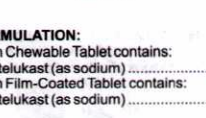
MONTELUKAST

LEUKAST®

5 mg Chewable Tablet
10 mg Film-Coated Tablet
Leukotriene Receptor Antagonist



(montelukast)

FORMULATION:
Each Chewable Tablet contains:
Montelukast (as sodium) ..... 5 mg
Each Film-Coated Tablet contains:
Montelukast (as sodium) ..... 10 mg

PRODUCT DESCRIPTION:
5 mg chewable tablet: Orange, mottled, round, biconvex, orange-flavored uncoated tablet, plain on both sides.
10 mg film-coated tablet: Off-white to cream, barrel-shaped, film-coated tablet, bisected on both sides.

PHARMACOKINETICS:
Special Populations
Hepatic Insufficiency:
No dosage adjustment is required in patients with mild-to-moderate hepatic insufficiency. The pharmacokinetics of montelukast in patients with more severe hepatic impairment or with hepatitis have not been evaluated.
Renal Insufficiency: Since montelukast and its metabolites are not excreted in the urine, the pharmacokinetics of montelukast were not evaluated in patients with renal insufficiency. No dosage adjustment is recommended in these patients.
Adolescents and Pediatric Patients: Pharmacokinetic studies evaluated the systemic exposure of the 4-mg oral granule formulation in pediatric patients 6 to 23 months of age, the 4-mg chewable tablets in pediatric patients 2 to 5 years of age, the 5-mg chewable tablets in pediatric patients 6 to 14 years of age, and the 10-mg film-coated tablets in young adults and adolescent ≥15 years of age.
The plasma concentration profile of montelukast following administration of the 10-mg film-coated tablet is similar in adolescents ≥15 years of age and young adults. The 10-mg film-coated tablet is recommended for use in patients ≥15 years of age.
The mean systemic exposure of the 4-mg chewable tablet in pediatric patients 2 to 5 years of age and the 5-mg chewable tablets in pediatric patients 6 to 14 years of age is similar to the mean systemic exposure of the 10-mg film-coated tablet in adults. The 5-mg chewable tablet should be used in pediatric patients 6 to 14 years of age and the 4-mg chewable tablet should be used in pediatric patients 2 to 5 years of age.
In children 6 to 11 months of age, the systemic exposure to montelukast and the variability of plasma montelukast concentrations were higher than those observed in adults.
Drug-Drug Interactions
Theophylline, Prednisone, and Prednisolone: Montelukast has been administered with other therapies routinely used in the prophylaxis and chronic treatment of asthma with no apparent increase in adverse reactions. In drug-interaction studies, the recommended clinical dose of montelukast did not have clinically important effects on the pharmacokinetics of the following drugs: theophylline, prednisone and prednisolone.
Montelukast at a dose of 10 mg once daily dosed to pharmacokinetic steady state, did not cause clinically significant changes in the kinetics of a single intravenous dose of theophylline [predominantly a cytochrome P450 (CYP) 1A2 substrate]. Montelukast at doses of ≥100 mg daily dosed to pharmacokinetic steady state, did not cause any clinically significant change in plasma profiles of prednisone or prednisolone following administration of either oral prednisone or intravenous prednisolone.
Oral Contraceptives, Terfenadine, Digoxin, and Warfarin: In drug interaction studies, the recommended clinical dose of montelukast did not have clinically important effects on the pharmacokinetics of the following drugs: oral contraceptives (norethindrone 1 mg/ethinyl estradiol 35 mcg), terfenadine, digoxin, and warfarin. Montelukast at doses of ≥100 mg daily dosed to pharmacokinetic steady state did not significantly alter the plasma concentrations of either component of an oral contraceptive containing norethindrone 1 mg/ethinyl estradiol 35 mcg. Montelukast at a dose of 10 mg once daily dosed to pharmacokinetic steady did not change the plasma concentration profile of terfenadine (a substrate of CYP3A4) or fexofenadine, the carboxylated metabolite, and did not prolong the QTc interval following co-administration with terfenadine 60 mg twice daily; did not change the pharmacokinetic profile or urinary excretion of immunoreactive digoxin; did not change the pharmacokinetic profile of warfarin (primarily a substrate of CYP2C9, 3A4 and 1A2) or influence the effect of a single 30-mg oral dose of warfarin on prothrombin time or the International Normalized Ratio (INR).
Thyroid Hormones, Sedative Hypnotics, Non-Steroidal Anti-Inflammatory Agents, Benzodiazepines, and Decongestants: Although additional specific interaction studies were not performed, Montelukast was used concomitantly with a wide range of commonly prescribed drugs in clinical studies without evidence of clinical adverse interactions. These medications include thyroid hormones, sedative hypnotics, non-steroidal anti-inflammatory agents, benzodiazepines, and decongestants.
Cytochrome P450 (CYP) Enzyme Inducers: Phenobarbital, which induces hepatic metabolism, decreased the area under the plasma concentration curve (AUC) of montelukast approximately 40% following a single 10-mg dose of montelukast. No dosage adjustment for montelukast is recommended. It is reasonable to employ appropriate clinical monitoring when potent CYP enzyme inducers, such as phenobarbital or rifampin, are co-administered with montelukast.
Effect of Montelukast on Cytochrome P450 (CYP) Enzymes: Montelukast is not anticipated to alter the metabolism of drugs metabolized by this enzyme (e.g., paclitaxel, rosiglitazone, and repaglinide). Data from a clinical drug-drug interaction study involving montelukast and gemfibrozil (an inhibitor of both CYP 2C8 and 2C9) demonstrated that gemfibrozil, at a therapeutic dose, increased the systemic exposure of montelukast by 4.4-fold. Co-administration of itraconazole, gemfibrozil, and montelukast did not further increase the systemic exposure of montelukast. Based on available clinical experience, no dosage adjustment of montelukast is required upon co-administration with gemfibrozil.

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. In a placebo-controlled, crossover study (n=12), montelukast inhibited early- and late-phase bronchoconstriction due to antigen challenge by 75% and 57%, respectively.

INDICATIONS:
Asthma
Montelukast is indicated for the prophylaxis and chronic treatment of asthma in adults and pediatric patients 12 months of age and older.
Exercise-Induced Bronchoconstriction (EIB)
Montelukast is indicated for prevention of exercise-induced bronchoconstriction (EIB) in patients 6 years of age and older.
Allergic Rhinitis
Montelukast is indicated for the relief of symptoms of seasonal allergic rhinitis in patients 2 years of age and older and perennial allergic rhinitis in patients 6 months of age and older.

DOSAGE AND ADMINISTRATION:
Asthma
Montelukast should be taken once daily in the evening. The following doses are recommended:
For adults and adolescents 15 years of age and older: one 10-mg tablet.
For pediatric patients 6 to 14 years of age: one 5-mg chewable tablet.
For pediatric patients 2 to 5 years of age: one 4-mg chewable tablet.
The pharmacokinetics of montelukast are similar whether dosed in the morning or evening. Efficacy has been demonstrated for asthma when montelukast was administered in the evening without regard to time of food ingestion.

Exercise-Induced Bronchoconstriction (EIB)
For prevention of EIB, a single dose of Montelukast should be taken at least 2 hours before exercise.
The following doses are recommended:
For adults and adolescents 15 years of age and older: one 10-mg tablet.
For pediatric patients 6 to 14 years of age: one 5-mg chewable tablet.
An additional dose of Montelukast should not be taken within 24 hours of previous dose. Patients already taking Montelukast daily for another indication (including chronic asthma) should not take an additional dose to prevent EIB. All patients should have available for rescue a short-acting β-agonist.
Safety and efficacy in patients younger than 6 years of age have not been established. Daily administration of Montelukast for the chronic treatment of asthma has not been established to prevent acute episodes of EIB.

Allergic Rhinitis
For allergic rhinitis, Montelukast should be taken once daily. Efficacy was demonstrated for seasonal allergic rhinitis when montelukast was administered in the morning or the evening without regard to time of food ingestion. The time of administration may be individualized to suit patient needs.
The following doses for the treatment of symptoms of **seasonal allergic rhinitis** are recommended:
For adults and adolescents 15 years of age and older: one 10-mg tablet.
For pediatric patients 6 to 14 years of age: one 5-mg chewable tablet.
For pediatric patients 2 to 5 years of age: one 4-mg chewable tablet.
Safety and effectiveness in pediatric patients younger than 2 years of age with seasonal allergic rhinitis have not been established.

The following doses for the treatment of symptoms of **perennial allergic rhinitis** are recommended:
For adults and adolescents 15 years of age and older: one 10-mg tablet.
For pediatric patients 6 to 14 years of age: one 5-mg chewable tablet.
For pediatric patients 2 to 5 years of age: one 4-mg chewable tablet.
Safety and effectiveness in pediatric patients younger than 6 months of age with perennial allergic rhinitis have not been established.

Asthma and Allergic Rhinitis
Patients with both asthma and allergic rhinitis should take only one montelukast dose daily in the evening.

Montelukast chewable tablets should be taken by mouth, chewed and swallowed. Montelukast film-coated tablets should be taken by mouth and swallowed whole.

CONTRAINDICATIONS:
It is contraindicated in patients with hepatic impairment or cirrhosis and hypersensitivity to any component of the product.

WARNINGS AND PRECAUTIONS:
Acute Asthma
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. Patients who have exacerbations of asthma after exercise should have available for rescue a short-acting inhaled β-agonist.

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. Post-marketing reports with Montelukast use include agitation, aggressive behavior or hostility, anxiousness, depression, disorientation, disturbance in attention, dream abnormalities, hallucinations, insomnia, irritability, memory impairment, restlessness, somnambulism, suicidal thinking and behavior (including suicide), and tremor. The clinical details of some post-marketing reports involving Montelukast appear consistent with a drug-induced effect.

Patients and prescribers should be alert for neuropsychiatric events. Patients should be instructed to notify their prescribers if these changes occur. Prescribers should carefully evaluate the risks and benefits of continuing treatment with Montelukast if such event occur.

Eosinophilic Conditions
Patients with asthma on therapy with Montelukast may present with systematic 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.

Phenylketonuria
Phenylketonuric patients should be informed that the 4-mg and 5-mg chewable tablets contain phenylalanine (a component of aspartame), 0.674 and 0.842 mg per 4-mg and 5-mg chewable tablet, respectively.

ADVERSE REACTIONS:
Most common adverse reactions (incidence >5% and greater than placebo listed in descending order of frequency): upper respiratory infection, fever, headache, pharyngitis, cough, abdominal paln, diarrhea, otitis media, influenza, rhinorrhea, sinusitis, otitis.

DRUG INTERACTIONS:
No dose adjustment is needed when montelukast is co-administered with theophylline, prednisone, prednisolone, oral contraceptives, terfenadine, digoxin, warfarin, gemfibrozil, itraconazole, thyroid hormones, sedative hypnotics, non-steroidal anti-inflammatory agents, benzodiazepines, decongestants and Cytochrome P450 (CYP) enzyme inducers.

USE IN SPECIFIC POPULATIONS:
Pregnancy
There are no adequate and well-controlled studies in pregnant women.
Montelukast should be used during pregnancy only if clearly needed.
Nursing Mothers
Studies in rats have shown that montelukast is excreted in milk. 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.
Pediatric Use
Safety and efficacy of montelukast have been established in adequate and well-controlled studies in pediatric patients with asthma 6 to 14 years of age. Safety and efficacy profiles in this age group are similar to those seen in adults.
The efficacy of Montelukast for the treatment of seasonal allergic rhinitis in pediatric patients 2 to 14 years of age and for the treatment of perennial allergic rhinitis in pediatric patients 6 months to 14 years of age is supported by extrapolation from the demonstrated efficacy in patients 15 years of age and older with allergic rhinitis as well as the assumption that the disease course, pathophysiology and the drug's effect are substantially similar among these populations.
The safety of Montelukast 4-mg chewable tablets in pediatric patients 2 to 5 years of age with asthma has been demonstrated by adequate and well-controlled data. Efficacy of Montelukast in this age group is extrapolated from the demonstrated efficacy in patients 6 years of age and older with asthma and is based on similar pharmacokinetic data, as well as the assumption that the disease course, pathophysiology and the drug's effect are substantially similar among these populations.
Geriatric Use
The plasma half-life of montelukast is slightly longer in the elderly. No dosage adjustment in the elderly is required.
Hepatic Insufficiency
No dosage adjustment is required in patients with mild-to-moderate hepatic insufficiency.
Renal Insufficiency
No dosage adjustment is recommended in patients with renal insufficiency.

OVERDOSAGE:
No specific information is available on the treatment of overdose with montelukast. In chronic asthma studies, montelukast has been administered at doses up to 200 mg/day to patients for 22 weeks and in short term studies, up to 900 mg/day to patients for approximately one week without clinically important adverse experiences. There were no adverse experiences in the majority of overdosage 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 dialysable by peritoneal or haemodialysis.

CAUTION:
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

ADR REPORTING:
For suspected adverse drug reaction, report to FDA: www.fda.gov.ph
Patient should seek medical attention immediately at the first sign of any adverse drug reaction.

AVAILABILITY:
5 mg Chewable Tablet: Alu-Alu Blister Pack x 10's (Box of 30's)
10 mg Film-coated Tablet: Alu-Alu Blister Pack x 10's (Box of 30's)

REGISTRATION NUMBER:
5 mg Chewable Tablet: DRP-6840-03
10 mg Film-coated Tablet: DRP-6741-03

STORE AT TEMPERATURES NOT EXCEEDING 30°C.

DATE OF FIRST AUTHORIZATION:
5 mg Chewable Tablet: 03 March 2022
10 mg Film-coated Tablet: 11 March 2022

DATE OF REVISION:
March 2022

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Manufactured by:
HIZON LABORATORIES, INC.
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