For consumer information only

EPIMON® - L

(Montelukast Sodium & Levocetirizine Dihydrochloride Tablets)

Composition:

Each Film coated tablet Contains:

Montelukast Sodium IP
eq. to Montelukast..... 10 mg
Levocetirizine Dihydrochloride IP..... 5 mg
Excipients... .....q.s.
Colour... .....Titanium Dioxide IP

Pharmacology:

Montelukast sodium is a selective and orally active leukotriene receptor antagonist that inhibits the Cysteinyl leukotriene (CysLT1), receptor.

Levocetirizine is the R-enantiomer of cetirizine. Levocetirizine is an orally active, potent, selective and long acting H1 -histamine receptor antagonist with no anticholinergic activity.

Recent studies have demonstrated that Allergic Rhinitis [AR] when treated concomitantly with an antileukotriene (montelukast) and an antihistamine (levocetirizine), shows significantly better symptom relief compared with the modest improvement of rhinitis symptoms with each of the treatments alone.

Pharmacodynamics:

Montelukast causes inhibition of airway cysteinyl leukotriene receptors as demonstrated by the ability to inhibit bronchoconstriction due to inhaled LTD4 in asthmatics. Doses as low as 5 mg cause substantial blockage of LTD4 –induced bronchoconstriction.

Pharmacokinetics:

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.

Elimination:
The plasma clearance of montelukast averages 45 mL/min in healthy adults. Coupled with estimates of montelukast oral bioavailability, this indicates that montelukast and its metabolites are excreted almost exclusively via the bile.

Levocetirizine:
The pharmacokinetics of levocetirizine is linear with dose and time-independent with low inter-subject variability.

Absorption:
Levocetirizine is rapidly and extensively absorbed following oral administration. Peak plasma concentrations are achieved 0.9h after dosing. Steady state is achieved after two days. Peak concentrations are typically 270 ng/ml and 308 ng/ml following a single and a repeated 5 mg o.d. dose, respectively.

Distribution:
Levocetirizine is 90% bound to plasma proteins.

Biotransformation:
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.

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 half-life in adults is 7.9 + 1.9 hours.
The major route of excretion of levocetirizine and metabolites is via urine.

Indications:

Extrinsic asthma, Seasonal allergic rhinitis, Perennial rhinitis, Chronic Idiopathic Urticaria (CIU), Eczema, Acute allergic reactions & Prophylaxis treatment of asthma , Exercise induced Broncho constriction, Allergic Dermatitis.

Contraindication:

Contraindicated in patients with known hypersensitivity to montelukast sodium, levocetirizine or cetirizine or to any other component of this product. Epimon-L is 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.

Warnings and Precautions:

Monteleukast:

Eosinophilic Conditions In rare cases, patients on therapy with Montelukast may present with systemic eosinophilia, sometimes presenting with clinical features of vasculitis consistent with Churg-Strauss syndrome, a condition, which is often treated with systemic corticosteroid therapy. These events usually, but not always, have been associated with the reduction of oral corticosteroid therapy.

Levocetirizine:

Patients should avoid engaging in hazardous occupation requiring complete mental alertness such as driving or operating machinery when taking levocetirizine. Precaution is recommended with intake of alcohol and in those who are on CNS depressants

Use in special population:

Renal Impairment

As levocetrizine is mainly excreted through urine, dosage adjustment may be required in patients with impaired renal function. Hence this combination should be used with caution in such patients.

Hepatic Impairment

As montelukast is mainly excreted through bile, caution is to be exercised while prescribing this combination in patients with impaired hepatic function.

Pregnancy

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

Lactation

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

Geriatric Use

Montelukast:

No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Levocetirizine:

Clinical studies of levocetirizine for each approved indication did not include sufficient numbers of patients aged 65 years and older to determine whether they respond differently than younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, 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.

Adverse Effects:

Montelukast:

Common side effects include dyspepsia, abdominal pain, rash, dizziness, headache, fatigue, fever, trauma, cough, nasal congestion.

Levocetirizine:

Use of levocetirizine has been associated with somnolence, fatigue, nasopharyngitis, dry mouth, and pharyngitis in subjects 12 years of age and older. Further uncommon incidences of adverse reactions like asthenia or abdominal pain were observed.

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 consistent with the safety profile in adults and pediatric patients.

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 levocetrizine. Should

overdose occur, symptomatic or supportive treatment is recommended. Levocetrizine is not effectively removed by dialysis and dialysis will be ineffective unless a dialyzable agent has been concomitantly ingested.

Dosage:
As directed by the Physician.

For Therapeutic Use.

Route of administration: Oral

SCHEDULE H PRESCRIPITION DRUG-CAUTION
Not to be sold by retail without the prescription of a Registered Medical Practitioner.

Storage: Store at temperature below 25^0C. Protect from light and moisture.
Keep out of reach of children.

Presentation: EPIMON-L available as 10 X 10 Tablet

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