MONTAIR Tablets / Chewable Tablets / Oral Granules (Montelukast sodium)

**Composition**

**MONTAIR-10 Tablets**  
Each film coated tablet contains  
Montelukast sodium IP equivalent to montelukast.........10 mg

**MONTAIR-5 Chewable Tablets**  
Each film coated tablet contains  
Montelukast sodium IP equivalent to montelukast...........5 mg

**MONTAIR-4 Chewable Tablets**  
Each film coated tablet contains  
Montelukast sodium IP equivalent to montelukast...........4mg

**MONTAIR Oral Granules**  
Each sachet contains  
Montelukast sodium IP equivalent to montelukast...........4mg

**Dosage Form**

Oral tablets and granules

**Pharmacology**

**Pharmacodynamics**

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 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 CysLT\(_1\) receptor (in preference to other pharmacologically important airway receptors, such as the prostanoid, cholinergic, or beta-adrenergic receptor. Montelukast inhibits physiologic actions of LTD\(_4\) at the CysLT\(_1\) receptor without any agonist activity. 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 5 mg cause substantial blockage of LTD\(_4\)-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.

The effect of montelukast on eosinophils in the peripheral blood was examined in clinical trials. In patients with asthma aged 2 years and older who received montelukast, a decrease in mean peripheral blood eosinophil counts ranging from 9% to 15% was noted, compared with placebo, over the double-blind treatment periods. In patients with seasonal allergic rhinitis aged 15 years and older who received montelukast, a mean increase of 0.2% in peripheral blood eosinophil counts was noted, compared with a mean increase of 12.5% in placebo-treated patients, over the double-blind treatment periods; this reflects a mean difference of 12.3% in favor of montelukast. The relationship between these observations and the clinical benefits of montelukast noted in the clinical trials is not known.

### 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 ($C_{\text{max}}$) is achieved in 3 to 4 hours ($T_{\text{max}}$). The mean oral bioavailability is 64%. The oral bioavailability and $C_{\text{max}}$ are not influenced by a standard meal in the morning.

For the 5 mg chewable tablet, the mean $C_{\text{max}}$ 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.

For the 4 mg chewable tablet, the mean $C_{\text{max}}$ is achieved 2 hours after administration in pediatric patients 2 to 5 years of age in the fasted state.

The 4 mg oral granule formulation is bioequivalent to the 4 mg chewable tablet when administered to adults in the fasted state. The co-administration of the oral granule formulation with applesauce did not have a clinically significant effect on the pharmacokinetics of montelukast. A high fat meal in the morning did not affect the AUC of montelukast oral granules; however, the meal decreased $C_{\text{max}}$ by 35% and prolonged $T_{\text{max}}$ from 2.3 ± 1.0 hours to 6.4 ± 2.9 hours.

The safety and efficacy of montelukast in patients with asthma were demonstrated in clinical trials in which the 10 mg film-coated tablet and 5 mg chewable tablet formulations were administered in the evening without regard to the time of food ingestion. The safety of montelukast in patients with asthma was also demonstrated in clinical trials in which the 4 mg chewable tablet and 4 mg oral granule formulations were administered in the evening without regard to the time of food ingestion. The safety and efficacy of montelukast in patients with seasonal allergic rhinitis were demonstrated in clinical trials in which the 10 mg 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 10 mg film-coated tablet has 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 litres. 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 cytochromes P450 3A4, 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. Clinical studies investigating the effect of known inhibitors of cytochromes P450 3A4 (e.g., ketoconazole, erythromycin) or 2C9 (e.g., fluconazole) on montelukast pharmacokinetics have not been conducted. Based on further *in
vitro results in human liver microsomes, therapeutic plasma concentrations of montelukast do not inhibit cytochromes P450 3A4, 2C9, 1A2, 2A6, 2C19 or 2D6. However, in vitro studies have shown that montelukast is a potent inhibitor of cytochrome P450 2C8; however, data from a clinical drug-drug interaction study involving montelukast and rosiglitazone (a probe substrate representative of drugs primarily metabolized by CYP2C8) demonstrated that montelukast does not inhibit CYP2C8 in vivo, and therefore is not anticipated to alter the metabolism of drugs metabolized by this enzyme.

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 is 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 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.

Gender: The pharmacokinetics of montelukast are similar in males and females.

Race: Pharmacokinetic differences due to race have not been studied.

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 adolescents ≥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.

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. Based on population analyses, the mean AUC (4296 ng•hr/mL) was 60% higher and the mean Cmax (667 ng/mL) was 89% higher than those observed in adults (mean AUC 2689 ng•hr/mL) and mean Cmax (353 ng/mL). The systemic exposure in children 12 to 23 months of age was less variable, but was still higher than that observed in adults. The mean AUC (3574 ng•hr/mL) was 33% higher and the mean Cmax (562 ng/mL) was 60% higher than those observed in adults. Safety and tolerability of montelukast in a single-dose pharmacokinetic study in 26 children 6 to 23 months of age were similar to that of patients two years and above. The 4-mg oral granule formulation should be used for pediatric patients 12 to 23 months of age for the treatment of asthma, or
for pediatric patients 6 to 23 months of age for the treatment of perennial allergic rhinitis. Since the 4-mg oral granule formulation is bioequivalent to the 4-mg chewable tablet, it can also be used as an alternative formulation to the 4-mg chewable tablet in pediatric patients 2 to 5 years of age.

**Indications**

- **Asthma**
  
  MONTAIR is indicated for the prophylaxis and chronic treatment of asthma in adults and pediatric patients 12 months of age and older.

- **Exercise-Induced Bronchospasm**
  
  MONTAIR is indicated for prevention of exercise-induced bronchoconstriction (EIB) in patients 6 years of age and older.

- **Allergic Rhinitis**
  
  MONTAIR is indicated in 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**
  
  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 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 or one packet of 4-mg oral granules.
  - For pediatric patients 12 to 23 months of age: one packet of 4-mg oral granules.

  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 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**
  
  For prevention of EIB, a single dose of MONTAIR 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 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 beta-agonist. Safety and efficacy in patients younger than 6 years of age have not been established. Daily administration of MONTAIR for the chronic treatment of asthma has not been established to prevent acute episodes of EIB.

- **Allergic Rhinitis**
  
  For allergic rhinitis, MONTAIR 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 or one packet of 4-mg oral granules.

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 or one packet of 4-mg oral granules.
For pediatric patients 6 to 23 months of age: one packet of 4-mg oral granules.

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 MONTAIR dose daily in the evening.

Administration of MONTAIR Oral Granules

MONTAIR Oral granules (4 mg) can be administered either directly in the mouth, dissolved in 1 teaspoonful (5 mL) of cold or room temperature baby formula or breast milk, or mixed with a spoonful of cold or room temperature soft foods; based on stability studies, only apple sauce, carrots, rice, or ice cream should be used. The packet should not be opened until ready to use. After opening the packet, the full dose (with or without mixing with baby formula, breast milk, or food) must be administered within 15 minutes. If mixed with baby formula, breast milk, or food, MONTAIR Oral granules must not be stored for future use. Discard any unused portion. MONTAIR Oral granules are not intended to be dissolved in any liquid other than baby formula or breast milk for administration. However, liquids may be taken subsequent to administration. MONTAIR Oral granules can be administered without regard to the time of meals.

Contraindications

Hypersensitivity to any component of this product

Warnings And Precautions

Acute Asthma

MONTAIR-10/5/4 Tablets/ Chewable tablets/ Oral granules are 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. While the dose of inhaled corticosteroid may be reduced gradually under medical supervision, MONTAIR-10/5/4 Tablets/ Chewable tablets/ Oral granules should not be abruptly substituted for inhaled or oral corticosteroids. There are no data demonstrating that oral corticosteroids can be reduced when montelukast is given concomitantly.

Patients who have exacerbations of asthma after exercise should have available for rescue a short-acting inhaled beta2-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.

### 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 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.

### 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, 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. 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 if such events occur.

### 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.

### Drug Interactions

Montelukast may be administered with other therapies routinely used in the prophylaxis and chronic treatment of asthma. 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, prednisolone, oral contraceptives (norethindrone 1 mg/ethinyl estradiol 35 mcg), terfenadine, digoxin, warfarin, gemfibrozil, itraconazole, thyroid hormones, sedative hypnotics, non-steroidal anti-inflammatory agents, benzodiazepines, decongestants, and Cytochrome P450 (CYP) enzyme inducers.

The area under the plasma concentration curve (AUC) for montelukast was decreased approximately 40% in subjects with co-administration of phenobarbital. Since montelukast is metabolised by CYP 3A4, it is reasonable to employ appropriate clinical monitoring in children, when montelukast is co-administered with inducers of CYP 3A4, such as phenytoin, phenobarbital and rifampicin. 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 included thyroid hormones, sedative hypnotics, non-steroidal anti-inflammatory agents, benzodiazepines,
and decongestants. 

In vitro studies have shown that montelukast is a potent inhibitor of CYP 2C8. However, data from a clinical drug-drug interaction study involving montelukast and rosiglitazone (a probe substrate representative of medicinal products primarily metabolised by CYP 2C8) demonstrated that montelukast does not inhibit CYP 2C8 in vivo. Therefore, montelukast is not anticipated to markedly alter the metabolism of medicinal products metabolised by this enzyme (e.g., paclitaxel, rosiglitazone, and repaglinide).

In vitro studies have shown that montelukast is a substrate of CYP 2C8, and to a less significant extent, of 2C9, and 3A4. In a clinical drug-drug interaction study involving montelukast and gemfibrozil (an inhibitor of both CYP 2C8 and 2C9) gemfibrozil increased the systemic exposure of montelukast by 4.4-fold. No routine dosage adjustment of montelukast is required upon co-administration with gemfibrozil or other potent inhibitors of CYP 2C8, but the physician should be aware of the potential for an increase in adverse reactions.

Based on in vitro data, clinically important drug interactions with less potent inhibitors of CYP 2C8 (e.g., trimethoprim) are not anticipated. Co-administration of montelukast with itraconazole, a strong inhibitor of CYP 3A4, resulted in no significant increase in the systemic exposure of montelukast.

### Hepatic Impairment

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 Impairment

No dosage adjustment is recommended in these patients.

### Pregnancy

**Pregnancy Category B**

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. During worldwide marketing experience, congenital limb defects have been rarely reported in the offspring of women being treated with montelukast during pregnancy. Most of these women were also taking other asthma medications during their pregnancy. A causal relationship between these events and montelukast has not been established.

### 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 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 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

No overall differences in safety or effectiveness were observed between subjects aged 65 years and above and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. The pharmacokinetic profile and the oral bioavailability of a single 10-mg oral dose of montelukast are similar in elderly and younger adults. The plasma half-life of montelukast is slightly longer in the elderly. No dosage adjustment in the elderly is required.

Effects on Ability to Drive and Use Machines

Montelukast is not expected to affect a patient’s ability to drive a car or operate machinery. However, in very rare cases, individuals have reported drowsiness or dizziness.

Undesirable Effects

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

The most common adverse reactions (incidence ≥5% and greater than placebo; listed in descending order of frequency) in controlled clinical trials were: upper respiratory infection, fever, headache, pharyngitis, cough, abdominal pain, diarrhea, otitis media, influenza, rhinorrhea, sinusitis, otitis.

Adults and Adolescents 15 Years of Age and Older

Asthma

Montelukast has been evaluated for safety in approximately 2950 adult and adolescent patients with asthma 15 years of age and older in clinical trials. In placebo-controlled clinical trials, the following adverse experiences reported with montelukast occurred in greater than or equal to 1% of patients and at an incidence greater than that in patients treated with placebo:

- **Body as a whole:** Abdominal pain, asthenia/fatigue, fever, trauma
- **Digestive system disorders:** Dyspepsia, dental pain, infectious gastroenteritis
- **Nervous/Psychiatric disorders:** Headache, dizziness
- **Respiratory system disorders:** Influenza, cough, nasal congestion
- **Skin/Skin appendages disorder:** Rash
- **Laboratory adverse experiences:** Increased alanine amino transaminase (ALT) and aspartate amino transaminase (AST) and pyuria

The frequency of less common adverse events was comparable between montelukast and placebo. The safety profile of montelukast, when administered as a single dose for prevention of EIB in adult and adolescent patients 15 years of age and older, was consistent with the safety profile previously described for montelukast.

Cumulatively, 569 patients were treated with montelukast for at least 6 months, 480 for one year, and 49 for two years in clinical trials. With prolonged treatment, the adverse experience profile did not significantly change.

Seasonal Allergic Rhinitis

Montelukast has been evaluated for safety in 2199 adult and adolescent patients with seasonal allergic rhinitis 15 years of age and older in clinical trials. Montelukast administered once daily in the morning or in the evening had a safety profile similar to that of placebo. In placebo-controlled clinical trials, the following event was reported with montelukast with a frequency ≥1% and at an incidence greater than placebo: upper respiratory infection, 1.9% of patients receiving
montelukast vs. 1.5% of patients receiving placebo. In a 4-week, placebo-controlled clinical study, the safety profile was consistent with that observed in 2-week studies. The incidence of somnolence was similar to that of placebo in all studies.

**Perennial Allergic Rhinitis**

Montelukast has been evaluated for safety in 3357 adult and adolescent patients 15 years of age and older with perennial allergic rhinitis of whom 1632 received montelukast in two, 6-week, clinical studies. Montelukast administered once daily had a safety profile consistent with that observed in patients with seasonal allergic rhinitis and similar to that of placebo. In these two studies, the following events were reported with montelukast with a frequency ≥ 1% and at an incidence greater than placebo: sinusitis, upper respiratory infection, sinus headache, cough, epistaxis, and increased ALT. The incidence of somnolence was similar to that of placebo.

**Pediatric Patients 6 to 14 Years of Age**

**Asthma**

Montelukast has been evaluated for safety in 476 pediatric patients with asthma 6 to 14 years of age. Cumulatively, 289 pediatric patients were treated with montelukast for at least 6 months, and 241 for one year or longer in clinical trials. The safety profile of montelukast in the 8-week, double-blind, pediatric efficacy trial was generally similar to the adult safety profile. In pediatric patients 6 to 14 years of age receiving montelukast, the following events occurred with a frequency ≥ 2% and more frequently than in pediatric patients who received placebo: pharyngitis, influenza, fever, sinusitis, nausea, diarrhea, dyspepsia, otitis, viral infection, and laryngitis. The other adverse effect reported frequently in clinical trials with montelukast in this age group was headache. The frequency of less common adverse events was comparable between montelukast and placebo. With prolonged treatment, the adverse experience profile did not significantly change.

The safety profile of montelukast, when administered as a single dose for prevention of EIB in pediatric patients 6 years of age and older, was consistent with the safety profile previously described for montelukast. In studies evaluating growth rate, the safety profile in these pediatric patients was consistent with the safety profile previously described for montelukast. In a 56-week, double-blind study evaluating growth rate in pediatric patients 6 to 8 years of age receiving montelukast, the following events not previously observed with the use of montelukast in this age group occurred with a frequency ≥ 2% and more frequently than in pediatric patients who received placebo: headache, rhinitis ( Infective ), varicella, gastroenteritis, atopic dermatitis, acute bronchitis, tooth infection, skin infection, and myopia.

**Pediatric Patients 2 to 5 Years of Age**

**Asthma**

Montelukast has been evaluated for safety in 573 pediatric patients 2 to 5 years of age in single- and multiple-dose studies. Cumulatively, 426 pediatric patients 2 to 5 years of age were treated with montelukast for at least 3 months, 230 for 6 months or longer, and 63 patients for one year or longer in clinical trials. In pediatric patients 2 to 5 years of age receiving montelukast, the following events occurred with a frequency ≥ 2% and more frequently than in pediatric patients who received placebo: fever, cough, abdominal pain, diarrhea, headache, rhinorrhea, sinusitis, otitis, influenza, rash, ear pain, gastroenteritis, eczema, urticaria, varicella, pneumonia, dermatitis, and conjunctivitis. Another adverse effect commonly reported in the clinical trials with montelukast in this age-group was thirst.

**Pediatric Patients 2 to 14 Years of Age**

**Seasonal Allergic Rhinitis**

Montelukast has been evaluated in 280 pediatric patients with seasonal allergic rhinitis 2 to 14 years of age in a 2-week, multicenter, double-blind, placebo-controlled, parallel-group safety study. Montelukast administered once daily in the evening had a safety profile similar to that of placebo. In this study, the following events occurred with a frequency ≥ 2% and at an incidence greater than placebo: headache, otitis media, pharyngitis, and upper respiratory infection.
The safety in patients 2 to 14 years of age with perennial allergic rhinitis is supported by the safety in patients 2 to 14 years of age with seasonal allergic rhinitis. The safety in patients 6 to 23 months of age is supported by data from pharmacokinetic and safety and efficacy studies in asthma in this pediatric population and from adult pharmacokinetic studies.

**Pediatric Patients 6 to 23 Months of Age with Asthma**

Safety and effectiveness in pediatric patients younger than 12 months of age with asthma have not been established. Montelukast has been evaluated for safety in 175 pediatric patients 6 to 23 months of age. The safety profile of montelukast in a 6-week, double-blind, placebo-controlled clinical study was generally similar to the safety profile in adults and pediatric patients 2 to 14 years of age. In pediatric patients 6 to 23 months of age receiving montelukast, the following events occurred with a frequency ≥ 2% and more frequently than in pediatric patients who received placebo: upper respiratory infection, wheezing; otitis media; pharyngitis, tonsillitis, cough; and rhinitis. The frequency of less common adverse events was comparable between montelukast and placebo.

**Pediatric Patients 6 Months to 14 Years of Age**

**Perennial Allergic Rhinitis**

The safety in patients 2 to 14 years of age with perennial allergic rhinitis is supported by the safety in patients 2 to 14 years of age with seasonal allergic rhinitis. The safety in patients 6 to 23 months of age is supported by data from pharmacokinetic and safety and efficacy studies in asthma in this pediatric population and from adult pharmacokinetic studies.

### Postmarketing Experience

The following adverse reactions have been reported in post-marketing use:

**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 including nightmares, hallucinations, insomnia, irritability, memory impairment, restlessness, somnambulism, suicidal thinking and behavior (including suicide), tic, and tremor

**Nervous system disorders:** Drowsiness, dizziness, paraesthesia/hypoesthesia, seizures.

**Respiratory, thoracic and mediastinal disorders:** Epistaxis, pulmonary eosinophilia

**Cardiac disorders:** Palpitations.

**Gastro-intestinal disorders:** Diarrhoea, dyspepsia, nausea, vomiting, pancreatitis

**Hepatobiliary disorders:** Cases of cholestatic hepatitis, hepatocellular liver-injury, and mixed-pattern liver injury have been reported in patients treated with montelukast. Most of these occurred in combination with other confounding factors, such as use of other medications, or when 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, urticaria, pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome/toxic epidermal necrolysis.

**Musculoskeletal and connective tissue disorders:** Arthralgia, myalgia including muscle cramps

**Renal and urinary disorders:** enuresis in children

**General disorders and administration site conditions:** Pyrexia, asthenia/fatigue, malaise, oedema.

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 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.
If you experience any side-effects, talk to your doctor or pharmacist or write to drugsafety@cipla.com. You can also report side effects directly via the national pharmacovigilance program of India by calling on 1800 180 3024. By reporting side-effects, you can help provide more information on the safety of this product.

**Overdosage**

No specific information is available on the treatment of overdosage with montelukast. In chronic asthma studies, montelukast has been administered at doses up to 200 mg/day to adult patients for 22 weeks and in short-term studies, up to 900 mg/day to patients for approximately a week without clinically important adverse experiences. 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.

There have been reports of acute overdosage in post-marketing experience and clinical studies of up to at least 150 mg/day with montelukast. These include reports in adults and children with a dose as high as 1000 mg. The clinical and laboratory findings observed were consistent with the safety profile in adults and older pediatric patients. There were no adverse experiences reported in the majority of overdosage reports. The most frequent adverse experiences observed were thirst, somnolence, vomiting, psychomotor hyperactivity, and abdominal pain.

It is not known whether montelukast is removed by peritoneal dialysis or hemodialysis.

**Storage And Handling Instructions**

Store below 30°C

Protect from light and moisture.

**Packaging Information**

MONTAIR-10 Tablets.................................Blister pack of 10 tablets
MONTAIR-5 Chewable Tablets..............Blister pack of 10 tablets
MONTAIR-4 Chewable Tablets..............Blister pack of 10 tablets
MONTAIR Oral Granules.........................Sachet of 0.5 gm

Last Updated: December 2018
Last reviewed: December 2018

**MONTAIR Tablets / Chewable Tablets / Oral Granules**

Source URL: https://ciplamed.com/content/montair-tablets-chewable-tablets-oral-granules