LEVOCETIRIZINE DIHYDROCHLORIDE

ALLERZET®

℞

2.5 mg per 5 mL Syrup
Antihistamine

FORMULATION

Each 5 mL (1 teaspoonful) syrup contains:
Levocetirizine dihydrochloride,-- ..... 2.5 mg

PRODUCT DESCRIPTION

Levocetirizine dihydrochloride (Allerzet®) 2.5 mg/5 mL Syrup is a clear, colorless to slightly yellow syrup with a grape odor and taste using the TasteRite® Technology. TasteRite® technology is a unique tastemasking system developed specifically for liquid dosage forms. This technology significantly reduces the bitterness of medicine so that children taste the flavor and not the medicine.

CLINICAL PHARMACOLOGY

PHARMACODYNAMICS

Levocetirizine, the active enantiomer of cetirizine, is a second generation antihistamine. It selectively antagonizes histamine H_1-receptors. In vitro studies have shown that levocetirizine has twice the H_1-receptor affinity of cetirizine.

Levocetirizine (at half of cetirizine dosage) appears to be as potent as cetirizine in inhibiting histamine-induced sneezing, increased nasal airway resistance, and skin wheal and flare. Compared with other antihistamines (e.g., desloratadine, fexofenadine, loratadine), it exhibits greater and more consistent inhibition of histamine-induced wheal and flare.

PHARMACOKINETICS

Levocetirizine is rapidly and extensively absorbed after oral administration. Peak plasma concentrations are seen at 0.5 hour for oral solution following oral administration. Food has no effect on the extent of exposure of levocetirizine, but time to peak plasma concentration is delayed by approximately 1.25 hours and peak plasma concentration is decreased by approximately 36% after administration with a high fat meal. Levocetirizine can, therefore, be administered with or without food.

No tissue distribution data are available in humans, neither concerning the passage of levocetirizine through the blood-brain barrier. Levocetirizine is 90% bound to plasma proteins. The apparent volume of distribution is approximately 0.4 L/kg.

In humans, the extent of levocetirizine metabolism is less than 14% of the dose. Therefore, differences resulting from genetic polymorphism or concomitant intake of enzyme inhibitors are expected to be negligible. Metabolic pathways include aromatic oxidation, N- and O-dealkylation, and taurine conjugation. Due to its low metabolism and absence of metabolic inhibition potential, the interaction of levocetirizine with other substances, or vice-versa, is unlikely.

The plasma elimination half-life of levocetirizine is approximately 8 to 9 hours following oral administration. Mean oral total body clearance is 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.

Special Population:

Renal Impairment: The area under the plasma concentration-time curve (AUC) is increased by 1.8-, 3.2-, 4.3-, or 5.7-fold in those with mild, moderate, severe impairment, or end-stage renal disease, respectively. The corresponding increases of half-life estimates were 1.4-, 2.0-, 2.9-, and 4-fold, respectively.

Additional pharmacokinetics for syrup:
In children 6 months to 5 years old, the administration of levocetirizine 1.25 mg once a day resulted in plasma concentrations similar to those in adults receiving 5 mg once a day. In children 6 to 11 years old given a single oral dose of levocetirizine 5 mg, peak plasma concentration and AUC values are about 2-fold greater than those in adults. Total body clearance is 30% greater and elimination half-life is 24%

INDICATIONS

Allergic rhinitis
• For the relief of symptoms associated with seasonal allergic rhinitis in children ≥ 2 years old and in adults
• For the relief of symptoms associated with perennial allergic rhinitis in children ≥ 6 months old and in adults

Chronic idiopathic urticaria
• For the treatment of uncomplicated skin manifestations of chronic idiopathic urticaria in children ≥ 6 months old and in adults

DOSAGE AND ADMINISTRATION

This medicine should be taken orally, once a day at bedtime, with or without food.

Children 6 months to 5 years old ..... 2.5 mL (½ teaspoonful)
Children 6 to 11 years old ..... 5 mL (1 teaspoonful)
Adults and Children ≥ 12 years old .... 10 mL (2 teaspoonsful)

Renal Impairment
Dosage adjustment should be done according to the degree of renal impairment, as follows:

Dosage for Symptomatic Treatment of Allergic Rhinitis and Chronic Idiopathic Urticaria in Children ≥ 12 Years Old and Adults with Renal Impairment		
Degree of Renal Impairment	**Creatinine Clearance (mL/min)**	**Oral Levocetirizine Dose**
Mild	50 to 79	2.5 mg (5 mL) once a day
Moderate	30 to 49	2.5 mg (5 mL) once every 2 days
Severe	< 30	2.5 mg (5 mL) once every 3 days
End-stage Renal Disease; Patients Undergoing Dialysis	< 10	CONTRAINDICATED

Hepatic Impairment
No dosage adjustment is necessary for patients with hepatic impairment.

CONTRAINDICATIONS

• Hypersensitivity to levocetirizine, cetirizine, other piperazine derivatives, or to any component of the product
• Patients with end-stage renal disease (creatinine clearance < 10 mL/min) or undergoing hemodialysis
• Children 6 months to 11 years of age with renal impairment
• Breastfeeding

WARNINGS AND PRECAUTIONS

• Patients with predisposing factors of urinary retention (e.g., spinal cord lesion, prostatic hyperplasia) should use levocetirizine with caution.
• Concomitant use of levocetirizine with alcohol or other central nervous system (CNS) depressants should be avoided. (See Interactions with Other Medicaments)
• Caution should be observed in epileptic patients and patients at risk of convulsions.
• Levocetirizine should only be used during pregnancy when clearly needed.

Effects on Ability to Drive and Use Machine
Somnolence, fatigue and asthenia are associated with levocetirizine treatment. Patients should exercise caution when performing hazardous activities requiring mental alertness and physical coordination (e.g., driving, operating

INTERACTIONS WITH OTHER MEDICAMENTS

CNS Depressants (e.g., Alcohol): Avoid concomitant use due to possible additive effect (i.e., additional reduction in alertness, additional impairment of CNS performance).

Ritonavir: Ritonavir disposition is not altered but this may cause increased AUC (42%), increased half-life (53%), and decreased clearance (29%) of cetirizine.

Theophylline: Theophylline disposition is not altered but this may cause decreased clearance (16%) of cetirizine.

Ketoconazole: Concomitant administration with cetirizine caused prolongation of QT_c interval (increase of 17.4 msec). However, this interaction was not considered clinically important.

Antipyrine, Azithromycin, Cimetidine, Erythromycin, Ketoconazole, Pseudoephedrine: No clinically important changes in electrocardiogram parameters and no pharmacokinetic interactions were observed with cetirizine.

STATEMENT ON USAGE FOR HIGH RISK GROUPS

Pregnancy: Pregnancy Category B. There are no adequate and well-controlled studies in pregnant women. Levocetirizine should only be used during pregnancy when clearly needed.

Lactation: The use of levocetirizine is not recommended in breastfeeding women as it is possibly distributed into milk (cetirizine is distributed into milk).

Elderly: Clinical experience with levocetirizine has not identified differences in responses between the elderly and younger patients. However, dose should be carefully selected for elderly patients, usually starting at the lowest dose due to greater frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other drug therapy.

Renal Impairment: Levocetirizine is mainly excreted by the kidneys and the risk of adverse effects may be greater in patients with renal impairment. (See Dosage and Mode of Administration)

UNDESIRABLE EFFECTS

The most frequently reported adverse effects with levocetirizine include diarrhea, constipation, otitis media, vomiting, cough, pyrexia, epistaxis, asthenia, dry mouth, fatigue, headache, nasopharyngitis, pharyngitis, and somnolence.

Immune system disorders: Hypersensitivity (anaphylaxis)
Metabolism and nutrition disorders: Edema, increased appetite, weight gain
Psychiatric disorders: Aggression, agitation, depression, hallucination, suicidal ideation
Nervous system disorders: Convulsion, dizziness, dysgeusia, extrapyramidal symptoms, febrile seizure, insomnia, movement disorders (including dystonia and oculogyric crisis), myoclonus, orofacial dyskinesia, paresthesia, seizure, syncope, tic, tremor
Eye disorders: Blurred vision, visual disturbances
Ear and labyrinth disorders: Vertigo
Cardiac disorders: Palpitations, tachycardia
Vascular disorders: Severe hypotension
Respiratory, thoracic and mediastinal disorders: Dyspnea
Gastrointestinal disorders: Nausea
Hepatobiliary disorders: Cholestasis, hepatitis
Skin and subcutaneous tissue disorders: Acute generalized exanthematous pustulosis (AGEP), angioedema, fixed drug eruption, pruritus, rash, urticaria
Musculoskeletal and connective tissue disorders: Arthralgia, myalgia
Renal and urinary disorders: Dysuria, glomerulonephritis, urinary retention
Pregnancy, puerperium and perinatal conditions: Stillbirth
Investigations: Abnormal liver function tests, blood bilirubin increased, transaminases increased

OVERDOSE AND TREATMENT

Symptoms of levocetirizine overdose in adults may include drowsiness. In children, symptoms are initially agitation and restlessness, followed by drowsiness. No specific antidote is known and overdose is addressed by symptomatic or supportive treatment. Following short-term ingestion, gastric lavage may be considered. Dialysis may be ineffective unless a dialyzable agent was concomitantly ingested.

STORAGE CONDITION

Keep the product out of sight and reach of children
Store at temperatures not exceeding 30°C

AVAILABILITY

Levocetirizine dihydrochloride (**Allerzet®**) 2.5 mg / 5 mL Syrup - in bottles of 30 mL, 60 mL and 120 mL

DATE OF FIRST AUTHORIZATION: October 2012
DATE OF REVISION OF PACKAGE INSERT: September 2017

CAUTION

Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription

ADVERSE DRUG REACTION REPORTING STATEMENT
For suspected adverse drug reaction, seek medical attention immediately and report to the FDA at www.fda.gov.ph AND Unilab at (+632) 858-1000 or productsafety@unilab.com.ph. By reporting undesirable effects, you can help provide more information on the safety of this medicine.

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