Montelukast sodium

Kastair®

10 mg F ilm-coated Tablet

Leuk otriene Receptor Antagonist

FORMULATION

Each film-coated tablet contains:

Montelukast (as sodium), USP ..... 10 mg

PRODUCT DESCRIPTION

Montelukast (Kastair) 10 mg film-coated tablet contains 10.4 mg montelukast sodium which is equivalent to 10 mg of montelukast. It is a white, round, convex, film-coated tablet.

PHARMACODYNAMICS

Montelukast is a selective leukotriene-receptor antagonist that specifically inhibits the cysteinyl leukotriene $CysLT_1$ receptor. The cysteinyl leukotrienes [CysLT (LTC_4, LTD_4, and LTE_4)] are potent inflammatory eicosanoids released from various cells including mast cells and eosinophils that bind to CysLT receptors. The CysLT type 1 ($CysLT_1$) receptor is present in the human airway (including airway smooth muscle cells and airway macrophages). CysLTs contribute to the pathophysiology of asthma and allergic rhinitis. In asthma, CysLTs are found to increase mucus secretion, vascular permeability, and bronchoconstriction. In allergic rhinitis, CysLTs are released from the nasal mucosa after exposure to allergens and are associated with symptoms of allergic rhinitis. Montelukast inhibits bronchoconstriction and reduces inflammation of the nasal mucosa induced by exposure to known precipitants.

PHARMACOKINETICS

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

In two pharmacokinetic trials in asthmatic pediatric patients aged 2 to 5 years and 6 to 14 years, peak plasma concentrations of montelukast 4 mg (471 ± 65 ng/mL) and 5 mg (495 ± 129 ng/mL) as chewable tablets are attained within 2.07 ± 0.3 hours and 2.6 ± 1 hours, respectively.

In a pharmacokinetic trial in asthmatic pediatric patients 6 to 24 months old, peak plasma concentrations (514.4 ng/mL) of montelukast 4 mg as oral granules are attained within 2.2 hours.

Montelukast's steady state volume of distribution is 8 to 11 liters. Plasma protein binding is more than 99%.

Montelukast is extensively metabolized in the liver by cytochrome P450 isoenzymes CYP2C8, CYP3A4, and CYP2C9, and is excreted principally in the feces via the bile.

INDICATIONS

- For the relief of symptoms of allergic rhinitis.
- For the prophylaxis and chronic treatment of asthma.

  Montelukast is effective alone or when used together with other agents for the management of chronic asthma. Montelukast may be used concomitantly with inhaled corticosteroids to control asthma and to reduce the dose of inhaled corticosteroids required by patients with moderate to severe asthma.
- For the prevention of exercise-induced bronchoconstriction.

DOSAGE AND ADMINISTRATION

Adults and children 15 years and older: Orally, 1 tablet once daily. Or as prescribed by a physician.

Directions for Use:

- **For patients with allergic rhinitis:**
  - The time of administration may be individualized to suit patient needs.
  - Take everyday, at about the same time each day, or, as prescribed by a physician.
- **For patients with asthma with or without coexisting allergic rhinitis:**
  - The dose should be taken in the evening to obtain simultaneous peak plasma concentration and peak airway reactivity in the morning.
  - Take at regular intervals (i.e., daily) to be therapeutically effective, even if the patient has no asthma symptoms, or, as prescribed by a physician.
- **For the prevention of exercise-induced bronchoconstriction:**
  - Take at least 2 hours before exercise.
  - Do not take an additional dose within 24 hours of a previous dose.
  - Do not take an additional dose to prevent exercise-induced bronchoconstriction if the patient is taking Montelukast daily for chronic asthma or allergic rhinitis. Consult a physician about treatment of exercise-induced bronchoconstriction.
- May be taken with or without food.

CONTRAINDICATION

- Hypersensitivity to montelukast or other ingredients in the product

WARNINGS AND PRECAUTIONS

Acute Asthma

Montelukast is not indicated for the treatment of acute asthma attacks, including status asthmaticus. Patients should have appropriate short-acting inhaled beta-agonist medication available to treat asthma exacerbations. However, therapy with montelukast can be continued during acute asthmatic attacks.
Patients taking montelukast should not discontinue or reduce the dosage of other medicines for asthma unless directed by a physician.

Aspirin Sensitivity

Avoid aspirin or nonsteroidal anti-inflammatory drugs (NSAIDs) while taking montelukast in patients with known aspirin sensitivity.

Neuropsychiatric Events

Neuropsychiatric events have been reported in patients taking montelukast. These postmarketing reports 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. Patients should inform their physician if these changes occur.

Eosinophilic Conditions

Eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy consistent with Churg-Strauss syndrome have been reported in patients with asthma being treated with montelukast.

Effects on Ability to Drive and Use Machines

Montelukast is not expected to affect patients' physical coordination (e.g., driving, operating machinery). However, in very rare cases, individuals have reported dizziness or drowsiness.

INTERACTIONS WITH OTHER MEDICAMENTS

Montelukast may be administered with other drugs routinely used in the prophylaxis and chronic treatment of asthma and in the treatment of allergic rhinitis.

No clinically important effects were observed when montelukast was concomitantly administered with: benzodiazepines, decongestants, digoxin, nonsteroidal anti-inflammatory agents, oral contraceptives (ethinyl estradiol with norethindrone), prednisone, prednisolone, sedative hypnotics, terfenadine, theophylline, thyroid hormones, and warfarin.

Montelukast-treated patients with known aspirin sensitivity should continue to avoid aspirin and other NSAIDs. Although montelukast can improve airway function in asthmatics with aspirin sensitivity, the drug has not been shown to shorten the bronchoconstrictor response to aspirin or other NSAIDs in such patients.

The area under the plasma concentration-time curve of montelukast is decreased by approximately 40% with coadministration of phenobarbital. No dosage adjustment for montelukast is recommended. However, appropriate clinical monitoring should be initiated with concomitant administration of montelukast with potent cytochrome P450 enzyme inducers such as phenobarbital, phenytoin, and rifampicin.

STATEMENT ON USAGE FOR HIGH RISK GROUPS

Pregnancy: Pregnancy Category B. No adequate and well-controlled studies in pregnant women are available for montelukast. Montelukast should only be used during pregnancy when clearly needed.

There have been reports of congenital limb defects in children of patients treated with montelukast. Some of the mothers, however, were receiving various medications in the course of their pregnancies. Since there is no consistent pattern of congenital abnormality development, a relationship between the use of montelukast and the development of congenital anomalies cannot be established.

Lactation: It is not known if montelukast is excreted in human milk. Therefore, do not administer to breastfeeding women unless, in the opinion of a physician, the potential benefit of the drug justifies the possible risk to the infant.

Children: The safety and efficacy of montelukast in infants younger than 6 months old have not been established.

Elderly: There were no age-related differences in the efficacy or safety profile of montelukast, but greater sensitivity of some older individuals cannot be ruled out.

UNDESIRABLE EFFECTS

The most frequently reported adverse effects with montelukast include upper respiratory infection, fever, headache, pharyngitis, cough, abdominal pain, diarrhea, otitis media, influenza, rhinorrhea, sinusitis, and otitis.

Infection and infestations: Pyuria, skin infection, tooth infection, varicella, viral infection
Blood and lymphatic system disorders: Increased bleeding tendency, thrombocytopenia
Immune system disorders: Hypersensitivity reactions including anaphylaxis
Psychiatric disorders: Agitation including 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, tremor
Nervous system disorders: Dizziness, drowsiness, hyperkinesia, hypoesthesia, paresthesia, seizure
Eye disorders: Conjunctivitis, myopia
Ear and labyrinth disorders: Ear pain
Cardiac disorders: Palpitations
Vascular disorders: Vasculitis
Respiratory, thoracic and mediastinal disorders: Acute bronchitis, asthma, Churg-Strauss syndrome, epistaxis, laryngitis, nasal congestion, pneumonia, pulmonary eosinophilia, rhinitis/infective rhinitis, sinus headache, tonsillitis, wheezing
Gastrointestinal disorders: Dry mouth, dyspepsia, gastroenteritis/infectious gastroenteritis, nausea, pancreatitis, vomiting
Hepatobiliary disorders: Hepatic infiltration eosinophilic, hepatitis cholestatic, hepatocellular liver injury, mixed-pattern liver injury, increased alanine aminotransferase (ALT) and aspartate aminotransferase (AST)
Skin and subcutaneous tissue disorders: Angioedema, atopic dermatitis, bruising, dermatitis, eczema, erythema multiforme, erythema nodosum, Stevens-Johnson syndrome, pruritus, rash, toxic epidermal necrolysis, urticaria
Musculoskeletal and connective tissue disorders: Arthralgia, myalgia including muscle cramps
Renal and urinary disorders: Enuresis in children
General disorders and administration site conditions: Asthenia, dental pain, edema, fatigue, leg pain, malaise, thirst
Injury, poisoning and procedural complications: Trauma

OVERDOSE AND TREATMENT

Montelukast given in doses up to 200 mg/day for 22 weeks and up to 900 mg/day for approximately a week to adult patients showed no clinically important adverse reactions. Acute overdosages in adults and children given montelukast with a dose as high as 1000 mg have been reported. There were no adverse effects reported in majority of overdosage reports. The most frequent adverse effects observed were abdominal pain, headache, psychomotor hyperactivity, somnolence, thirst, vomiting, and less frequently convulsion.

There is no specific information available on the treatment of overdosage with montelukast. In case of overdose, institute supportive and symptomatic therapy, i.e., remove unabsorbed material from the gastrointestinal tract. There is no adequate evidence to support the use of dialysis in the treatment of montelukast overdose.

STORAGE CONDITION

Keep the product out of sight and reach of children.
Store at temperatures not exceeding 30°C.

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

ADVERSE DRUG REACTION REPORTING STATEMENT

For suspected adverse drug reaction, seek medical attention immediately and report to the FDA at www.fda.gov.ph **AND** Unilab at (+632) 858-1000 or productsafety@unilab.com.ph. By reporting undesirable effects, you can help provide more information on the safety of this medicine.

AVAILABILITY: Kastair 10 mg Tablet - Boxes of 28's (in flex foil)

Manufactured by AMHERST LABORATORIES, INC.
UNILAB Pharma Campus, Barangay Mamplasan, Biñan, Laguna, Philippines
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