Airmont®

(USP Specification)

Montelukast

(USP Specification)

5mg chewable & **10**mg Film Coated Tablets

COMPOSITION

AIRMONT 5mg Tablets: Each chewable tablet contains:
Montelukast as sodium 5mg
(USP Specification)
AIRMONT 10mg Tablets: Each film coated tablet contains:
Montelukast as sodium 10mg
(USP Specification)
Dissolution Test 2

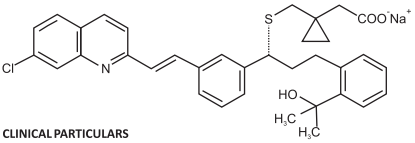
DESCRIPTION

Montelukast sodium, the active ingredient in AIRMONT, is a selective and orally active leukotriene receptor antagonist that inhibits the cysteinyl leukotriene $CysLT_1$ receptor.

Montelukast sodium is described chemically as [R-(E)]-1-[[1-[3-[2-(7-chloro-2-uinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl] propyl]thio]methyl]cyclopropaneacetic acid, monosodium salt.

The empirical formula is $C_{35}H_{35}ClNNaO_3S$, and its molecular weight is 608.18.

The structural formula is:



CLINICAL PARTICULARS

Therapeutic Indications:

AIRMONT (Montelukast) is a leukotriene receptor antagonist indicated for prophylaxis and chronic treatment of asthma in patients 12 months of age and older, acute prevention of exercise-induced bronchoconstriction (EIB) in patients 6 years of age and older and relief of symptoms of allergic rhinitis (AR): seasonal allergic rhinitis (SAR) in patients 2 years of age and older, and perennial allergic rhinitis (PAR) in patients 6 months of age and older.

Dosage and administration:

Asthma: **AIRMONT** (Montelukast) should be taken once daily in the evening. The following doses are recommended:
For pediatric patients 6 to 14 years of age: one 5mg chewable tablet.
For adults and adolescents 15 years of age and older: one 10mg tablet.
Safety and effectiveness in pediatric patients less than 12 months of age with asthma have not been established. There have been no clinical trials in patients with asthma to evaluate the relative efficacy of morning versus evening dosing. The pharmacokinetics of **AIRMONT** (Montelukast) are similar whether dosed in the morning or evening. Efficacy has been demonstrated for asthma when **AIRMONT** (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 **AIRMONT** (Montelukast) should be taken at least 2 hours before exercise. The following doses are recommended:
For pediatric patients 6 to 14 years of age: one 5mg chewable tablet.
For adults and adolescents 15 years of age and older: one 10mg tablet.
An additional dose of **AIRMONT** (Montelukast) should not be taken within 24 hours of a previous dose. Patients already taking **AIRMONT** (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 **AIRMONT** (Montelukast) for the chronic treatment of asthma has not been established to prevent acute episodes of EIB.

Allergic Rhinitis:
For allergic rhinitis, **AIRMONT** (Montelukast) should be taken once daily. Efficacy was demonstrated for seasonal allergic rhinitis when **AIRMONT** (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 pediatric patients 6 to 14 years of age: one 5mg chewable tablet.
For adults and adolescents 15 years of age and older: one 10mg 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 pediatric patients 6 to 14 years of age: one 5mg chewable tablet.
For adults and adolescents 15 years of age and older: one 10mg 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 **AIRMONT** (Montelukast) dose daily in the evening.

Contraindications:

Hypersensitivity to any component of this product

Precautions:

Acute Asthma: **AIRMONT** (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 **AIRMONT** (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, **AIRMONT** (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 **AIRMONT** (Montelukast). Although **AIRMONT** (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 **AIRMONT** (Montelukast). Post-marketing reports with **AIRMONT** (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 **AIRMONT** (Montelukast) appear consistent with a drug-induced effect.
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 **AIRMONT** (Montelukast) if such events occur.

Eosinophilic Conditions: Patients with asthma on therapy with **AIRMONT** (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 **AIRMONT** (Montelukast) and these underlying conditions has not been established.

Drug Interactions:

No dose adjustment is needed when **AIRMONT** (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.

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, **AIRMONT** (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.

Lactation:

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 **AIRMONT** (Montelukast) is given to a nursing mother.

Pediatric Use:

Safety and efficacy of **AIRMONT** (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 **AIRMONT** (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 **AIRMONT** (Montelukast) 5-mg chewable tablets in pediatric patients aged 2 to 14 years with allergic rhinitis is supported by data from studies conducted in pediatric patients aged 2 to 14 years with asthma. A safety study in pediatric patients 2 to 14 years of age with seasonal allergic rhinitis demonstrated a similar safety profile.
The safety and effectiveness in pediatric patients below the age of 12 months with asthma, 6 months with perennial allergic rhinitis, and 6 years with exercise-induced bronchoconstriction have not been established.

Geriatric Use:

Of the total number of subjects in clinical studies of montelukast, 3.5% were 65 years of age and over, and 0.4% were 75 years of age and over. No overall differences in safety or effectiveness were observed during clinical studies on elderly population.

Adverse Reactions:

The following adverse reactions have been identified during post-approval use of **AIRMONT** (Montelukast). Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.
Blood and lymphatic system disorders: increased bleeding tendency, thrombocytopenia.

Immune system disorders: hypersensitivity reactions including anaphylaxis, hepatic eosinophilic infiltration.
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, and tremor.
Nervous system disorders: drowsiness, paraesthesia/hypoesthesia, seizures.
Cardiac disorders: palpitations.
Respiratory, thoracic and mediastinal disorders: epistaxis, pulmonary eosinophilia.
Gastrointestinal disorders: diarrhea, dyspepsia, nausea, pancreatitis, vomiting.
Hepatobiliary disorders: Cases of cholestatic hepatitis, hepatocellular liver-injury, and mixed-pattern liver injury have been reported in patients treated with **AIRMONT** (Montelukast). Most of these occurred in combination with other confounding factors, such as use of other medications, or when **AIRMONT** (Montelukast) was administered to patients who had underlying potential for liver disease such as alcohol use or other forms of hepatitis.
Skin and subcutaneous tissue disorders: angioedema, bruising, erythema multiforme, erythema nodosum, pruritus, Stevens-Johnson syndrome/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: edema.
Patients with asthma on therapy with **AIRMONT** (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.

CLINICAL PHARMACOLOGY
Mechanism of Action
The cysteinyl leukotrienes (LTC_4, LTD_4, LTE_4) 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 ($CysLT_1$) 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 earlyand 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 $CysLT_1$ receptor (in preference to other pharmacologically important airway receptors, such as the prostanoid, cholinergic, or -adrenergic receptor). Montelukast inhibits physiologic actions of LTD_4 at the $CysLT_1$ receptor without any agonist activity.
Pharmacodynamics
Montelukast causes inhibition of airway cysteinyl leukotriene receptors as demonstrated by the ability to inhibit bronchoconstriction due to inhaled LTD_4 in asthmatics. Doses as low as 5mg cause substantial blockage of LTD_4-induced bronchoconstriction. In a placebo-controlled, crossover study (n=12), **AIRMONT** (Montelukast) inhibited early- and late-phase bronchoconstriction due to antigen challenge by 75% and 57%, respectively.
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 **AIRMONT** (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 ingestion. The safety and efficacy of **AIRMONT** (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. The comparative pharmacokinetics of montelukast when administered as two 5-mg chewable tablets versus one 10mg film coated tablet have not been evaluated.
Distribution: Montelukast is more than 99% bound to plasma proteins. The steady state volume of distribution of montelukast averages 8 to 11 liters. Studies in rats with radiolabeled montelukast indicate minimal distribution across the blood-brain barrier. In addition, concentrations of radiolabeled material at 24 hours postdose were minimal in all other tissues.
Metabolism: Montelukast is extensively metabolized. In studies with therapeutic doses, plasma concentrations of metabolites of montelukast are undetectable at steady state in adults and pediatric patients. In vitro studies using human liver microsomes indicate that CYP3A4, 2C8, and 2C9 are involved in the metabolism of montelukast. At clinically relevant concentrations, 2C8 appears to play a major role in the metabolism of montelukast.
Elimination: The plasma clearance of montelukast averages 45 mL/min in healthy adults. Following an oral dose of radiolabeled montelukast, 86% of the radioactivity was recovered in 5-day fecal collections and <0.2% was recovered in urine. Coupled with estimates of montelukast oral bioavailability, this indicates that 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 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 had evidence of decreased metabolism of montelukast resulting in 41% (90% CI=7%, 85%) higher mean montelukast AUC following a single 10-mg dose. The elimination of montelukast was slightly prolonged compared with that in healthy subjects (mean half-life, 7.4 hours). No dosage adjustment is required in patients with mild-to-moderate hepatic insufficiency. The pharmacokinetics of **AIRMONT** (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.

STORAGE:
Store at 20-25°C. Protect from light and moisture.
(excursions permitted to 15°C to 30°C)

HOW SUPPLIED
AIRMONT 5mg Tablets: Pack of 14 chewable tablets.
AIRMONT 10mg Tablets: Pack of 14 film coated tablets.

TO BE SOLD ON THE PRESCRIPTION OF A REGISTERED MEDICAL PRACTITIONER ONLY.

KEEP ALL MEDICINES OUT OF THE REACH OF CHILDREN.

Lactose & Gluten Free

ایئرمونٹ
(مونٹیلوکاسٹ)

5 ملی گرام چبانے والی گولیاں
10 ملی گرام فلم کوٹڈ گولیاں

خوراک وہدایات
ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔
صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا فروخت کی جائے۔
تمام ادویات بچوں کی پہنچ سے دور رکھیں۔
دوا کو 25°C-20°C درجہ حرارت پر نمی اور روشنی سے محفوظ رکھیں۔
(درجہ حرارت کی حد 15°C سے 30°C ہے)

NEXT PHARMACEUTICAL
Manufactured by:
NEXT Pharmaceutical Products (Pvt.) Ltd.
Plot no. 44-A&B, Sunder Industrial Estate Lahore-Pakistan