# Alatrol® Syrup 5mg/5ml

## Cetirizine Hydrochloride BP

**Alatrol® Syrup:** Each 5 ml Syrup contains Cetirizine Hydrochloride BP 5.0 mg.
**Product Description:** A light yellow colored flavored clear liquid, filled and sealed in transparent PET bottle with "SQUARE" printed white color PP cap.

**Pharmacodynamics:** Cetirizine hydrochloride, a human metabolite of hydroxyzine, is a potent antihistamine that selectively inhibits the effect of peripheral H(1)-receptors. Cetirizine belongs to the piperazine class of antihistamines and is the major carboxylated metabolite of hydroxyzine. However, it is less lipophilic than hydroxyzine and thus less likely to distribute into the central nervous system (CNS) and produce sedation. Generally, antihistamines contain 1 or 2 heterocyclic or aromatic rings attached to the side chain of histamine. Cetirizine has more polar or less lipophilic functional groups attached to the ethylamine side chain which has resulted in less CNS penetration, greater selectivity for the H1-receptor, and less anticholinergic side effects. Cetirizine may also have a modulatory effect on inflammatory cells by inhibiting eosinophil migration or eosinophilotactic mediators. Additionally, cetirizine may also have inhibitory effects on other infiltrating inflammatory cells, such as neutrophils. Cetirizine has shown to be safe for allergic patients with mild to moderate asthma and does not cause prolongation of QT interval.

**Pharmacokinetics:** *Absorption:* Cetirizine is rapidly absorbed from the gastrointestinal tract after oral doses and peak plasma concentrations occur within about an hour. Food delays the time to peak plasma concentrations but does not decrease the amount of drug absorbed.
*Bioavailability, oral:* 70%. The extent of bioavailability is similar when cetirizine is given as solutions, capsules or tablets.
*Distribution:* Cetirizine is highly bound to plasma proteins (93%).Volume of distribution is 0.5 to 0.8 L/kg. It does not appear to cross the blood-brain barrier to a significant extent. It has been detected in breast milk.
*Metabolism:* Cetirizine is not extensively metabolized by the liver. The inactive O- dealkylated metabolite has been identified in both the plasma and feces, but not in the urine.
*Elimination:* Cetirizine is excreted primarily in the urine (60%) mainly as unchanged drug and has an elimination half-life of about 10 hours. Cetirizine is poorly cleared by hemodialysis.
Special populations: 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. Renal insufficiency: The elimination half-life of cetirizine may be prolonged. Dosing adjustment is necessary in patients with moderate or severe renal impairment. Hemodialysis is unlikely to be of value in removing cetirizine from the plasma.
Elderly or hepatic insufficiency: The elimination half-life is prolonged by 50% in geriatrics and in patients with chronic liver disease as compared to normal healthy adults. Dosing adjustment is only necessary in hepatically impaired patients if concomitant renal impairment is present.

**Indication:**
Adults and children of 2 year and above: symptomatic treatment of seasonal allergic rhinitis, perennial allergic rhinitis and urticaria of allergic origin.

**Recommended Dosage:**
Adults: 10 mg (20 drops or 10 ml oral solution or 1 tablet) once daily. A 5 mg starting dose (10 drops or 5 ml of oral solution or half of the tablet) may be proposed if this leads to satisfactory control of the symptoms.
Children: Children aged from 2 to 6 years 2.5 mg (5 drops or 2.5 ml of oral solution bid) twice daily. Children aged from 6 to 12 years 5 mg (10 drops or 5 ml of oral solution or half of the tablet) twice daily. Children over 12 years of age 10 mg (20 drops or 10 ml of oral solution or 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: 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 (ClCcr) in ml/min is needed. The ClCr (ml/min) may be estimated from serum creatinine (mg/dl) determination using the following formula:

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

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 paediatric 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 renal impairment above).

**Mode of Administration:** Oral

**Contraindications:**
- History of hypersensitivity to any of the constituents of the formulation, to hydroxyzine or to any piperazine derivatives.
- Cetirizine is contraindicated during lactation.
- 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 is recommended in epileptic patients and patients at risk of convulsions.
Sodium benzoate may cause allergic reactions (possibly delayed).
Patients with rare hereditary problems of fructose intolerance should not take cetirizine 1 mg/ml oral solution.
Response to allergy skin tests are inhibited by antihistamines and a wash-out period (of 3 days) is required before performing them. 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.

**Paediatric population:** Due to the amount of some excipients in the formulation, the use of the product is not recommended in children aged less than 2 years.

**Effects on the 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.

**Interactions with Other Medicaments:** 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).

**Pregnancy and Lactation:**

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.

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

**Adverse Effects / Undesirable 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 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.

Undesirable effects are described according to MedDRA System Organ Class and by estimated frequency.

Frequencies are defined as follows: Very common; common; uncommon; rare; very rare, not known.

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: diarrhoea
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: oedema
Investigations
Rare: weight increased

Description of selected adverse reactions

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

**Overdose and Treatment:** *Symptoms:* Overdose symptoms include 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. Activated charcoal should be considered after extremely large ingestions or if more toxic coingestants are involved within 2 hours from the ingestion. Cetirizine is not effectively removed by dialysis.

**Storage Conditions:** Store below 30°C

**Dosage Forms and Packaging Available**

60 ml Syrup in a round transparent PET bottle

**Date of Revision:** October 2023

**Manufactured by :**

**SQUARE PHARMACEUTICALS PLC.**
Square Road, Salgaria,
Pabna 6600, Bangladesh



200002691 4