cetirizine is rapidly absorbed after oral administration. In adults, peak plasma levels after a 10 mg dose are approximately 300 ng/mL and occur at about one hour. Co-administration with food decreases the rate of absorption by 1.7 hour (lower Cmax and greater Tmax), but does not affect bioavailability as measured by the AUC. Plasma protein binding is 93%. The apparent volume of distribution is 0.45 L/kg, suggestive of significant extravascular distribution. The plasma elimination half-life in adults is approximately 8 hours and does not change with multiple dosing. Plasma levels are proportional to the dose administered over the range of 5 to 20 mg.

Distribution and Protein Binding: The bioavailability of Cetirizine hydrochloride is similar from the different dosage forms of Cetirizine. The mean time taken to reach the peak serum Cetirizine concentration (Tmax) was 0.67 hour after a single 10 mg dose of the film coated tablets.

In children, as with adults, Cetirizine is eliminated mostly in the urine. Children over 6 years of age show peak plasma levels and times to peak similar to adults, with slightly more rapid elimination. Children younger than 6 years have more rapid clearance and a shorter half-life relative to adults. The half-life of Cetirizine is approximately; 6 hours in children aged 6-12 years; 5 hours in children aged 2-6 years, and; 3 hours in infants and toddlers aged 6-24 months.

Metabolism: In contrast to other known antihistamines, Cetirizine is less extensively metabolised, and approximately 2/3 of an administered dose is excreted unchanged in the urine. This results in high bioavailability with low inter- or intrasubject variation in blood levels. A study using 14-C-labelled Cetirizine showed that most of the plasma radioactivity is associated with the parent compound. Only one metabolite has been identified in human plasma, the product of oxidative dealkylation of the terminal Carboxymethyl group. The antihistaminic activity of this metabolite is negligible.

Elimination: The total body clearance of Cetirizine is reduced in subjects with renal dysfunction but below a creatinine clearance of about 30 to 50 mL/minute, little further change occurs. The pharmacokinetics of the drug was similar in patients with mild impairment (creatinine clearance higher than 40 mL/min) and normal volunteers. Moderately renally impaired patients had a 3-fold increase in half-life and 70% decrease in clearance compared to normal volunteers. Plasma levels of Cetirizine are essentially unaffected by hemodialysis, and the plasma elimination half-life in dialysis patients is approximately 20 hours. The plasma AUC is increased about threefold in these patients. The clearance of Cetirizine is reduced in elderly patients, but only in proportion to the decrease in creatinine clearance. Thus, in 16 patients with a mean age of 77 years, half-life increased to 12 hours. Cetirizine blood levels were monitored in a clinical trial of 59 patients, aged 60 to 82, who received 10 mg of Cetirizine daily for three weeks, and no undue accumulation of Cetirizine, was found.

INDICATIONS:

In adults and pediatric patients 6 year 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.

DOSAGE AND MODE / ROUTE OF ADMINISTRATION:

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).

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.

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 excreted 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. To use this dosing table, an estimate of the patient's creatinine clearance (CLcr) in mL/min is needed. The CLcr (mL/min) may be estimated from serum creatinine (mg/dL) determination using the following formula:

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

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 taking into account 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.

CONTRAINDICATIONS & PRECAUTION(S), WARNING(S):

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

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose- galactose malabsorption should not take Cetirizine film-coated tablet.

PRECAUTIONS & WARNINGS:

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 at risk of convulsions are recommended. 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. Allergy skin tests are inhibited by antihistamines and a wash-out period (of 3 days) is required before performing them.

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 sensitive patients, concurrent use with alcohol or other CNS depressants may cause additional reductions in alertness and impairment of performance.

PREGNANCY AND LACTATION:

Pregnancy: 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 women.

Lactation: Cetirizine is excreted in human milk at concentrations representing 0.25 to 0.90 those measured in plasma, depending on sampling time after administration. Therefore, caution should be exercised when prescribing Cetirizine to lactating women.

INTERACTIONS:

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.

240 mm

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ADVERSE EFFECTS:

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 this resolves upon discontinuation of the treatment with Cetirizine dihydrochloride.

Clinical trials: 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 reactions were reported for Cetirizine 10 mg in the placebo-controlled trials at rates of 1.0 % or greater:

Adverse reactions (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	1.10 %	0.98 %
Headache	7.42 %	8.07 %
Gastro-intestinal system 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 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 reactions at rates of 1 % or greater in children aged from 6 months to 12 years, included in placebo-controlled clinical trials are:

Adverse reactions (WHO-ART)	Cetirizine (n=1656)	Placebo (n =1294)
Gastro-intestinal system disorders		
Diarrhea	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 reactions 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, hallucination, insomnia

Very rare: tics

Not known: suicidal ideation

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, oculogyration

Ear and labyrinth disorders:

Not known: vertigo

Cardiac disorders:

Rare: tachycardia

Gastro-intestinal disorders:

Uncommon: diarrhea

Hepatobiliary disorders:

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

Skin and subcutaneous tissue disorders:

Uncommon: pruritus, rash

Rare: urticaria

Very rare: angioneurotic oedema, fixed drug eruption

Renal and urinary disorders:

Very rare: dysuria, enuresis

Not known: urinary retention

General disorders and administration site conditions:

Uncommon: asthenia, malaise

Rare: edema

Investigations:

Rare: weight increased

OVERDOSAGE AND TREATMENT:

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, diarrhea, 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.

STORAGE CONDITION:

Store at temperatures not exceeding 30°C.

DOSAGE FORMS AND PACKAGING AVAILABLE:

Film coated Tablet, Alu/PVC Blister Pack of 10's (Box of 100's)

INSTRUCTIONS AND SPECIAL PRECAUTIONS FOR HANDLING AND DISPOSAL (IF APPLICABLE):

Not Applicable

NAME AND ADDRESS OF MARKETING AUTHORIZATION HOLDER:

Marketing Authorization Holder

Brown & Burk Philippines Inc
U-501, 5/F., SEDCCO 1 Bldg., 120 Rada cor.,
Legaspi Sts., Legaspi Village, Makati City, Philippines

NAME AND ADDRESS OF MANUFACTURER:

MICRO LABS LIMITED
67/68A, 3rd Phase, Peenya,
Bangalore - 560 058, INDIA.

CAUTION STATEMENT:

FOODS, DRUGS, DEVICES, AND COSMETICS ACT PROHIBITS DISPENSING WITHOUT PRESCRIPTION.

ADR REPORTING STATEMENT:

"FOR SUSPECTED ADVERSE DRUG REACTION, REPORT TO THE FDA:

www.fda.gov.ph

Seek medical attention immediately at the first sign of Adverse Drug Reaction.

REGISTRATION NUMBER:

DRP-275

DATE OF FIRST AUTHORIZATION:

10 MARCH, 2008

DATE OF REVISION OF PACKAGE INSERT:

Mar. 2018

EXG-ML12I-0521/C

240 mm

MICRO LABS LIMITED, BANGALORE, INDIA						
1	Product Name	Askey			Colours Used <input checked="" type="checkbox"/> BLACK	
2	Strength	10 mg				
3	Component	Leaflet				
4	Category	Export - Philippines				
5	Dimension	210 x 240 mm				
6	Artwork Code	EXG-ML12I-0521/C				
7	Pharma Code	N/A				
8	Reason for Change	Text corrections as per Customer				
		Prepared by (DTP)	Checked by (PD)	Approved by		
Sign		Kantharaju L.		Head CQA	Head Production/ Packing (Site)	
Date		24-05-2021		Head QC (Site)	Head QA (Site)	