BioWell ATRIZINE TABLET 10MG

VIATR01-0
BW04UM-220617

DESCRIPTION
Oblong, white to off-white film-coated tablet, bevel edged, shallow convex and scored on one face. This tablet can be broken into two.

COMPOSITION
Each tablet contains Cetirizine HC/ BP 10 mg.

PHARMACODYNAMICS
Cetirizine, a human metabolite of hydroxyzine, is a potent and selective antagonist of peripheral 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.
At the recommended dosage, cetirizine has demonstrated that it improves the quality of life of patients with perennial and seasonal allergic rhinitis.

PHARMACOKINETICS
Peak blood levels in the order of 0.3µg/ml are reached within about one hour after the oral administration of cetirizine.
The terminal half-life is approximately ten hours in adults and six hours in children aged 6 - 12 years.
This is consistent with the urinary excretion half-life of the drug.
The cumulative urinary excretion represents about two thirds of the dose given for both adults and children.
Consequently, the apparent plasma clearance in children is higher than that measured in adults. Plasma levels are linearly related to the dose given. A high proportion of cetirizine is bound to human plasma proteins.

INDICATIONS
Adults and children of 2 years and above: symptomatic treatment of seasonal allergic rhinitis, perennial allergic rhinitis and urticaria of allergic origin.

CONTRAINDICATIONS
Hypersensitivity to the active substance, to any of the excipients, to hydroxyzine or to any piperazine derivatives.
Caution for patients with lactose intolerance as this product contains lactose monohydrate. Patients with severe renal impairment at less than 10 ml/min creatinine clearance.

WARNINGS AND PRECAUTIONS
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 is 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.
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.
Allergy skin tests are inhibited by antihistamines and a wash-out period (of 3 days) is required before performing them.
Activities Requiring Mental Alertness: In clinical trials the occurrence of somnolence has been reported in some patients taking Cetirizine: due caution should therefore be exercised when driving a car or operating potentially dangerous machinery.

PREGNANCY AND LACTATION
Data on a limited number of exposed pregnancies indicate no adverse effects of cetirizine on pregnancy or on health of foetus/new born child. To date no other relevant epidemiological data are available. Caution should be exercised when prescribing to pregnant women.

Breast feeding
Caution should be exercised when prescribing cetirizine to lactating women. Cetirizine is excreted in human milk at concentrations representing 25% to 90% of those measured in plasma, depending on sampling time after administration.

SIDE EFFECTS
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 antichloinergic 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.

MedDRA SOC	Adverse reaction	Frequency
Blood and lymphatic disorders	Thrombocytopenia	Very rare
Metabolism and nutrition disorders	Increased appetite	Not known
Psychiatric disorders	Agitation	Uncommon
	Aggression, confusion, depression, hallucinations, insomnia	Rare
	Tic	Very rare
	Suicidal ideation, nightmare	Not known
Nervous system disorders	Paraesthesia	Uncommon
	Convulsions	Rare
	Dysgeusia, syncope, tremor, dystonia, dyskinesia	Very rare
	Amnesia, memory impairment	Unknown
Eye disorders	Accommodation disorder, blurred vision, oculogyration	Very rare
Ear and labyrinth disorders	Vertigo	Not known
Cardiac disorders	Tachycardia	Rare
Gastro-intestinal disorders	Diarrhoea	Uncommon
Hepatobiliary disorders	Hepatic function abnormal (increased transaminases, alkaline phosphates, γ -GT and bilirubin)	Rare
	Hepatitis	Unknown
Skin and subcutaneous tissue disorders	Pruritus, rash	Uncommon
	Urticaria	Rare
	Angioneurotic oedema, fixed drug eruption	Very rare
	Acute generalized exanthematous pustulosis (AGEP)	Unknown

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MedDRA SOC	Adverse reaction	Frequency
Musculoskeletal and connective tissue disorder	Arthralgia	Not known
Renal and urinary disorders	Dysuria, enuresis	Very rare
	Urinary retention (see section Warnings and Precautions)	Not known

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

Effects on Ability to Drive and Use Machine
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.

DRUG INTERACTIONS

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.

Alcohol and other CNS depressants
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.

OVERDOSE 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, diarrhoea, dizziness, fatigue, headache, malaise, mydriasis, pruritus, restlessness, sedation, somnolence, stupor, tachycardia, tremor, and urinary retention.

Treatment
There is no known specific antidote to cetirizine.
Should overdose occur, symptomatic or supportive treatment is recommended. Cetirizine is not effectively removed by dialysis.

DOSAGE AND ADMINISRATION

For oral use.
Adults
10mg (1 tablet) once daily.
A 5mg starting dose (half of the tablet) may be proposed if this lead to satisfactory control of the symptoms.

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

Children
Children aged from 2 to 6 years
2.5 mg twice daily.

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

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

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
Since cetirizine is mainly excreted via renal route, in cases no alternative treatment can be used, the dosing intervals must be individualised 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:

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

Dosing adjustments for adults 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 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.

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 renal impairment above).

Note: The information given here is limited. For further information, consult your doctor or pharmacist.

Storage : Store below 30°C. Protect from direct sunlight and moisture.
Presentation/Packing : Blister pack of 10 x 10's

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