

ABRIDGED PRESCRIBING INFORMATION FOR MEDICAL PROFESSIONALS

Juvexy

(Montelukast Sodium USP)

جوویکسی
(مونٹیلوکاست سوڈیم یو ایس پی)

COMPOSITION

Each **Juvexy** 5mg chewable tablet contains Montelukast Sodium equivalent to Montelukast 5mg.
Each **Juvexy** 10mg film coated tablet contains Montelukast Sodium equivalent to Montelukast 10mg.
"Product contains Lactose"

CLINICAL PHARMACOLOGY

The cysteinyl leukotrienes (LTC₄, LTD₄, 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. Montelukast inhibits physiologic actions of LTD₄ at the CysLT₁ receptor without any agonist activity.

PHARMACOKINETICS

Absorption: Montelukast is rapidly absorbed following oral administration. After administration of the 10mg film-coated tablet to fasted adults the mean peak Montelukast plasma concentration (C_{max}) is achieved in 3 to 4 hours (T_{max}). The mean oral bioavailability is 64%. The oral bioavailability and C_{max} are not influenced by a standard meal in the morning.

For the 5mg chewable tablet the mean C_{max} is achieved in 2 to 2.5 hours after administration to adults in the fasted state. The mean oral bioavailability is 73% in the fasted state versus 63% when administered with a standard meal in the morning.

The safety and efficacy of Montelukast in patients with asthma were demonstrated in clinical trials in which the 10mg film-coated tablet and 5mg chewable tablet formulations were administered in the evening without regard to the time of food. The safety and efficacy of Montelukast in patients with seasonal allergic rhinitis were demonstrated in clinical trials in which the 10mg film-coated tablet was administered in the morning or evening without regard to the time of food ingestion.

Distribution: Montelukast is more than 99% bound to plasma proteins.

Metabolism: Montelukast is extensively metabolized. CYP3A4, 2C8, and 2C9 are involved in the metabolism of Montelukast. 2C8 appears to play a major role in the metabolism of Montelukast.

Elimination: Montelukast and its metabolites are excreted almost exclusively via the bile.

In several studies, the mean plasma half-life of Montelukast ranged from 2.7 to 5.5 hours in healthy young adults. The pharmacokinetics of Montelukast are nearly linear for oral doses up to 50mg. During once-daily dosing with 10mg Montelukast there is little accumulation of the parent drug in plasma (14%).

INDICATIONS

Asthma: **Juvexy** 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): **Juvexy** is indicated for prevention of exercise-induced bronchoconstriction (EIB) in patients 6 years of age and older.

Allergic Rhinitis: **Juvexy** 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: **Juvexy** should be taken once daily in the evening. The following doses are recommended:

- - For adults and adolescents 15 years of age and older: one 10mg tablet.
- - For pediatric patients 6 to 14 years of age: one 5mg chewable tablet.

There have been no clinical trials in patients with asthma to evaluate the relative efficacy of morning versus evening dosing. 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 **Juvexy** 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 10mg tablet.
- - For pediatric patients 6 to 14 years of age: one 5mg chewable tablet.

An additional dose of **Juvexy** should not be taken within 24 hours of a previous dose. Patients already taking **Juvexy** 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

Juvexy for the chronic treatment of asthma has not been established to prevent acute episodes of EIB.

Allergic Rhinitis: For allergic rhinitis, **Juvexy** 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 10mg tablet.
- - For pediatric patients 6 to 14 years of age: one 5mg chewable tablet.

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 10mg tablet.
- - For pediatric patients 6 to 14 years of age: one 5mg chewable tablet.

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

ADVERSE EFFECTS

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

WARNINGS AND PRECAUTION

Acute asthma: Montelukast is not indicated for use in the reversal of bronchospasm in acute asthma attacks including status asthmaticus.

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.

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), tic and tremor. The clinical details of some post-marketing reports involving Montelukast appear consistent with a drug-induced effect.

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 have been sometimes 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 5mg chewable tablets contain phenylalanine (a component of aspartame).

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: 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.

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 given to a nursing mother.

Pediatric Use: The safety and effectiveness in pediatric patients below the age of 12 months with asthma, 6 months with perennial allergic rhinitis, 2 years with seasonal allergic rhinitis and 6 years with exercise-induced bronchoconstriction have not been established.

Geriatric Use: 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.

CONTRAINDICATIONS

Hypersensitivity to any component of this product.

OVERDOSAGE

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.

PRESENTATION

Juvexy Tablet 5mg- : 2X7's/pack.

Juvexy Tablet 10mg : 2X7's/pack.

DOSAGE

As directed by the physician.

INSTRUCTIONS

Store below 30°C.

Protect from sunlight and moisture

Keep out of reach of children

Detailed prescribing information is available on request.

 Manufactured by:
AsianContinental (Pvt.) Ltd.
D-32, S.I.T.E. II, Super Highway,
Karachi-Pakistan.



LFT/036/01