MONTair®

(Montelukast)

Tablet

مونٹ ائیر

COMPOSITION

Each film coated tablet contains:
Montelukast Sodium equivalent to
Montelukast (USP) ..... 10 mg.

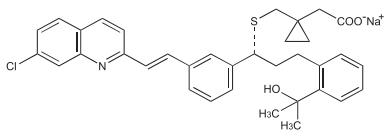
Product Specs.: USP

WARNING:

- Monitor all patients treated with montelukast for neuropsychiatric symptoms with and without pre-existing psychiatric disease.
- Patient should stop taking montelukast and contact a health care professional immediately if changes in behavior or new neuropsychiatric symptoms, suicidal thoughts or behavior occur.

DESCRIPTION:

Montair (Montelukast sodium) is a leukotriene receptor antagonist (LTRA) used for the maintenance and treatment of asthma and to relieve symptoms of seasonal allergic rhinitis. Montelukast sodium is described chemically as [R-(E)]-1-[[[1-[3-[2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio]methyl] cyclopropaneacetic acid, monosodium salt. The molecular formula is $C_{35}H_{35}ClNNaO_3S$ and the structural formula is.



CLINICAL PHARMACOLOGY:

Mechanism of Action:

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. 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 10 mg 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. The mean oral bioavailability is 73% in the fasted state versus 63% when administered with a standard meal in the morning. A high fat meal in the morning did not affect the AUC of montelukast oral granules; however, the meal decreased C_{max} by 35% and prolonged T_{max} from 2.3 ± 1.0 hour to 6.4 ± 2.9 hours.

Distribution: Montelukast is more than 99% bound to plasma proteins. The steady state volume of distribution of montelukast averages 8 to 11 liters. Montelukast sodium is extensively metabolized in the liver by cytochrome P450 isoenzymes CYP3A4, CYP2A6 and CYP2C9. Therapeutic plasm concentrations of montelukast sodium do not inhibit cytochromes P450 3A4, 2C9, 1A2, 2A6, 2C19, or 2D6.

Metabolism: 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 ranges from 2.7 to 5.5 hours in young adults. The pharmacokinetics of montelukast are nearly linear for oral doses up to 50 mg. During once-daily dosing with 10 mg montelukast, there is little accumulation of the parent drug in plasma (14%).

Excretion: 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 ranges from 2.7 to 5.5 hours in young adults. The pharmacokinetics of montelukast are nearly linear for oral doses up to 50 mg. During once-daily dosing with 10 mg montelukast, there is little accumulation of the parent drug in plasma (14%).

Special Populations:

Hepatic insufficiency: Patients with mild-to-moderate hepatic insufficiency and clinical evidence of cirrhosis has evidence of decreased metabolism and prolonged elimination half-life of montelukast sodium resulting in 41% higher mean montelukast sodium area under the plasma concentration curve (AUC) following a single 10mg dose. The mean elimination half-life is 7.4 hours. No dosage adjustment is required in patients with mild-to-moderate hepatic insufficiency.

THERAPEUTIC INDICATIONS:

Asthma: Montair is indicated for the prophylaxis and chronic treatment of asthma in adults and pediatric patients 15 years of age and older.

Exercise-Induced bronchoconstriction: Montair is indicated for prevention of exercise-induced bronchoconstriction (EIB) in patients 15 years of age and older.

Allergic rhinitis: Montair is indicated for the relief of symptoms of seasonal allergic rhinitis in patients 15 years of age and older and perennial allergic rhinitis in patients 15 years of age and older.

DOSAGE AND ADMINISTRATION:

Asthma: Montair 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 film coated tablet.

The pharmacokinetics of montelukast are similar whether dosed in the morning or evening.

Exercise-Induced bronchoconstriction (EIB): In patients 15 Years of Age and Older-For prevention of EIB, a single 10mg dose of Montair should be taken at least 2 hours before exercise. An additional dose of Montair should not be taken within 24 hours of a previous dose. Patients already taking Montair 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 -agonist.

Allergic rhinitis: For allergic rhinitis, Montair should be taken once daily. Montelukast should be administered in the morning or the evening without regard to time of food ingestion.

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 film coated tablet.

Perennial allergic rhinitis:

The following dose for the treatment of symptoms of perennial allergic rhinitis is:

For adults and adolescents 15 years of age and older. One 10 mg film coated tablet.

Asthma and allergic rhinitis: Patients with both asthma and allergic rhinitis should take only one Montair dose daily in the evening.

ADVERSE REACTIONS:

Montelukast sodium is generally well tolerated. However, following are the adverse effects reported which usually were mild and did not require discontinuation of therapy.

- Increased bleeding tendency.
- Hypersensitivity reactions including anaphylaxis, hepatic eosinophilic infiltration.
- Dream abnormalities including nightmares, hallucinations, insomnia, irritability, anxiety, restlessness, agitation including aggressive behaviour, tremor, depression, suicidal thinking and behaviour (suicidality) in very rare cases.
- Dizziness, drowsiness, paraesthesia/ hypoesthesia, seizure.
- Palpitations.
- Epistaxis.
- Diarrhoea, dry mouth, dyspepsia, nausea, vomiting.
- Elevated levels of serum transaminases (ALT, AST), cholestatic hepatitis.
- Angioedema, bruising, urticaria, pruritus, rash, erythema nodosum.
- Arthralgia, myalgia including muscle cramps.
- Asthenia/fatigue, malaise, oedema, pyrexia.

CONTRAINDICATIONS:

Montelukast sodium is contraindicated in a patient who has shown hypersensitivity to the drug or any of its components. Montelukast sodium is not indicated for use in acute asthma attacks including status asthmaticus.

WARNINGS AND PRECAUTIONS:

Acute asthma: Montair 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 Montair 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-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: Have been reported in adult, adolescent, and pediatric patients taking Montelukast sodium. Patients and prescribers should be alert for neuropsychiatric events. Patients should be instructed to notify their prescriber if these changes occur. Prescribers should carefully evaluate the risks and benefits of continuing treatment with montelukast sodium if such events occur. Patients/ parents/care giver are advised that patient should stop taking montelukast and notify a health care professional right away if anyone taking the medicine experiences behavior or mood-related changes while taking the medicine.

These may include:

• agitation, including aggressive behavior or hostility • attention problems • bad or vivid dreams • depression • disorientation or confusion • feeling anxious • hallucinations (seeing or hearing • things that are not really there) • irritability	• memory problems • obsessive-compulsive symptoms • restlessness • sleepwalking • stuttering • suicidal thoughts and actions • tremor or shakiness • trouble sleeping • uncontrolled muscle movements

Eosinophilic conditions: Patients with asthma on therapy with Montelukast sodium 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.

Phenylketonuria: Phenylketonuric patients should be informed that the 4mg and 5mg chewable tablets contain phenylalanine (a component of aspartame).

Pregnancy: Montelukast sodium should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing mothers: It is not known if montelukast sodium is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Montair is given to a nursing mother.

DRUG INTERACTIONS:

The area under the plasma concentration curve (AUC) for montelukast is decreased approximately 40% with co-administration of phenobarbital. Since montelukast is metabolised by CYP 3A4, caution should be exercised, particularly in children, when montelukast is co-administered with inducers of CYP 3A4, such as phenytoin, phenobarbital and rifampicin.

INSTRUCTIONS:

– Store below 30°C.
– Protect from heat, sunlight & moisture.
– Keep out of the reach of children.
– To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:

Montair Tablet 10 mg : Pack of 1 x 14 tablets.

ہدایات:

۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

Manufactured by:
CCL Pharmaceuticals (Pvt.) Ltd.
Plot No. 710, Sundar Industrial Estate, Raiwind Road Lahore, Pakistan.

FOR FURTHER INFORMATION PLEASE CONTACT:

CCL

Manufactured for:
CCL Pharmaceuticals (Pvt.) Ltd.
62 Industrial Estate, Kot Lakhpat, Lahore, Pakistan.