MONKAST LC

Product Name

MONKAST LC Tablet
MONKAST LC Suspension
Name and Strength of Active Ingredient (s)

MONKAST LC Tablet
Each uncoated bilayered tablet contains:

Montelukast Sodium IP equivalent to Montelukast	10 mg
Levocetirizine Hydrochloride	5 mg

MONKASTLC Suspension
Each 5 ml contains: Montelukast Sodium IP equivalent to Montelukast 4 mg
Levocetirizine Dihydrochloride IP 2.5 mg

Product Description
MONKAST LC Tablet and MONKAST LC Suspension are a combination of Montelukast Sodium & Levocetirizine Hydrochloride.

Montelukast is a Leukotriene receptor antagonist (LTRA) used for the maintenance treatment of asthma and to relieve symptoms of seasonal allergies. Montelukast is usually taken once a day with or without food. Montelukast is a CysLT1 antagonist; it blocks the action of Leukotriene D4 (and secondary ligands LTC4 and LTE4) on the cysteinyl Leukotriene receptor CysLT1 in the lungs and bronchial tubes by binding to it. This reduces the bronchoconstriction otherwise caused by the Leukotriene and results in less inflammation.

Levocetirizine is a third-generation non-sedative antihistamine, developed from the second-generation antihistamine cetirizine. It is the L-enantiomer of the Cetirizine racemate. Levocetirizine works by blocking histamine receptors. It does not prevent the actual release of histamine from mast cells, but prevents its binding to its receptors. This in turn prevents the release of other allergy chemicals and increases blood supply to the area, and provides relief from the typical symptoms of hay fever

Pharmacodynamics & Pharmacokinetics

Pharmacodynamics:

Montelukast:

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.

The cysteinyl leukotrienes (LTC4, LTD4, and LTE4) are products of arachidonic acid metabolism and are released from various cells, including mast cells and eosinophils. These eicosanoids bind to cysteinyl Leukotriene (CysLT) receptors. The CysLT type-1 (CysLT1) receptor is found in the human airway (including airway smooth muscle cells and airway macrophages) and on other pro-inflammatory cells (including eosinophils and certain myeloid stem cells). CysLTs have been correlated with the pathophysiology of asthma and allergic rhinitis. In asthma, Leukotriene-mediated effects include airway edema, smooth muscle contraction, and altered cellular activity associated with the inflammatory process. In allergic rhinitis, CysLTs are released from the nasal mucosa after allergen exposure during both early and late-phase reactions and are associated with symptoms of allergic rhinitis. Montelukast is an orally active compound that binds with high affinity and selectivity to the CysLT1 receptor (in preference to other pharmacologically important airway receptors, such as the prostanoid, cholinergic, or β-adrenergic receptor). Montelukast inhibits physiologic actions of LTD4 at the CysLT1 receptor without any agonist activity.

Levocetirizine:

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.

Pharmacokinetics

Montelukast:

Absorption: Montelukast is rapidly absorbed following oral administration. After oral administration of the 10-mg film coated 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 averaged 8 to 11 liters. Distribution of Montelukast across the blood-brain barrier is minimal.

Metabolism: Montelukast is extensively metabolized in liver; CYP3A4 and 2C9 are involved in the metabolism of Montelukast.

Elimination:

The plasma clearance of Montelukast averages 45 ml/min in healthy adults. Montelukast and its metabolites are excreted almost exclusively via the bile. The mean plasma half-life of Montelukast ranged from 2.7 to 5.5 hours in healthy young adults.

Levocetirizine

Levocetirizine exhibited linear pharmacokinetics over the therapeutic dose range in adult healthy subjects.
Absorption: Rapidly and extensively absorbed from the GI tract (oral); peak plasma concentration in 0.9 hours. Cmax is 270 and 308ng/ml after single and repeated once-daily dosing, respectively. Steady state achieved after 2 days.
Distribution: Protein-binding: 91-92%. Vdis approximately 0.4 L/kg.
Metabolism: Less than 14%: Via aromatic oxidation, N- and O-dealkylation and taurine conjugation.
Excretion: Via urine (85.4%), via faeces (12.9%), as metabolites and unchanged drug; 8-9 hours (plasma half-life).

Indications

MONKAST LC Tablet and Suspension are indicated for relief of symptoms of allergic rhinitis (seasonal and perennial).

Recommended Dose and Administration

MONKAST LC Tablets

Adults and adolescents (>15 years):1 tablet once daily

MONKAST LC Suspension

Children (2-5 years): 5 ml Suspension from the given cup once daily.

Contraindication

Hypersensitivity to any component of this product.

Warnings and Precautions
Montelukast:

Acute Asthma:

Montelukastis 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. Patients who have exacerbations of asthma after exercise should have available a short-acting inhaled β-agonist for rescue.
Concomitant Corticosteroid Use:
While the dose of inhaled corticosteroid may be reduced gradually under medical supervision, Montelukast should not be abruptly substituted for inhaled or oral corticosteroids.

Aspirin Sensitivity:

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.

Neuropsychiatric Events:

Neuropsychiatric events have been reported in adult, adolescent, and pediatric patients taking Montelukast. They include agitation, aggressive behavior or hostility, anxiousness, depression, disorientation, dream abnormalities, hallucinations, insomnia, irritability, restlessness, somnambulism, suicidal thinking and behavior (including suicide), and tremor. Patients and prescribers should be alert for neuropsychiatric events. Patients should be instructed to notify their prescriber if these changes occur.

Eosinophilic Conditions:
Patients with asthma 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. Physicians should be alert to eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in their patients. A causal association between Montelukast and these underlying conditions has not been established.

Levocetirizine:

This medicine may cause some people to become dizzy, drowsy, or less alert than they are normally. Make sure you know how you react to this medicine before you drive, use machines, or do anything else that could be dangerous if you are dizzy or not alert. This medicine will add to the effects of alcohol and other CNS depressants (medicines that make you drowsy or less alert). Some examples of CNS depressants are antihistamines or medicine for hay fever, other allergies or colds, sedatives, tranquilizers, or sleeping medicine,

prescription pain medicine or narcotics, medicine for seizures, muscle relaxants, or anesthetics, including some dental anesthetics.
Avoid engaging in hazardous occupations requiring complete mental alertness such as driving or operating machinery when taking Levocetirizine.
Avoid concurrent use of alcohol or other central nervous system depressants with Levocetirizine.
Urinary retention has been reported post-marketing with Levocetirizine Dihydrochloride. Levocetirizine Dihydrochloride should be used with caution in patients with predisposing factors of urinary retention (e.g. spinal cord lesion, prostatic hyperplasia) as Levocetirizine Dihydrochloride may increase the risk of urinary retention. Discontinue Levocetirizine Dihydrochloride if urinary retention occurs.

Interactions With Other Medicaments

Montelukast:

No dose adjustment is needed when Montelukast is co-administered with Theophylline, Prednisone, Prednisolone, Oral contraceptives, Terfenadine, Digoxin, Warfarin, Thyroid hormones, Sedative hypnotics, Non-steroidal anti-inflammatory agents, Benzodiazepines, Decongestants, and Cytochrome P450 (CYP) enzyme inducers.

Levocetirizine:

Products that cause drowsiness including alcohol, other antihistamines (such as Diphenhydramine), drugs for sleep or anxiety (such as Alprazolam, Diazepam, Zolpidem), muscle relaxants, and narcotic pain relievers (such as codeine)
Levocetirizine is very similar to hydroxyzine and cetirizine. Do not use these medications while using Levocetirizine.
This medication may interfere with certain laboratory tests (including allergy skin testing), possibly causing false test results.

Pregnancy and Lactation
There are no adequate and well controlled studies of either montelukast or levocetirizine in pregnant women. Animal studies do not indicate harmful effects with respect to effects on pregnancy or embryonal/ foetal development.

Montelukast:

Pregnancy Category B

There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, Montelukast should be used during pregnancy only if clearly needed.
Teratogenic Effect: No teratogenicity was observed in rats and rabbits at doses approximately 100 and 110 times, respectively, the maximum recommended daily oral dose in adults based on AUCs.

Nursing Mothers:

It is not known if Montelukast is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Montelukast is given to a nursing mother.

Levocetirizine:

Pregnancy Category B
Either animal-reproduction studies have not demonstrated a foetal risk but there are no controlled studies in pregnant women or animal-reproduction studies have shown an adverse effect (other than a decrease in fertility) that was not confirmed in controlled studies in women in the 1st trimester (and there is no evidence of a risk in later trimesters).

Nursing Mothers:
Small occasional doses of Levocetirizine are probably acceptable during breastfeeding. Larger doses or more prolonged use may cause drowsiness and other effects in the infant or decrease the milk supply, particularly in combination with a sympathomimetic such as pseudoephedrine.

Undesirable Effects

Montelukast:

Side effects of Montelukast can include skin rash, mood changes, tremors, headache, stomach pain, heartburn, upset stomach, nausea, diarrhea, tooth pain, tiredness, fever, stuffy nose, sore throat, cough, and hoarseness.

Levocetirizine:

Levocetirizine is usually safe to use and rarely causes serious side effects. However if side effects do occur they may be unexplained rash, hives, itching, and unexplained swelling (especially of the lips, mouth, or throat). Fatigue, somnolence, dry mouth, nasopharyngitis, pyrexia, cough, epistaxis are rare adverse effects of the drug.

Overdose and treatment

Montelukast:

No specific information is available on the treatment of overdosage with Montelukast. In the event of overdose, it is reasonable to employ the usual supportive measures; e.g., remove unabsorbed material from the gastrointestinal tract, employ clinical monitoring, and institute supportive therapy, if required. 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: severe drowsiness. In children, mental/mood changes (such as restlessness, agitation) may occur before drowsiness.

Storage Condition

Protect from direct sunlight & moisture.
Store at dry & cool place.
Keep out of reach of children.

Dosage Forms and packaging available

MONKASTLC tablet : Box containing 10 x 10 tablets in strip pack.
MONKASTLC Suspension : Each bottle contains 50 ml suspension

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