ILR-G 5mg

(Levocetirizine Dihydrochloride)

Tablets U.S.P.

آئی ایل آر-جی ۵ ملی گرام

(لیوسیٹرزین ڈائی ہائیڈروکلورائیڈ) ٹیبلٹس یو۔ایس۔پی۔

QUALITATIVE AND QUANTITATIVE COMPOSITION

ILR-G (Levocetirizine Dihydrochloride) Tablets U.S.P. 5mg

Each tablet contains:

Levocetirizine Dihydrochloride U.S.P. 5mg

DESCRIPTION

Levocetirizine is anti-histamine used to relieve allergy symptoms such as watery eyes, runny nose, itching eyes/nose, and sneezing. It is also used to relieve itching and hives. It works by blocking a certain natural substance (histamine) that your body makes during an allergic reaction.

CLINICAL PHARMACOLOGY

Mechanism of Action: Levocetirizine, the active enantiomer of cetirizine, is an antihistamine; its principal effects are mediated via selective inhibition of H1 receptors. The antihistaminic activity of levocetirizine has been documented in a variety of animal and human models. In vitro binding studies revealed that levocetirizine has an affinity for the human H1-receptor 2-fold higher than that of cetirizine (Ki = 3 nmol/L vs. 6 nmol/L, respectively). The clinical relevance of this finding is unknown. **Pharmacokinetics:** ***Absorption:*** Levocetirizine is rapidly and extensively absorbed following oral administration. In adults, peak plasma concentrations are achieved 0.9 hour after administration of the oral tablet. The accumulation ratio following daily oral administration is 1.12 with steady state achieved after 2 days. Peak concentrations are typically 270ng/mL and 308 ng/mL following a single and a repeated 5 mg once daily dose, respectively. Food had no effect on the extent of exposure (AUC) of the levocetirizine tablet, but Tmax was delayed by about 1.25 hours and Cmax was decreased by about 36% after administration with a high fat meal; therefore, levocetirizine can be administered with or without food. ***Distribution:*** The mean plasma protein binding of levocetirizine in vitro ranged from 91 to 92%, independent of concentration in the range of 90-5000 ng/mL, which includes the therapeutic plasma levels observed. Following oral dosing, the average apparent volume of distribution is approximately 0.4L/kg, representative of distribution in total body water. ***Metabolism:*** The extent of metabolism of levocetirizine in humans is less than 14% of the dose and therefore differences resulting from genetic polymorphism or concomitant intake of hepatic drug metabolizing enzyme inhibitors are expected to be negligible. Metabolic pathways include aromatic oxidation, N-and O-dealkylation, and taurine conjugation. Dealkylation pathways are primarily mediated by CYP3A4 while aromatic oxidation involves multiple and/or unidentified CYP isoforms.

Excretion: The plasma half-life in adult healthy subjects was about 8 to 9 hours after administration of oral tablets , and the mean oral total body clearance for levocetirizine was approximately 0.63 mL/kg/min. The major route of excretion of levocetirizine and its metabolites is via urine, accounting for a mean of 85.4% of the dose. Excretion via feces accounts for only 12.9% of the dose. Levocetirizine is excreted both by glomerular filtration and active tubular secretion. Renal clearance of levocetirizine correlates with that of creatinine clearance. In patients with renal impairment the clearance of levocetirizine is reduced.

INDICATIONS AND USAGE

• Perennial Allergic Rhinitis: ILR-G is indicated for the relief of symptoms associated with perennial allergic rhinitis in children 6 months to 2 years of age.

• Chronic Idiopathic Urticaria: ILR-G is indicated for the treatment of the uncomplicated skin manifestations of chronic idiopathic urticaria in adults and children 6 months of age and older.

CONTRAINDICATIONS

The use of ILR-G is contraindicated in:

• Patients with Known Hypersensitivity: Patients with known hypersensitivity to levocetirizine or any of the ingredients of ILR-G, or to cetirizine. Observed reactions range from urticaria to anaphylaxis.

• Patients with End-Stage Renal Disease: Patients with end-stage renal disease (CLCR <10mL/min) and patients undergoing hemodialysis

• Pediatric Patients with Impaired Renal Function: Children 6 months to 11 years of age with impaired renal function

INTERACTIONS

In vitro data indicate that levocetirizine is unlikely to produce pharmacokinetic interactions through inhibition or induction of liver drug-metabolizing enzymes. Antipyrine, Azithromycin, Cimetidine, Erythromycin, Ketoconazole, Theophylline, and Pseudoephedrine: cetirizine did not interact with antipyrine, pseudoephedrine, erythromycin, azithromycin, ketoconazole, and cimetidine. There was a small decrease (~16%) in the clearance of cetirizine caused by a 400 mg dose of theophylline. It is possible that higher theophylline doses could have a greater effect.

Ritonavir: Ritonavir increased the plasma AUC of cetirizine by about 42% accompanied by an increase in half-life (53%) and a decrease in clearance (29%) of cetirizine. The disposition of ritonavir was not altered by concomitant cetirizine administration.

USE IN SPECIFIC POPULATION

Pregnancy: Most manufacturers of antihistamines advise avoiding their use during pregnancy; however, there is no evidence of teratogenicity. ***Breast Feeding:*** Most antihistamines are present in breast milk in varying amounts; although not known to be harmful, most manufacturers advise avoiding their use in mothers who are breast feeding. ***Renal impairment:*** In adults Avoid if eGFR less than 10 mL/minute/1.73m2. In children Avoid if estimated glomerular filtration rate less than 10 mL/minute/1.73m2. ***Dose adjustments:*** In adults 5mg on alternate days if eGFR 30–50 mL/minute/1.73m2. 5 mg every 3 days if eGFR 10–30

mL/minute/1.73m2. In children Reduce dose frequency to alternate days if estimated glomerular filtration rate 30–50 mL/minute/1.73m2. Reduce dose frequency to every 3 days if estimated glomerular filtration rate 10–30 mL/minute/1.73m2. ***Geriatric Use:*** Dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range reflecting the greater frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other drug therapy. ***Hepatic Impairment:*** As levocetirizine is mainly excreted unchanged by the kidneys, it is unlikely that the clearance of levocetirizine is significantly decreased in patients with solely hepatic impairment.

PRECAUTIONS

Somnolence: In clinical trials the occurrence of somnolence, fatigue, and asthenia has been reported in some patients under therapy with levocetrizine. Patients should be cautioned against engaging in hazardous occupations requiring complete mental alertness, and motor coordination such as operating machinery or driving a motor vehicle after ingestion of ILR-G. Concurrent use of ILR-G with alcohol or other central nervous system depressants should be avoided because additional reductions in alertness and additional impairment of central nervous system performance may occur. ***Urinary Retention:*** Urinary retention has been reported post marketing with levocetrizine. ILR-G should be used with caution in patients with predisposing factors of urinary retention (e.g. spinal cord lesion, prostatic hyperplasia) as ILR-G may increase the risk of urinary retention. Discontinue ILR-G if urinary retention occurs.

ADVERSE REACTIONS

Use of ILR-G has been associated with somnolence, fatigue, asthenia, and urinary retention.

DOSAGE AND ADMINISTRATION

ILR-G can be taken without regard to food consumption. ***Perennial Allergic Rhinitis:*** Children 6 months to 2 Years of Age: The recommended initial dose of ILR-G is 1.25 mg (1/2 tea-spoon oral solution) (2.5 mL) once daily in the evening. The 1.25 mg once daily dose should not be exceeded based on comparable exposure to adults receiving 5 mg. Chronic Idiopathic Urticaria. ***Adults and Children 12 Years of Age and Older:*** The recommended dose of ILR-G is 5mg (1 tab-let or 2 teaspoons [10 mL] oral solution) once daily in the evening. Some patients may be adequately controlled by 2.5 mg (1/2 tablet or 1 teaspoon [5 mL] oral solution) once daily in the evening. ***Children 6 to 11 Years of Age:*** The recommended dose of ILR-G is 2.5 mg (1/2 tablet or 1 tea-spoon [5 mL] oral solution) once daily in the evening. The 2.5 mg dose should not be exceeded because the systemic exposure with 5 mg is approximately twice that of adults. ***Children 6 months to 5 Years of Age:*** The recommended initial dose of ILR-G is 1.25 mg (1/2 tea-spoon oral solution) (2.5 mL) once daily in the evening. The 1.25 mg once daily dose should not be exceeded based on comparable exposure to adults receiving 5mg. ***Dose Adjustment for Renal and Hepatic Impairment:*** In adults and children 12 years of age and older with:

- Mild renal impairment (creatinine clearance [CLCR] = 50-80 mL/min): a dose of 2.5 mg once daily is recommended
- Moderate renal impairment (CLCR = 30-50 mL/min): a dose of 2.5 mg once every other day is recommended.
- Severe renal impairment (CLCR = 10-30 mL/min): a dose of 2.5 mg twice weekly (administered once every 3-4 days) is recommended;
- End-stage renal disease patients (CLCR <10 mL/min) and patients undergoing hemodialysis should not receive ILR-G.

No dose adjustment is needed in patients with solely hepatic impairment. In patients with both hepatic impairment and renal impairment, adjustment of the dose is recommended.

OVERDOSAGE

Overdosage has been reported with ILR-G.Symptoms of overdose may include drowsiness in adults. In children agitation and restlessness may initially occur, followed by drowsiness. There is no known specific antidote to ILR-G. Should overdose occur, symptomatic or supportive treatment is recommended. ILR-G is not effectively removed by dialysis, and dialysis will be effective unless a dialyzable agent has been concomitantly ingested. The acute maximal non-lethal oral dose of levocetirizine was 240 mg/kg in mice (approximately 190 times the maximum recommended daily oral dose in adults, approximately 230 times the maximum recommended daily oral dose in children 6 to 11 years of age, and approximately 180 times the maximum recommended daily oral dose in children 6 months to 5 years of age on a mg/m2 basis).

INSTRUCTIONS

Dosage as directed by the physician. Store at 20°C to 25°C, excursions permitted to 15°C to 30°C. Protect from light and moisture. Keep all medicines out of the reach of children. To be sold on the prescription of registered medical practitioner only.

PRESENTATION

ILR-G (Levocetirizine Dihydrochloride) Tablets 5mg are available in Alu-PVC blister pack of 10's.

ہدایات: خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔ ۲۰ سے ۲۵ ڈگری سینٹی گریڈ پر رکھیں، محفوظ رکھنے کی حد ۱۵ سے ۳۰ ڈگری سینٹی گریڈ ہے۔ روشنی اور نمی سے محفوظ رکھیں۔ تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔ صرف رجسٹرڈ ڈاکٹر کے نسخہ پر فروخت کریں۔

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