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Front side

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XERIN

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only.

Levocetirizine & Montelukast Tablets

COMPOSITION

Each film coated tablet contains:
Levocetirizine Hydrochloride 5 mg
Montelukast Sodium USP
eq. to Montelukast 10 mg
Colour: Titanium Dioxide BP

PHARMACEUTICAL FORM

Tablet

THERAPEUTIC INDICATIONS

For Chronic Allergic conditions like seasonal allergic rhinitis, perennial allergic rhinitis, Rhinitis associated with Asthma.

DOSAGE AND ADMINISTRATION

The film-coated tablet must be taken orally, swallowed whole with liquid and may be taken with or without food.

The daily recommended dose for the adults is one tablet daily.

CONTRAINDICATIONS

Contraindicated in patients with known hypersensitivity to montelukast sodium, levocetirizine or cetirizine or to any other component of this product. Also contraindicated in patients with severe renal impairment at less than 10ml/min creatinine clearance. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medication.

SPECIAL WARNINGS AND PRECAUTIONS

Montelukast is not indicated for use in the reversal of bronchospasm in acute asthma attacks, including status asthmaticus. Patients should be advised to have appropriate rescue medication available. Therapy with montelukast can be continued during acute exacerbations of asthma. While the dose of inhaled corticosteroid may be reduced gradually under medical supervision, Montelukast should not be abruptly substituted for inhaled or oral corticosteroids.

Montelukast should not be used as monotherapy for the treatment and management of exercise-induced bronchospasm. Patients who have exacerbations of asthma after exercise should continue to use their usual regimen of inhaled (beta)-agonists as prophylaxis and have available for rescue a short-acting inhaled (beta)-agonist. Patients with known aspirin sensitivity should continue avoidance of aspirin or non-steroidal anti-inflammatory agents while taking montelukast. Although montelukast is effective in improving airway function in asthmatics with documented aspirin sensitivity, it has not been shown to truncate bronchoconstrictor response to aspirin and other non-steroidal anti-inflammatory drugs in aspirin-sensitive asthmatic patients.

Comparative clinical trials have revealed no evidence that levocetirizine at the recommended dose impairs mental alertness, reactivity or the ability to drive. In clinical trials the occurrence of somnolence, fatigue, and asthenia has been reported in some patients under therapy with levocetirizine. 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 levocetirizine. Concurrent use of levocetirizine 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.

DRUG INTERACTIONS

Montelukast may be administered with other therapies routinely used in the prophylaxis and chronic treatment of asthma. In drug-interactions studies, the recommended clinical dose of montelukast did not have clinically important effects on the pharmacokinetics of the following medicinal products: theophylline, prednisone, prednisolone, oral contraceptives (ethinyl estradiol/ norethindrone 35/1), terfenadine, digoxin and warfarin. The area under the plasma concentration curve (AUC) for montelukast was decreased approximately 40% in subjects with co-administration of phenobarbital. Since montelukast is metabolised by CYP 3A4, 2C8, and 2C9, caution should be exercised, particularly in children, when montelukast is co-administered with inducers of CYP 3A4, 2C8, and 2C9, such as phenytoin, phenobarbital and rifampicin.

Due to the pharmacokinetic, pharmacodynamic and tolerance profile of levocetirizine, 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 levocetirizine is not reduced with food, although the rate of absorption is decreased.

PREGNANCY AND LACTATION

Pregnancy
There are no adequate and well-controlled studies of either montelukast or levocetirizine in pregnant women. Hence this combination should not be used during pregnancy.

Breastfeeding
Since levocetirizine is excreted in breast-milk the combination is not recommended during lactation

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Combination is not expected to affect a patient's ability to drive a car or operate machinery. However, in very rare cases, individuals have reported drowsiness or dizziness. In these sensitive patients, concurrent use with alcohol or other CNS depressants may cause additional reductions in alertness and impairment of performance.

UNDESIRABLE EFFECTS

Dyspepsia, Abdominal pain, Rash, Dizziness, Headache, Fatigue,

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Fever, Trauma, Cough, Nasal congestion, Somnolence, Fatigue, Nasopharyngitis, Dry mouth, and Pharyngitis.

OVERDOSAGE

There is no data to prove the overdosage of this combination. However, overdosage has been reported with individual molecules.

MONTELUKAST

There have been reports of acute over-dosage in post-marketing experience and clinical studies with montelukast. These include reports in adults and children with a dose as high as 1000 mg. The clinical and laboratory findings observed were 6 consistent with the safety profile in adults and pediatric patients. There were no adverse experiences in the majority of over-dosage reports. The most frequently occurring adverse experiences were consistent with the safety profile of montelukast and included abdominal pain, somnolence, thirst, headache, vomiting and psychomotor hyperactivity. It is not known whether montelukast is removed by peritoneal dialysis or hemodialysis.

LEVOCETIRIZINE

Symptoms of overdose may include drowsiness in adults and initially agitation and restlessness followed by drowsiness, in children. There is no known specific antidote to Levocetirizine. Should overdose occur, symptomatic or supportive treatment is recommended. Levocetirizine is not effectively removed by dialysis and dialysis will be ineffective unless a dialyzable agent has been concomitantly ingested.

PHARMACODYNAMIC PROPERTIES

Montelukast sodium is a selective and orally active leukotriene receptor antagonist that inhibits the cysteinyl leukotriene (CysLT1), receptor. Montelukast causes inhibition of airway cysteinyl leukotriene receptors as demonstrated by the ability to inhibit bronchoconstriction due to inhaled LTD4 in asthmatics.

Levocetirizine, the active enantiomer of cetirizine, is an anti-histamine; its principal effects are mediated via selective inhibition of H1 receptors. Levocetirizine inhibits the histamine-mediated early phase of the allergic reaction and also reduces the migration of certain inflammatory cells and the release of certain mediators associated with the late allergic response.

PHARMACOKINETIC PROPERTIES

MONTELUKAST

Absorption : After administration of a 10-mg tablet to fasted adults, the mean peak montelukast plasma concentration (Cmax) is achieved in 3 to 4 hours (Tmax). The mean oral bioavailability is 64%. The oral bioavailability and Cmax are not influenced by a standard meal in the morning.

Distribution : Montelukast is more than 99% bound to plasma proteins. The steady-state volume of distribution of montelukast averages 8 to 11 liters.

Metabolism : Montelukast is extensively metabolized. In studies with therapeutic doses, plasma concentrations of metabolites of montelukast are undetectable at steady state in adults and pediatric patients.

Elimination : The plasma clearance of montelukast averages 45 mL/min in healthy adults. Following an oral dose of radiolabeled montelukast, 86% of the radioactivity was recovered in 5-day fecal collections and <0.2% was recovered in urines. Coupled with estimates of montelukast oral bioavailability, this indicates that montelukast and its metabolites are excreted almost exclusively via the bile.

LEVOCETIRIZINE

Absorption : Levocetirizine is rapidly and extensively absorbed following oral administration. Peak plasma concentrations are achieved 0.9 h after dosing.

Distribution : 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 distribution of levocetirizine is restrictive, as the volume of distribution is 0.4 l/kg.

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 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 CYP 3A4 while aromatic oxidation involved multiple and/or unidentified CYP isoforms. Levocetirizine had no effect on the activities of CYP isoenzymes 1A2, 2C9, 2C19, 2D6, 2E1 and 3A4 at concentrations well above peak concentrations achieved following a 5 mg oral dose.

Elimination : The plasma half-life in adults is 7.9 ± 1.9 hours. The mean apparent total body clearance is 0.63 ml/min/kg. The major route of excretion of levocetirizine and 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.

STORAGE CONDITIONS

Store below 30°C, protected from light & moisture.

Keep all medicines out of reach of children.

PRESENTATION

10 Tablets packed in Alu-Alu blister.

Product from
Unosource Pharma Ltd.

Manufactured by:
Akums Drugs & Pharmaceuticals Ltd.
19,20,21, Sector-6A, I.I.E., SIDCUL,
Ranipur, Haridwar-249 403, INDIA.

250 mm