Montelukast Sodium Tablets and Chewable Tablets, USP

Part 1 of 2

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use MONTELUKAST SODIUM TABLETS and MONTELUKAST SODIUM CHEWABLE TABLETS safely and effectively. See full prescribing information for MONTELUKAST SODIUM TABLETS and MONTELUKAST SODIUM CHEWABLE TABLETS.

MONTELUKAST SODIUM tablets and MONTELUKAST SODIUM chewable tablets, for oral use.
Initial U.S. Approval: 1998

---------- RECENT MAJOR CHANGES ----------

Warnings and Precautions
Neuropsychiatric Events (5.4) 12/2016

---------- INDICATIONS AND USAGE ----------

Montelukast sodium tablets are a leukotriene receptor antagonist indicated for:
- Prophylaxis and chronic treatment of asthma in patients 2 years of age and older (1.1).
- Acute prevention of exercise-induced bronchoconstriction (EIB) in patients 6 years of age and older (1.2).
- 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 2 years of age and older (1.3).

---------- DOSAGE AND ADMINISTRATION ----------

Administration (by indications):
- Asthma (2.1): Once daily in the evening for patients 2 years and older.
- Acute prevention of EIB (2.2): One tablet at least 2 hours before exercise for patients 6 years of age and older.
- Seasonal allergic rhinitis (2.3): Once daily for patients 2 years and older.
- Perennial allergic rhinitis (2.3): Once daily for patients 2 years and older.

Dosage (by age) (2):
- 15 years and older: one 10-mg tablet.
- 6 to 14 years: one 5-mg chewable tablet.
- 2 to 5 years: one 4-mg chewable tablet.

Patients with both asthma and allergic rhinitis should take only one dose daily in the evening (2.4).

---------- DOSAGE FORMS AND STRENGTHS ----------

- Montelukast sodium Film-Coated Tablets, 10 mg
- Montelukast sodium Chewable Tablets, 4 mg and 5 mg

---------- CONTRAINDICATIONS ----------

- Hypersensitivity to any component of this product (4).

---------- WARNINGS AND PRECAUTIONS ----------

- Do not prescribe montelukast sodium to treat an acute asthma attack (5.1).
- Advise patients to have appropriate rescue medication available (5.1).
- Inhaled corticosteroid may be reduced gradually. Do not abruptly substitute montelukast sodium for inhaled or oral corticosteroids (5.2).
- Patients with known aspirin sensitivity should continue to avoid aspirin or non-steroidal anti-inflammatory agents while taking montelukast sodium (5.3).
- Neuropsychiatric events have been reported with montelukast sodium. Instruct patients to be alert for neuropsychiatric events. Evaluate the risks and benefits of continuing treatment with montelukast sodium if such events occur (5.4 and 6.2).
- Systemic eosinophilia, sometimes presenting with clinical features of vasculitis consistent with Churg-Strauss syndrome, has been reported. These events have been sometimes associated with the reduction of oral corticosteroid therapy (5.5 and 6.2).
- Inform patients with phenylketonuria that the 4-mg and 5-mg chewable tablets contain phenylalanine (5.6).

---------- ADVERSE REACTIONS ----------

Most common adverse reactions (incidence ≥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 (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Par Pharmaceutical at 1-800-828-9393 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 12/2016

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Asthma

Montelukast sodium is indicated for the prophylaxis and chronic treatment of asthma in adults and pediatric patients 2 years of age and older.

-mg and 5-mg chewable tablets contain
mg per 4-mg and 5-mg chewable tablet, respectively.

ing conditions, adverse reaction rates observed in the ates in the clinical trials of another drug and may not owing description of clinical trials experience, adverse

nd greater than placebo; listed in descending order spiratory infection, fever, headache, pharyngitis, a, rhinorrhea, sinusitis, otitis.

with Asthma

pproximately 2950 adult and adolescent patients 15 rolled clinical trials, the following adverse experiences han or equal to 1% of patients and at an incidence

of Patients with an Incidence Greater than that

Montelukast 10 mg/day (%) (n=1955)	Placebo (%) (n=1180)
2.9	2.5
1.8	1.2
1.5	0.9
1.0	0.8
2.1	1.1
1.7	1.0
1.5	0.5
18.4	18.1
1.9	1.4
4.2	3.9
2.7	2.4
1.6	1.3
1.6	1.2
2.1	2.0
1.6	1.2
1.0	0.9

respectively): ALT and AST, 1935, 1170; pyuria, 1924, 1159.

mparable between montelukast sodium and placebo.

stered as a single dose for prevention of EIB in r, was consistent with the safety profile previously

ast sodium for at least 6 months, 480 for one year, atment, the adverse experience profile did not

76 pediatric patients 6 to 14 years of age. montelukast sodium for at least 6 months, and 241 of montelukast sodium in the 8-week, double- adult safety profile. In pediatric patients 6 to 14 ng events occurred with a frequency ≥2% and more bo: pharyngitis, influenza, fever, sinusitis, nausea, . The frequency of less common adverse events was . With prolonged treatment, the adverse experience

stered as a single dose for prevention of EIB in tent with the safety profile previously described for

ese pediatric patients was consistent with the ium. In a 56-week, double-blind study evaluating eiving montelukast sodium, the following events not n in this age group occurred with a frequency ≥2% ived placebo: headache, rhinitis (infective), varicella, infection, skin infection, and myopia.

73 pediatric patients 2 to 5 years of age in single- and nts 2 to 5 years of age were treated with montelukast r, and 63 patients for one year or longer in clinical montelukast sodium, the following events occurred iatric patients who received placebo: fever, cough, tis, otitis, influenza, rash, ear pain, gastroenteritis, conjunctivitis.

with Seasonal Allergic Rhinitis

199 adult and adolescent patients 15 years of age tered once daily in the morning or in the evening had ntrolled clinical trials, the following event was reported an incidence greater than placebo: upper respiratory n vs. 1.5% of patients receiving placebo. In a 4-week, consistent with that observed in 2-week studies. The in all studies.

al Allergic Rhinitis

ic patients 2 to 14 years of age in a 2-week, roup safety study. Montelukast sodium 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.

Adults and Adolescents 15 Years of Age and Older with Perennial Allergic Rhinitis

Montelukast sodium 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 sodium in two, 6-week, clinical studies. Montelukast sodium 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 sodium 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 2 Years to 14 Years of Age with 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.

6.2 Post-Marketing Experience

The following adverse reactions have been identified during post-approval use of montelukast sodium. 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 *[see Warnings and Precautions (5.4)]*.

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 montelukast sodium. Most of these occurred in combination with other confounding factors, such as use of other medications, or when montelukast sodium 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 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 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 *[see Warnings and Precautions (5.5)]*.

7 DRUG INTERACTIONS

No dose adjustment is needed when montelukast sodium 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 *[see Clinical Pharmacology (12.3)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 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 sodium 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 *[see Nonclinical Toxicology (13.2)]*.

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

8.3 Nursing Mothers

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 sodium is given to a nursing mother.

8.4 Pediatric Use

Safety and efficacy of montelukast sodium 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 *[see Adverse Reactions (6.1)*, *Clinical Pharmacology, Special Populations (12.3)*, and *Clinical Studies (14.1, 14.2)]*.

The efficacy of montelukast sodium 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 2 years 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 montelukast sodium 4-mg chewable tablets in pediatric patients 2 to 5 years of age with asthma has been demonstrated by adequate and well-controlled data *[see Adverse Reactions (6.1)]*. Efficacy of montelukast sodium in this age group is extrapolated from the demonstrated efficacy in patients 6 years of age and older with asthma and is based on similar pharmacokinetic data, as well as the assumption that the disease course, pathophysiology and the drug's effect are substantially similar among these populations. Efficacy in this age group is supported by exploratory efficacy assessments from a large, well-controlled safety study conducted in patients 2 to 5 years of age.

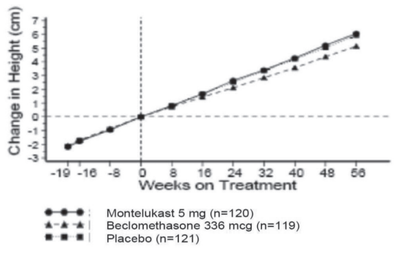
The safety of montelukast sodium 4-mg and 5-mg chewable tablets in pediatric patients aged 2 to 14 years with allergic rhinitis is supported by data from studies conducted in pediatric patients aged 2 to 14 years with asthma. A safety study in pediatric patients 2 to 14 years of age with seasonal allergic rhinitis demonstrated a similar safety profile *[see Adverse Reactions (6.1)]*.

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.

Growth Rate in Pediatric Patients

A 56-week, multi-center, double-blind, randomized, active- and placebo-controlled parallel group study was conducted to assess the effect of montelukast sodium on growth rate in 360 patients with mild asthma, aged 6 to 8 years. Treatment groups included montelukast sodium 5 mg once daily, placebo, and beclomethasone dipropionate administered as 168 mcg twice daily with a spacer device. For each subject, a growth rate was defined as the slope of a linear regression line fit to the height measurements over 56 weeks. The primary comparison was the difference in growth rates between montelukast sodium and placebo groups. Growth rates, expressed as least-squares (LS) mean (95% CI) in cm/year, for the montelukast sodium placebo, and beclomethasone treatment groups were 5.67 (5.46, 5.88), 5.64 (5.42, 5.86), and 4.86 (4.64, 5.08), respectively. The differences in growth rates, expressed as least-squares (LS) mean (95% CI) in cm/year, for montelukast sodium minus placebo, beclomethasone minus placebo, and montelukast sodium minus beclomethasone treatment groups were 0.03 (-0.26, 0.31), -0.78 (-1.06, -0.49); and 0.81 (0.53, 1.09), respectively. Growth rate (expressed as mean change in height over time) for each treatment group is shown in FIGURE 1.

Figure 1: Change in Height (cm) from Randomization Visit by Scheduled Week (Treatment Group Mean ± Standard Error* of the Mean)



*The standard errors of the treatment group means in change in height are too small to be visible on the plot

8.5 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 between these subjects 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.

8.6 Hepatic Insufficiency

No dosage adjustment is required in patients with mild-to-moderate hepatic insufficiency *[see Clinical Pharmacology (12.3)]*.

8.7 Renal Insufficiency

No dosage adjustment is recommended in patients with renal insufficiency *[see Clinical Pharmacology (12.3)]*.

10 OVERDOSAGE

No specific information is available on the treatment of overdosage with montelukast sodium. 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 with montelukast sodium. 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 pediatric patients. There were no adverse experiences in the majority of overdosage reports. The most frequently occurring adverse experiences were consistent with the safety profile of montelukast sodium and included abdominal pain, somnolence, thirst, headache, vomiting and psychomotor hyperactivity.

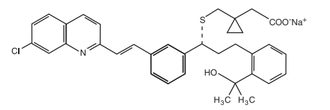
It is not known whether montelukast is removed by peritoneal dialysis or hemodialysis.

11 DESCRIPTION

Montelukast sodium, the active ingredient in montelukast sodium tablets, USP, 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-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio]methyl]cyclopropaneacetic acid, monosodium salt.

The empirical formula is $C_{35}H_{35}ClNNa_2O_3S$, and its molecular weight is 608.18. The structural formula is:



Montelukast sodium is a hygroscopic, optically active, white to off-white powder. Montelukast sodium is soluble in water (0.03 g/mL) and freely soluble in methanol, ethanol, DMSO and DMF and practically insoluble in acetonitrile.

Each 10-mg film-coated montelukast sodium tablet, USP contains 10.4 mg montelukast sodium, which is equivalent to 10 mg of montelukast, and the following inactive ingredients: croscarmellose sodium, hydroxypropyl cellulose, lactose monohydrate, magnesium stearate, and silicified microcrystalline cellulose. The film coating consists of: hydroxypropyl cellulose, hypromellose, red ferric oxide, titanium dioxide, and yellow ferric oxide.

Each 4-mg and 5-mg chewable montelukast sodium tablet, USP contains 4.2 and 5.2 mg montelukast sodium, respectively, which are equivalent to 4 and 5 mg of montelukast, respectively. Both chewable tablets contain the following inactive ingredients: aspartame, croscarmellose sodium, flavor black cherry, hydroxypropyl cellulose, magnesium stearate, mannitol, red ferric oxide, and silicified microcrystalline cellulose.

Meets USP Dissolution Test II.

12 CLINICAL PHARMACOLOGY

12.1 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 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 β-adrenergic receptor). Montelukast inhibits physiologic actions of LTD_4 at the $CysLT_1$ receptor without any agonist activity.

12.2 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 5 mg cause substantial blockage of LTD_4-induced bronchoconstriction. In a placebo-controlled, crossover study (n=12), montelukast sodium inhibited early- and late-phase bronchoconstriction due to antigen challenge by 75% and 57%, respectively.

The effect of montelukast sodium on eosinophils in the peripheral blood was examined in clinical trials. In patients with asthma aged 2 years and older who received montelukast sodium, 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 sodium, 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 sodium. The relationship between these observations and the clinical benefits of montelukast noted in the clinical trials is not known *[see Clinical Studies (14)]*.

12.3 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.

For the 5-mg 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.

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

The safety and efficacy of montelukast sodium 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 sodium 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 sodium 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 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 montelukast sodium 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 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.

The mean systemic exposure of the 4-mg chewable tablet in pediatric patients 2 to 5 years of age and the 5-mg chewable tablets in pediatric patients 6 to 14 years of age is similar to the mean systemic exposure of the 10-mg film-coated tablet in adults. The 5-mg chewable tablet should be used in pediatric patients 6 to 14 years of age and the 4-mg chewable tablet should be used in pediatric patients 2 to 5 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 [range 1200 to 7153]) was 60% higher and the mean C_{max} (667 ng/mL [range 201 to 1058]) was 89% higher than those observed in adults (mean AUC 2689 ng•hr/mL [range 1521 to 4595]) and mean C_{max} (353 ng/mL [range 180 to 548]). 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 [range 2229 to 5408]) was 33% higher and the mean C_{max} (562 ng/mL [range 296 to 814]) 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 *[see Adverse Reactions (6.1)]*. 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.

18.5000"

Front

Drug-Drug Interactions

Theophylline, Prednisone, and Prednisolone: montelukast sodium has been administered with other therapies routinely used in the prophylaxis and chronic treatment of asthma with no apparent increase in adverse reactions. 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, and prednisolone.

Montelukast at a dose of 10 mg once daily dosed to pharmacokinetic steady state, did not cause clinically significant changes in the kinetics of a single intravenous dose of theophylline [predominantly a cytochrome P450 (CYP) 1A2 substrate]. Montelukast at doses of ≥100 mg daily dosed to pharmacokinetic steady state, did not cause any clinically significant change in plasma profiles of prednisone or prednisolone following administration of either oral prednisone or intravenous prednisolone.

Oral Contraceptives, Terfenadine, Digoxin, and Warfarin: In drug interaction studies, the recommended clinical dose of montelukast did not have clinically important effects on the pharmacokinetics of the following drugs: oral contraceptives (norethindrone 1 mg/ethinyl estradiol 35 mcg), terfenadine, digoxin, and warfarin. Montelukast at doses of ≥100 mg daily dosed to pharmacokinetic steady state did not significantly alter the plasma concentrations of either component of an oral contraceptive containing norethindrone 1 mg/ethinyl estradiol 35 mcg. Montelukast at a dose of 10 mg once daily dosed to pharmacokinetic steady state did not change the plasma concentration profile of terfenadine (a substrate of CYP3A4) or fexofenadine, the carboxylated metabolite, and did not prolong the QTc interval following co-administration with terfenadine 60 mg twice daily; did not change the pharmacokinetic profile or urinary excretion of immunoreactive digoxin; did not change the pharmacokinetic profile of warfarin (primarily a substrate of CYP2C9, 3A4 and 1A2) or influence the effect of a single 30-mg oral dose of warfarin on prothrombin time or the International Normalized Ratio (INR).

Thyroid Hormones, Sedative Hypnotics, Non-Steroidal Anti-Inflammatory Agents, Benzodiazepines, and Decongestants: 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.

Cytochrome P450 (CYP) Enzyme Inducers: Phenobarbital, which induces hepatic metabolism, decreased the area under the plasma concentration curve (AUC) of montelukast approximately 40% following a single 10-mg dose of montelukast. No dosage adjustment for montelukast sodium is recommended. It is reasonable to employ appropriate clinical monitoring when potent CYP enzyme inducers, such as phenobarbital or rifampin, are co-administered with montelukast sodium.

Effect of Montelukast on Cytochrome P450 (CYP) Enzymes: Montelukast is a potent inhibitor of CYP2C8 *in vitro*. However, data from a clinical drug-drug interaction study involving montelukast and rosiglitazone (a probe substrate representative of drugs primarily metabolized by CYP2C8) in 12 healthy individuals demonstrated that the pharmacokinetics of rosiglitazone are not altered when the drugs are coadministered, indicating that montelukast does not inhibit CYP2C8 *in vivo*. Therefore, montelukast is not anticipated to alter the metabolism of drugs metabolized by this enzyme (e.g., paclitaxel, rosiglitazone, and repaglinide). Based on further *in vitro* results in human liver microsomes, therapeutic plasma concentrations of montelukast do not inhibit CYP 3A4, 2C9, 1A2, 2A6, 2C19, or 2D6.

Cytochrome P450 (CYP) Enzyme Inhibitors: In vitro studies have shown that montelukast is a substrate of CYP 2C8, 2C9, and 3A4. Co-administration of montelukast with itraconazole, a strong CYP 3A4 inhibitor, resulted in no significant increase in the systemic exposure of montelukast. Data from a clinical drug-drug interaction study involving montelukast and gemfibrozil (an inhibitor of both CYP 2C8 and 2C9) demonstrated that gemfibrozil, at a therapeutic dose, increased the systemic exposure of montelukast by 4.4-fold. Co-administration of itraconazole, gemfibrozil, and montelukast did not further increase the systemic exposure of montelukast. Based on available clinical experience, no dosage adjustment of montelukast is required upon co-administration with gemfibrozil *[see Overdosage (10)]*.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No evidence of tumorigenicity was seen in carcinogenicity studies of either 2 years in Sprague-Dawley rats or 92 weeks in mice at oral gavage doses up to 200 mg/kg/day or 100 mg/kg/day, respectively. The estimated exposure in rats was approximately 120 and 75 times the AUC for adults and children, respectively, at the maximum recommended daily oral dose. The estimated exposure in mice was approximately 45 and 25 times the AUC for adults and children, respectively, at the maximum recommended daily oral dose.

Montelukast demonstrated no evidence of mutagenic or clastogenic activity in the following assays: the microbial mutagenesis assay, the V-79 mammalian cell mutagenesis assay, the alkaline elution assay in rat hepatocytes, the chromosomal aberration assay in Chinese hamster ovary cells, and in the *in vivo* mouse bone marrow chromosomal aberration assay.

Pediatric Patients 6 to 14 Years of Age with Asthma

The efficacy of montelukast sodium in pediatric patients 6 to 14 years of age was demonstrated in one 8-week, double-blind, placebo-controlled trial in 336 patients (201 treated with montelukast sodium and 135 treated with placebo) using an inhaled β-agonist on an "as-needed" basis. The patients had a mean baseline percent predicted FEV_1 of 72% (approximate range, 45 to 90%) and a mean daily inhaled β-agonist requirement of 3.4 puffs of albuterol. Approximately 36% of the patients were on inhaled corticosteroids. The median age was 11 years (range 6 to 15); 35.4% were females and 64.6% were males. The ethnic/racial distribution in this study was 80.1% Caucasian, 12.8% Black, 4.5% Hispanic, and 2.7% other origins.

Compared with placebo, treatment with one 5-mg montelukast sodium chewable tablet daily resulted in a significant improvement in mean morning FEV_1 percent change from baseline (8.7% in the group treated with montelukast sodium vs. 4.2% change from baseline in the placebo group, p<0.001). There was a significant decrease in the mean percentage change in daily "as-needed" inhaled β-agonist use (11.7% decrease from baseline in the group treated with montelukast sodium vs. 8.2% increase from baseline in the placebo group, p<0.05). This effect represents a mean decrease from baseline of 0.56 and 0.23 puffs per day for the montelukast and placebo groups, respectively. Subgroup analyses indicated that younger pediatric patients aged 6 to 11 had efficacy results comparable to those of the older pediatric patients aged 12 to 14.

Similar to the adult studies, no significant change in the treatment effect was observed during continuous once-daily administration in one open-label extension trial without a concurrent placebo group for up to 6 months.

Pediatric Patients 2 to 5 Years of Age with Asthma

The efficacy of montelukast sodium for the chronic treatment of asthma in pediatric patients 2 to 5 years of age was explored in a 12-week, placebo-controlled safety and tolerability study in 689 patients, 461 of whom were treated with montelukast sodium. The median age was 4 years (range 2 to 6); 41.5% were females and 58.5% were males. The ethnic/racial distribution in this study was 56.5% Caucasian, 20.9% Hispanic, 14.4% other origins, and 8.3% Black.

While the primary objective was to determine the safety and tolerability of montelukast sodium in this age group, the study included exploratory efficacy evaluations, including daytime and overnight asthma symptom scores, β-agonist use, oral corticosteroid rescue, and the physician's global evaluation. The findings of these exploratory efficacy evaluations, along with pharmacokinetics and extrapolation of efficacy data from older patients, support the overall conclusion that montelukast sodium is efficacious in the maintenance treatment of asthma in patients 2 to 5 years of age.

Effects in Patients on Concomitant Inhaled Corticosteroids

Separate trials in adults evaluated the ability of montelukast sodium to add to the clinical effect of inhaled corticosteroids and to allow inhaled corticosteroid tapering when used concomitantly.

One randomized, placebo-controlled, parallel-group trial (n=226) enrolled adults with stable asthma with a mean FEV_1 of approximately 84% of predicted who were previously maintained on various inhaled corticosteroids (delivered by metered-dose aerosol or dry powder inhalers). The median age was 41.5 years (range 16 to 70); 52.2% were females and 47.8% were males. The ethnic/racial distribution in this study was 92.0% Caucasian, 3.5% Black, 2.2% Hispanic, and 2.2% Asian. The types of inhaled corticosteroids and their mean baseline requirements included beclomethasone dipropionate (mean dose, 1203 mcg/day), triamcinolone acetonide (mean dose, 2004 mcg/day), flunisolide (mean dose, 1971 mcg/day), fluticasone propionate (mean dose, 1083 mcg/day), or budesonide (mean dose, 1192 mcg/day). Some of these inhaled corticosteroids were non-U.S.-approved formulations, and doses expressed may not be ex-actuator. The pre-study inhaled corticosteroid requirements were reduced by approximately 37% during a 5- to 7-week placebo run-in period designed to titrate patients toward their lowest effective inhaled corticosteroid dose. Treatment with montelukast sodium resulted in a further 47% reduction in mean inhaled corticosteroid dose compared with a mean reduction of 30% in the placebo group over the 12-week active treatment period (p≤0.05). It is not known whether the results of this study can be generalized to patients with asthma who require higher doses of inhaled corticosteroids or systemic corticosteroids.

In another randomized, placebo-controlled, parallel-group trial (n=642) in a similar population of adult patients previously maintained, but not adequately controlled, on inhaled corticosteroids (beclomethasone 336 mcg/day), the addition of montelukast sodium to beclomethasone resulted in statistically significant improvements in FEV_1 compared with those patients who were continued on beclomethasone alone or those patients who were withdrawn from beclomethasone and treated with montelukast or placebo alone over the last 10 weeks of the 16-week, blinded treatment period. Patients who were randomized to treatment arms containing beclomethasone had statistically significantly better asthma control than those patients randomized to montelukast sodium alone or placebo alone as indicated by FEV_1, daytime asthma symptoms, PEFR, nocturnal awakenings due to asthma, and "as-needed" β-agonist requirements.

In adult patients with asthma with documented aspirin sensitivity, nearly all of whom were receiving concomitant inhaled and/or oral corticosteroids, a 4-week, randomized, parallel-group trial (n=80)

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Table 5: Effects of Montelukast Sodium on Daytime Nasal Symptoms Score* in a Placebo-and Active-controlled Trial in Patients with Seasonal Allergic Rhinitis (ANCOVA Model)

Treatment Group (N)	Baseline Mean Score	Mean Change from Baseline	Difference Between Treatment and Placebo (95% CI) Least-Squares Mean
Montelukast 10 mg (344)	2.09	-0.39	-0.13‡ (-0.21, -0.06)
Placebo (351)	2.10	-0.26	N.A.
Active Control† (Loratadine 10 mg) (599)	2.06	-0.46	-0.24‡ (-0.31, -0.17)

* Average of individual scores of nasal congestion, rhinorrhea, nasal itching, sneezing as assessed by patients on a 0-3 categorical scale.
† The study was not designed for statistical comparison between Montelukast Sodium and the active control (loratadine).
‡ Statistically different from placebo (p≤0.001).

Perennial Allergic Rhinitis

The efficacy of montelukast sodium tablets for the treatment of perennial allergic rhinitis was investigated in 2 randomized, double-blind, placebo-controlled studies conducted in North America and Europe. The two studies enrolled a total of 3357 patients, of whom 1632 received montelukast sodium 10-mg tablets. Patients 15 to 82 years of age with perennial allergic rhinitis as confirmed by history and a positive skin test to at least one relevant perennial allergen (dust mites, animal dander, and/or mold spores), who had active symptoms at the time of study entry, were enrolled.

In the study in which efficacy was demonstrated, the median age was 35 years (range 15 to 81); 64.1% were females and 35.9% were males. The ethnic/racial distribution in this study was 83.2% Caucasian, 8.1% Black, 5.4% Hispanic, 2.3% Asian, and 1.0% other origins. Montelukast sodium 10-mg tablets once daily was shown to significantly reduce symptoms of perennial allergic rhinitis over a 6-week treatment period (TABLE 6); in this study the primary outcome variable was mean change from baseline in daytime nasal symptoms score (the average of individual scores of nasal congestion, rhinorrhea, and sneezing).

Table 6: Effects of Montelukast Sodium on Daytime Nasal Symptoms Score* in a Placebo-controlled Trial in Patients with Perennial Allergic Rhinitis (ANCOVA Model)

Treatment Group (N)	Baseline Mean Score	Mean Change from Baseline	Difference Between Treatment and Placebo (95% CI) Least-Squares Mean
Montelukast 10 mg (1000)	2.09	-0.42	-0.08† (-0.12, -0.04)
Placebo (980)	2.10	-0.35	N.A.

* Average of individual scores of nasal congestion, rhinorrhea, sneezing as assessed by patients on a 0-3 categorical scale.
† Statistically different from placebo (p≤0.001).

The other 6-week study evaluated montelukast 10 mg (n=626), placebo (n=609), and an active-control (cetirizine 10 mg; n=120). The primary analysis compared the mean change from baseline in daytime nasal symptoms score for montelukast sodium vs. placebo over the first 4 weeks of treatment; the study was not designed for statistical comparison between montelukast sodium and the active-control. The primary outcome variable included nasal itching in addition to nasal congestion, rhinorrhea, and sneezing. The estimated difference between montelukast sodium and placebo was -0.04 with a 95% CI of (-0.09, 0.01). The estimated difference between the active-control and placebo was -0.10 with a 95% CI of (-0.19, -0.01).

16 HOW SUPPLIED/STORAGE AND HANDLING

Montelukast Sodium Chewable Tablets, USP, 4-mg (montelukast), are pink, oval-shaped chewable tablets, debossed with E223 on one side and plain on the other. They are supplied as follows:

NDC 0603-4653-16 unit of use high-density polyethylene (HDPE) bottles of 30 with a polypropylene child-resistant cap, an aluminum foil induction seal, and silica gel desiccant

NDC 0603-4653-02 unit of use high-density polyethylene (HDPE) bottles of 90 with a polypropylene child-resistant cap, an aluminum foil induction seal, and silica gel desiccant

NDC 0603-4653-28 bulk packaging high-density polyethylene (HDPE) bottles of 500 with a polypropylene cap, an aluminum foil induction seal, and silica gel desiccant

NDC 0603-4653-32 bulk packaging high-density polyethylene (HDPE) bottles of 1,000 with a polypropylene cap, an aluminum foil induction seal, and silica gel desiccant

Montelukast Sodium Chewable Tablets, USP, 5-mg (montelukast), are pink, round-shaped chewable tablets, debossed with E224 on one side and plain on the other. They are supplied as follows:

NDC 0603-4654-16 unit of use high-density polyethylene (HDPE) bottles of 30 with a polypropylene child-resistant cap, an aluminum foil induction seal, and silica gel desiccant

NDC 0603-4654-02 unit of use high-density polyethylene (HDPE) bottles of 90 with a polypropylene child-resistant cap, an aluminum foil induction seal, and silica gel desiccant

NDC 0603-4654-28 bulk packaging high-density polyethylene (HDPE) bottles of 500 with a polypropylene cap, an aluminum foil induction seal, and silica gel desiccant

NDC 0603-4654-32 bulk packaging high-density polyethylene (HDPE) bottles of 1,000 with a polypropylene cap, an aluminum foil induction seal, and silica gel desiccant

Montelukast Sodium Tablets, USP, 10 mg (montelukast) are round-shaped, beige tablets, debossed with E225 on one side and plain on the other. They are supplied as follows:

NDC 0603-4655-16 unit of use high-density polyethylene (HDPE) bottles of 30 with a polypropylene child-resistant cap, an aluminum foil induction seal, and silica gel desiccant

NDC 0603-4655-02 unit of use high-density polyethylene (HDPE) bottles of 90 with a polypropylene child-resistant cap, an aluminum foil induction seal, and silica gel desiccant

NDC 0603-4655-28 bulk packaging high-density polyethylene (HDPE) bottles of 500 with a polypropylene cap, an aluminum foil induction seal, and silica gel desiccant

NDC 0603-4655-32 bulk packaging high-density polyethylene (HDPE) bottles of 1,000 with a polypropylene cap, an aluminum foil induction seal, and silica gel desiccant

NDC 0603-4655-34 bulk packaging high-density polyethylene (HDPE) bottles of 5,000 with a polypropylene cap, an aluminum foil induction seal, and silica gel desiccant

Storage
Store montelukast 4-mg chewable tablets, 5-mg chewable tablets and 10-mg film-coated tablets at 25°C (77°F), excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature]. Protect from moisture and light. Store in original package.

17 PATIENT COUNSELING INFORMATION

See FDA-Approved Patient Labeling (Patient Information).

Information for Patients

- Patients should be advised to take montelukast sodium daily as prescribed, even when they are asymptomatic, as well as during periods of worsening asthma, and to contact their physicians if their asthma is not well controlled.
- Patients should be advised that oral montelukast sodium is not for the treatment of acute asthma attacks. They should have appropriate short-acting inhaled ß-agonist medication available to treat asthma exacerbations. Patients who have exacerbations of asthma after exercise should be instructed to have available for rescue a short-acting inhaled ß-agonist. Daily administration of montelukast sodium for the chronic treatment of asthma has not been established to prevent acute episodes of EIB.
- Patients should be advised that, while using montelukast sodium, medical attention should be sought if short-acting inhaled bronchodilators are needed more often than usual, or if more than the maximum number of inhalations of short-acting bronchodilator treatment prescribed for a 24-hour period are needed.
- Patients receiving montelukast sodium should be instructed not to decrease the dose or stop taking any other anti-asthma medications unless instructed by a physician.
- Patients should be instructed to notify their physician if neuropsychiatric events occur while using montelukast sodium.
- Patients with known aspirin sensitivity should be advised to continue avoidance of aspirin or non-steroidal anti-inflammatory agents while taking montelukast sodium.
- Phenylketonuric patients should be informed that the 4-mg and 5-mg chewable tablets contain phenylalanine (a component of aspartame).

FDA-Approved Patient Labeling

See the full patient prescribing information for montelukast sodium.

Patient Information

Read the Patient Information Leaflet that comes with montelukast sodium tablets and/or chewable tablets before you start taking it and each time you get a refill. There may be new information. This leaflet does not take the place of talking with your healthcare provider about your medical condition or your treatment.

What are montelukast sodium tablets and/or chewable tablets?

- Montelukast sodium tablets and/or chewable tablets are prescription medicines that block substances in the body called leukotrienes. This may help to improve symptoms of asthma and allergic rhinitis. Montelukast sodium tablets and/or chewable tablets do not contain a steroid.

Montelukast sodium tablets and/or chewable tablets are used to:

1. Prevent asthma attacks and for the long-term treatment of asthma in adults and children ages 2 years of age and older.
   Do not take montelukast sodium tablets and/or chewable tablets if you need relief right away for a sudden asthma attack. If you get an asthma attack, you should follow the instructions your healthcare provider gave you for treating asthma attacks.
2. Prevent exercise-induced asthma in people 6 years of age and older.
3. Help control the symptoms of allergic rhinitis (sneezing, stuffy nose, runny nose, itching of the nose). Montelukast sodium tablets and/or chewable tablets are used to treat:
   - outdoor allergies that happen part of the year (seasonal allergic rhinitis) in adults and children ages 2 years and older, **and**
   - indoor allergies that happen all year (perennial allergic rhinitis) in adults and children ages 2 years of age and older.

Who should not take montelukast sodium tablets and/or chewable tablets?

Do not take montelukast sodium tablets and/or chewable tablets if you are allergic to any of its ingredients.

See the end of this leaflet for a complete list of the ingredients in montelukast sodium tablets and montelukast sodium chewable tablets.

What should I tell my healthcare provider before taking montelukast sodium tablets and/or chewable tablets?

Before taking montelukast sodium tablets and/or chewable tablets, tell your healthcare provider if you:

- are allergic to aspirin
- have phenylketonuria. Montelukast sodium chewable tablets contain aspartame, a source of phenylalanine
- have any other medical conditions
- are pregnant or plan to become pregnant. Talk to your doctor if you are pregnant or plan to become pregnant, as montelukast sodium tablets and/or chewable tablets may not be right for you.
- are breast-feeding or plan to breast-feed. It is not known if montelukast sodium passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby while taking montelukast sodium tablets and/or chewable tablets.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. Some medicines may affect how montelukast sodium works, or montelukast sodium may affect how your other medicines work.

How should I take montelukast sodium tablets and/or chewable tablets?

For anyone who takes montelukast sodium tablets and/or chewable tablets:

- Take montelukast sodium tablets and/or chewable tablets exactly as prescribed by your healthcare provider. Your healthcare provider will tell you how much montelukast sodium to take, and **when to take it**.
- Do not stop taking montelukast sodium tablets and/or chewable tablets or change when you take it without talking with your healthcare provider.
- You can take montelukast sodium tablets and/or chewable tablets with food or without food.
- **If you or your child misses a dose of montelukast sodium tablets and/or chewable tablets, just take the next dose at your regular time**. Do not take 2 doses at the same time.
- If you take too much montelukast sodium, call your healthcare provider or a Poison Control Center right away.

For adults and children 2 years of age and older with asthma:

- Take montelukast sodium tablets and/or chewable tablets 1 time each day, in the evening. Continue to take montelukast sodium tablets and/or chewable tablets every day for as long as your healthcare provider prescribes it, even if you have no asthma symptoms.
- Tell your healthcare provider right away if your asthma symptoms get worse, or if you need to use your rescue inhaler medicine more often for asthma attacks.
- **Do not take montelukast sodium tablets and/or chewable tablets if you need relief right away from a sudden asthma attack**. If you get an asthma attack, you should follow the instructions your healthcare provider gave you for treating asthma attacks.
- Always have your rescue inhaler medicine with you for asthma attacks.
- Do not stop taking or lower the dose of your other asthma medicines unless your healthcare provider tells you to.

For patients 6 years of age and older for the prevention of exercise-induced asthma:

- Take montelukast sodium tablets and/or chewable tablets at least 2 hours before exercise.
- Always have your rescue inhaler medicine with you for asthma attacks.
- If you take montelukast sodium tablets and/or chewable tablets every day for chronic asthma or allergic rhinitis, **do not** take another dose to prevent exercise-induced asthma. Talk to your healthcare provider about your treatment for exercise-induced asthma.
- **Do not take 2 doses of montelukast sodium tablets and/or chewable tablets within 24 hours (1 day).**

For adults and children 2 years of age and older with seasonal allergic rhinitis, or for adults and children 2 years of age and older with perennial allergic rhinitis:

- Take montelukast sodium tablets and/or chewable tablets 1 time each day, at about the same time each day.

What is the dose of montelukast sodium tablets and chewable tablets?

The dose of montelukast sodium tablets and/or chewable tablets prescribed for you or your child's condition is based on age:

- 2 to 5 years: one 4-mg chewable tablet.
- 6 to 14 years: one 5-mg chewable tablet.
- 15 years and older: one 10-mg tablet.

What should I avoid while taking montelukast sodium tablets and/or chewable tablets?

If you have asthma and aspirin makes your asthma symptoms worse, continue to avoid taking aspirin or other medicines called non-steroidal anti-inflammatory drugs (NSAIDs) while taking montelukast sodium tablets and/or chewable tablets.

What are the possible side effects of montelukast sodium tablets and/or chewable tablets?

Montelukast sodium may cause serious side effects.

- **Behavior and mood-related changes**. Tell your healthcare provider right away if you or your child have any of these symptoms while taking montelukast sodium tablets and/or chewable tablets:
  - agitation including aggressive behavior or hostility
  - attention problems
  - bad or vivid dreams
  - depression
  - disorientation (confusion)
  - feeling anxious
  - hallucinations (seeing or hearing things that are not really there)
  - irritability
  - memory problems
  - restlessness
  - sleep walking
  - suicidal thoughts and actions (including suicide)
  - tremor
  - trouble sleeping
  - uncontrolled muscle movements
- **Increase in certain white blood cells (eosinophils) and possible inflamed blood vessels throughout the body (systemic vasculitis)**. Rarely, this can happen in people with asthma who take montelukast sodium. This sometimes happens in people who also take a steroid medicine by mouth that is being stopped or the dose is being lowered.

  Tell your healthcare provider right away if you get one or more of these symptoms:
  - a feeling of pins and needles or numbness of arms or legs
  - a flu-like illness
  - rash
  - severe inflammation (pain and swelling) of the sinuses (sinusitis)

The most common side effects with montelukast sodium tablets and/or chewable tablets include:

- upper respiratory infection
- fever
- headache
- sore throat
- cough
- stomach pain
- diarrhea
- earache or ear infection
- flu
- runny nose
- sinus infection

Other side effects with montelukast sodium tablets and/or chewable tablets include:

- increased bleeding tendency, low blood platelet count
- allergic reactions [including swelling of the face, lips, tongue, and/or throat (which may cause trouble breathing or swallowing), hives and itching]
- dizziness, drowsiness, pins and needles/numbness, seizures (convulsions or fits)
- palpitations
- nose bleed, stuffy nose, swelling (inflammation) of the lungs
- heartburn, indigestion, inflammation of the pancreas, nausea, stomach or intestinal upset, vomiting
- hepatitis
- bruising, rash, severe skin reactions (erythema multiforme, Stevens-Johnson syndrome/toxic epidermal necrolysis) that may occur without warning
- joint pain, muscle aches and muscle cramps
- bedwetting in children
- tiredness, swelling

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of montelukast sodium tablets and/or chewable tablets. For more information ask your healthcare provider or pharmacist.

Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store montelukast sodium tablets and/or chewable tablets?

- Store montelukast sodium tablets and/or chewable tablets at 59°F to 86°F (15°C to 30°C).
- Keep montelukast sodium tablets and/or chewable tablets in the container it comes in.
- Keep montelukast sodium tablets and/or chewable tablets in a dry place and away from light.

General Information about the safe and effective use of montelukast sodium tablets and/or chewable tablets

Medicines are sometimes prescribed for purposes other than those mentioned in Patient Information Leaflets. Do not use montelukast sodium tablets and/or chewable tablets for a condition for which it was not prescribed. Do not give montelukast sodium tablets and/or chewable tablets to other people even if they have the same symptoms you have. It may harm them. **Keep montelukast sodium tablets and/or chewable tablets and all medicines out of the reach of children**.

This leaflet summarizes information about montelukast sodium tablets and/or chewable tablets. If you would like more information, talk to your healthcare provider. You can ask your pharmacist or healthcare provider for information about montelukast sodium tablets and/or chewable tablets that is written for health professionals. For more information, call **Par Pharmaceutical at 1-800-828-9393.**

What are the ingredients in montelukast sodium tablets and chewable tablets?

Active ingredient: montelukast sodium

Inactive ingredients:

- 10-mg tablet: croscarmellose sodium, hydroxypropyl cellulose, lactose monohydrate, magnesium stearate, and silicified microcrystalline cellulose. The film coating contains: hydroxypropyl cellulose, hypromellose, red ferric oxide, titanium dioxide and yellow ferric oxide.
- 4-mg and 5-mg chewable tablets: aspartame, croscarmellose sodium, flavor black cherry, hydroxypropyl cellulose, magnesium stearate, mannitol, red ferric oxide, and silicified microcrystalline cellulose.

People with Phenylketonuria: montelukast sodium 4-mg chewable tablets contain 1.2 mg of phenylalanine, and montelukast sodium 5-mg chewable tablets contain 1.5 mg of phenylalanine.

Distributed by:
Par Pharmaceutical
Chestnut Ridge, NY 10977

Revised: 12/16

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Patient Information
Montelukast (mon-te-LOO-kast) Sodium Tablets, USP 10 mg
&
Montelukast Sodium Chewable Tablets, USP
4 mg & 5 mg

Read the Patient Information Leaflet that comes with montelukast sodium tablets and/or chewable tablets before you start taking it and each time you get a refill. There may be new information. This leaflet does not take the place of talking with your healthcare provider about your medical condition or your treatment.

What are montelukast sodium tablets and/or chewable tablets?

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Montelukast sodium tablets and/or chewable tablets are used to:

1. Prevent asthma attacks and for the long-term treatment of asthma in adults and children ages 2 years of age and older.

   Do not take montelukast sodium tablets and/or chewable tablets if you need relief right away for a sudden asthma attack. If you get an asthma attack, you should follow the instructions your healthcare provider gave you for treating asthma attacks.

Patient Information
Montelukast (mon-te-LOO-kast) Sodium Tablets, USP 10 mg
&
Montelukast Sodium Chewable Tablets, USP
4 mg & 5 mg

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gies that happen part of the year (seasonal allergic rhinitis) in adults and children ages older, **and**

ies that happen all year (perennial allergic rhinitis) in adults and children ages 2 years of age and

ontelukast sodium tablets and/or chewable tablets?

sodium tablets and/or chewable tablets if you are allergic to any of its ingredients.

let for a complete list of the ingredients in montelukast sodium tablets and montelukast sodium

ealthcare provider before taking montelukast sodium tablets and/or chewable tablets?

ast sodium tablets and/or chewable tablets, tell your healthcare provider if you:

spirin

onuria. Montelukast sodium chewable tablets contain aspartame, a source of phenylalanine

medical conditions

plan to become pregnant. Talk to your doctor if you are pregnant or plan to become pregnant, as dium tablets and/or chewable tablets may not be right for you.

ing or plan to breast-feed. It is not known if montelukast sodium passes into your breast milk. Talk are provider about the best way to feed your baby while taking montelukast sodium tablets and/or s.

vider about all the medicines you take, including prescription and non-prescription medicines, plements. Some medicines may affect how montelukast sodium works, or montelukast sodium r medicines work.

telukast sodium tablets and/or chewable tablets?

montelukast sodium tablets and/or chewable tablets:

st sodium tablets and/or chewable tablets exactly as prescribed by your healthcare provider. Your ider will tell you how much montelukast sodium to take, and **when to take it**.

ing montelukast sodium tablets and/or chewable tablets or change when you take it without talking care provider.

ontelukast sodium tablets and/or chewable tablets with food or without food.

hild misses a dose of montelukast sodium tablets and/or chewable tablets, just take the next egular time. Do not take 2 doses at the same time.

nuch montelukast sodium, call your healthcare provider or a Poison Control Center right away.

n 2 years of age and older with asthma:

st sodium tablets and/or chewable tablets 1 time each day, in the evening. Continue to take dium tablets and/or chewable tablets every day for as long as your healthcare provider prescribes ave no asthma symptoms.

care provider right away if your asthma symptoms get worse, or if you need to use your rescue e more often for asthma attacks.

ntelukast sodium tablets and/or chewable tablets if you need relief right away from a sudden If you get an asthma attack, you should follow the instructions your healthcare provider gave you ma attacks.

ur rescue inhaler medicine with you for asthma attacks.

ng or lower the dose of your other asthma medicines unless your healthcare provider tells you to.

age and older for the prevention of exercise-induced asthma:

st sodium tablets and/or chewable tablets at least 2 hours before exercise.

ur rescue inhaler medicine with you for asthma attacks.

telukast sodium tablets and/or chewable tablets every day for chronic asthma or allergic rhinitis, other dose to prevent exercise-induced asthma. Talk to your healthcare provider about your ercise-induced asthma.

doses of montelukast sodium tablets and/or chewable tablets within 24 hours (1 day).

2 years of age and older with seasonal allergic rhinitis, or for adults and children er with perennial allergic rhinitis:

st sodium tablets and/or chewable tablets 1 time each day, at about the same time each day.

ntelukast sodium tablets and chewable tablets?

sodium tablets and/or chewable tablets prescribed for you or your child's condition is based on age:

e 4-mg chewable tablet.

ne 5-mg chewable tablet.

der: one 10-mg tablet.

ile taking montelukast sodium tablets and/or chewable tablets?

aspirin makes your asthma symptoms worse, continue to avoid taking aspirin or other medicines inflammatory drugs (NSAIDs) while taking montelukast sodium tablets and/or chewable tablets.

side effects of montelukast sodium tablets and/or chewable tablets?

ay cause serious side effects.

-related changes. Tell your healthcare provider right away if you or your child have any of these ng montelukast sodium tablets and/or chewable tablets:

aggressive behavior or hostility

s

ns

Patient Information
Montelukast (mon-te-LOO-kast) Sodium Tablets, USP 10 mg
&
Montelukast Sodium Chewable Tablets, USP
4 mg & 5 mg

Read the Patient Information Leaflet that comes with montelukast sodium tablets and/or chewable tablets before you start taking it and each time you get a refill. There may be new information. This leaflet does not take the place of talking with your healthcare provider about your medical condition or your treatment.

What are montelukast sodium tablets and/or chewable tablets?

- Montelukast sodium tablets and/or chewable tablets are prescription medicines that block substances in the body called leukotrienes. This may help to improve symptoms of asthma and allergic rhinitis. Montelukast sodium tablets and/or chewable tablets do not contain a steroid.

Montelukast sodium tablets and/or chewable tablets are used to:

1. Prevent asthma attacks and for the long-term treatment of asthma in adults and children ages 2 years of age and older.

   Do not take montelukast sodium tablets and/or chewable tablets if you need relief right away for a sudden asthma attack. If you get an asthma attack, you should follow the instructions your healthcare provider gave you for treating asthma attacks.
2. Prevent exercise-induced asthma in people 6 years of age and older.
3. Help control the symptoms of allergic rhinitis (sneezing, stuffy nose, runny nose, itching of the nose). Montelukast sodium tablets and/or chewable tablets are used to treat:
   - outdoor allergies that happen part of the year (seasonal allergic rhinitis) in adults and children ages 2 years and older, **and**
   - indoor allergies that happen all year (perennial allergic rhinitis) in adults and children ages 2 years of age and older.

Who should not take montelukast sodium tablets and/or chewable tablets?

Do not take montelukast sodium tablets and/or chewable tablets if you are allergic to any of its ingredients.

See the end of this leaflet for a complete list of the ingredients in montelukast sodium tablets and montelukast sodium chewable tablets.

What should I tell my healthcare provider before taking montelukast sodium tablets and/or chewable tablets?

Before taking montelukast sodium tablets and/or chewable tablets, tell your healthcare provider if you:

- are allergic to aspirin
- have phenylketonuria. Montelukast sodium chewable tablets contain aspartame, a source of phenylalanine
- have any other medical conditions
- are pregnant or plan to become pregnant. Talk to your doctor if you are pregnant or plan to become pregnant, as montelukast sodium tablets and/or chewable tablets may not be right for you.
- are breast-feeding or plan to breast-feed. It is not known if montelukast sodium passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby while taking montelukast sodium tablets and/or chewable tablets.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. Some medicines may affect how montelukast sodium works, or montelukast sodium may affect how your other medicines work.

How should I take montelukast sodium tablets and/or chewable tablets?

For anyone who takes montelukast sodium tablets and/or chewable tablets:

- Take montelukast sodium tablets and/or chewable tablets exactly as prescribed by your healthcare provider. Your healthcare provider will tell you how much montelukast sodium to take, and **when to take it**.
- Do not stop taking montelukast sodium tablets and/or chewable tablets or change when you take it without talking with your healthcare provider.
- You can take montelukast sodium tablets and/or chewable tablets with food or without food.
- **If you or your child misses a dose of montelukast sodium tablets and/or chewable tablets, just take the next dose at your regular time**. Do not take 2 doses at the same time.
- If you take too much montelukast sodium, call your healthcare provider or a Poison Control Center right away.

For adults and children 2 years of age and older with asthma:

- Take montelukast sodium tablets and/or chewable tablets 1 time each day, in the evening. Continue to take montelukast sodium tablets and/or chewable tablets every day for as long as your healthcare provider prescribes it, even if you have no asthma symptoms.
- Tell your healthcare provider right away if your asthma symptoms get worse, or if you need to use your rescue inhaler medicine more often for asthma attacks.
- **Do not take montelukast sodium tablets and/or chewable tablets if you need relief right away from a sudden asthma attack**. If you get an asthma attack, you should follow the instructions your healthcare provider gave you for treating asthma attacks.
- Always have your rescue inhaler medicine with you for asthma attacks.
- Do not stop taking or lower the dose of your other asthma medicines unless your healthcare provider tells you to.

For patients 6 years of age and older for the prevention of exercise-induced asthma:

- Take montelukast sodium tablets and/or chewable tablets at least 2 hours before exercise.
- Always have your rescue inhaler medicine with you for asthma attacks.
- If you take montelukast sodium tablets and/or chewable tablets every day for chronic asthma or allergic rhinitis, **do not** take another dose to prevent exercise-induced asthma. Talk to your healthcare provider about your treatment for exercise-induced asthma.
- **Do not take 2 doses of montelukast sodium tablets and/or chewable tablets within 24 hours (1 day).**

For adults and children 2 years of age and older with seasonal allergic rhinitis, or for adults and children 2 years of age and older with perennial allergic rhinitis:

- Take montelukast sodium tablets and/or chewable tablets 1 time each day, at about the same time each day.

What is the dose of montelukast sodium tablets and chewable tablets?

The dose of montelukast sodium tablets and/or chewable tablets prescribed for you or your child's condition is based on age:

- 2 to 5 years: one 4-mg chewable tablet.
- 6 to 14 years: one 5-mg chewable tablet.
- 15 years and older: one 10-mg tablet.

What should I avoid while taking montelukast sodium tablets and/or chewable tablets?

If you have asthma and aspirin makes your asthma symptoms worse, continue to avoid taking aspirin or other medicines called non-steroidal anti-inflammatory drugs (NSAIDs) while taking montelukast sodium tablets and/or chewable tablets.

What are the possible side effects of montelukast sodium tablets and/or chewable tablets?

Montelukast sodium may cause serious side effects.

- **Behavior and mood-related changes**. Tell your healthcare provider right away if you or your child have any of these symptoms while taking montelukast sodium tablets and/or chewable tablets:
  - agitation including aggressive behavior or hostility
  - attention problems
  - bad or vivid dreams

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- depression
- disorientation (confusion)
- feeling anxious
- hallucinations (seeing or hearing things that are not really there)
- irritability
- memory problems
- restlessness
- sleep walking
- suicidal thoughts and actions (including suicide)
- tremor
- trouble sleeping
- uncontrolled muscle movements

- **Increase in certain white blood cells (eosinophils) and possible inflamed blood vessels throughout the body (systemic vasculitis)**. Rarely, this can happen in people with asthma who take montelukast sodium. This sometimes happens in people who also take a steroid medicine by mouth that is being stopped or the dose is being lowered.

Tell your healthcare provider right away if you get one or more of these symptoms:

- a feeling of pins and needles or numbness of arms or legs
- a flu-like illness
- rash
- severe inflammation (pain and swelling) of the sinuses (sinusitis)

The most common side effects with montelukast sodium tablets and/or chewable tablets include:

- upper respiratory infection
- fever
- headache
- sore throat
- cough
- stomach pain
- diarrhea
- earache or ear infection
- flu
- runny nose
- sinus infection

Other side effects with montelukast sodium tablets and/or chewable tablets include:

- increased bleeding tendency, low blood platelet count
- allergic reactions [including swelling of the face, lips, tongue, and/or throat (which may cause trouble breathing or swallowing), hives and itching]
- dizziness, drowsiness, pins and needles/numbness, seizures (convulsions or fits)
- palpitations
- nose bleed, stuffy nose, swelling (inflammation) of the lungs
- heartburn, indigestion, inflammation of the pancreas, nausea, stomach or intestinal upset, vomiting
- hepatitis
- bruising, rash, severe skin reactions (erythema multiforme, Stevens-Johnson syndrome/toxic epidermal necrolysis) that may occur without warning
- joint pain, muscle aches and muscle cramps
- bedwetting in children
- tiredness, swelling

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of montelukast sodium tablets and/or chewable tablets. For more information ask your healthcare provider or pharmacist.

Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store montelukast sodium tablets and/or chewable tablets?

- Store montelukast sodium tablets and/or chewable tablets at 59°F to 86°F (15°C to 30°C).
- Keep montelukast sodium tablets and/or chewable tablets in the container it comes in.
- Keep montelukast sodium tablets and/or chewable tablets in a dry place and away from light.

General Information about the safe and effective use of montelukast sodium tablets and/or chewable tablets

Medicines are sometimes prescribed for purposes other than those mentioned in Patient Information Leaflets. Do not use montelukast sodium tablets and/or chewable tablets for a condition for which it was not prescribed. Do not give montelukast sodium tablets and/or chewable tablets to other people even if they have the same symptoms you have. It may harm them. **Keep montelukast sodium tablets and/or chewable tablets and all medicines out of the reach of children**.

This leaflet summarizes information about montelukast sodium tablets and/or chewable tablets. If you would like more information, talk to your healthcare provider. You can ask your pharmacist or healthcare provider for information about montelukast sodium tablets and/or chewable tablets that is written for health professionals. For more information, call **Par Pharmaceutical at 1-800-828-9393.**

What are the ingredients in montelukast sodium tablets and chewable tablets?

Active ingredient: montelukast sodium

Inactive ingredients:

- 10-mg tablet: croscarmellose sodium, hydroxypropyl cellulose, lactose monohydrate, magnesium stearate, and silicified microcrystalline cellulose. The film coating contains: hydroxypropyl cellulose, hypromellose, red ferric oxide, titanium dioxide and yellow ferric oxide.
- 4-mg and 5-mg chewable tablets: aspartame, croscarmellose sodium, flavor black cherry, hydroxypropyl cellulose, magnesium stearate, mannitol, red ferric oxide, and silicified microcrystalline cellulose.

People with Phenylketonuria: montelukast sodium 4-mg chewable tablets contain 1.2 mg of phenylalanine, and montelukast sodium 5-mg chewable tablets contain 1.5 mg of phenylalanine.

Distributed by:
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Chestnut Ridge, NY 10977

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