CVETOX

INSTRUCTIONS FOR THE MEDICINAL PRODUCT

Trade name: Cvetox.
International Nonproprietary Name: Cetirizine.
Dosage form: Oral solution**.**
Composition: 1 ml oral solution contains:
Cetirizine dihydrochloride 1 mg
Pharmacotherapeutic group: Piperazine derivatives .
ATC Code: R06A E07.
Pharmacologic property:
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.
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 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.
In a six-week, placebo-controlled study of 186 patients with allergic rhinitis and concomitant mild to moderate asthma, cetirizine 10 mg 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.
Pharmacokinetics:
Cetirizine is rapidly absorbed from the gastro-intestinal tract after oral administration with peak plasma levels after a 10mg dose are approximately 300ng/mL and occur about one hour after dosing. The onset of activity occurs within 20 to 60 minutes and persists for at least 24 hours following a single dose. Bioavailability is unchanged and time to peak plasma concentrations delayed when administered with food.Cetirizine is approximately 93% bound to plasma proteins. The plasma elimination half-life is approximately 8-9 hours and does not change with multiple dosing. Pharmacokinetics are dose independent and plasma levels are proportional to the dose administered over the clinically studied range of 5 to 20mg. Cetirizine is less extensively metabolised than other antihistamines and approximately 60% of an administered dose is excreted unchanged in 24 hours. The high bioavailability associated with generally low inter-subject variation in blood level is attributable primarily to first-pass metabolism. Only one metabolite has been identified in humans - the product of oxidative dealkylation of the terminal carboxymethyl group. The antihistaminic activity of this metabolite is negligible.
Indicationfor use:
- Relief of nasal and ocular-symptoms of seasonal and perennial rhinitis;
- Relief of symptoms of chronic idiopathic urticaria.
- **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

Caution in epileptic patients and patients at risk of convulsions is recommended.
Pregnancy and Nursing Mother:
For cetirizine very rare clinical data on exposed pregnancies are available.
Caution should be exercised when prescribing to pregnant or breast feeding women because cetirizine passes into breast milk.
Under 6 Months Old:
The safety and efficacy of this medication in patients under the age of 6 months have not been clinically evaluated. Patients younger than 6 months should not be administered cetirizine unless otherwise recommended by a medical provider.
Dosage:
Children aged from 2 to 6 years: 2,5 mg twice daily (2,5 ml oral solution twice daily (a half spoon twice daily)).
Children aged from 6 to 12 years: 5 mg twice daily (5 ml oral solution bid (a full spoon twice daily)).
Adults and adolescents over 12 years of age: 10 mg once daily (10 ml oral solution (2 full spoons)).
The solution can be swallowed as such.
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 impairement. 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.

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 (see Patients with moderate to severe renal impairment above).
Side-effects:
Blood and lymphatic disorders: Very rare: thrombocytopenia.
Immune system disorders: Rare: hypersensitivity; Very rare: anaphylactic shock.
Psychiatric disorders: Uncommon: agitation; Rare: aggression, confusion, depression, hallucination, insomnia; Very rare: tic.
Nervous system disorders: Uncommon: paraesthesia; Rare: convulsions, movement disorders; Very rare: dysgeusia, syncope, tremor, dystonia, dyskinesia.
Eye disorders: Very rare: accommodation disorder, blurred vision, oculogyration.
Cardiac disorders: Rare: tachycardia.
Gastro-intestinal disorders: Uncommon: diarrhoea.
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.
Investigations: Rare: weight increase.
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.
Treatment: should overdose occur, symptomatic or supportive treatment is recommended. Gastric lavage should be considered following ingestion of a short occurrence. There is no known specific antidote to cetirizine. Cetirizine is not effectively removed by dialysis.
Drug 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.
Cautions:
Cvetox oral solution contains sorbitol. Patients with rare hereditary problems of fructose intolerance should not take cetirizine oral solution.
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.
Effects on ability to drive and use machines:
This solution does not normally cause drowsiness. However, individuals can react differently to treatment. If you are affected you should not drive or operate machinery, but should persist with the oral solution as any drowsiness doesn't usually last very long.
Presentation:
Box with glass bottle with oral solution of 120 ml + plastic teaspoon.
Storage:
Keep in dry place, protected from light at a temperature below 25°C. Keep out of reach of children.
Shelf life:
Labeled. Do not use after expiry date.
Distribution Condition:
Non-prescribed medicine.