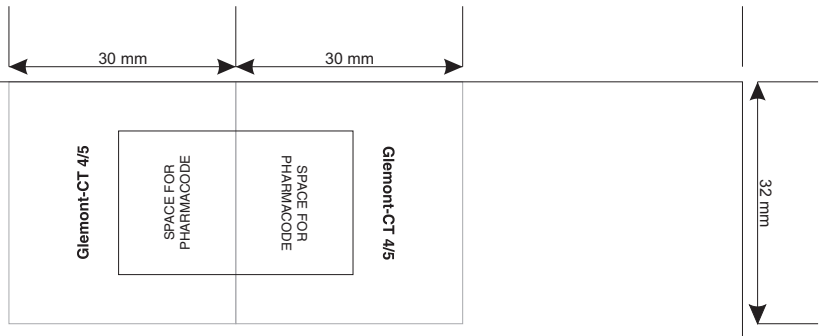
SAME SIZE ARTWORK
LEAFLET SIZE : 176 mm x 220 mm



important effects on the pharmacokinetics of the following drugs: theophylline, prednisone. Prednisolone, oral contraceptives (norethindrone 1 mg/ethinyl estradiol 35 mcg), terfenadine, digoxin, and warfarin.

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.

Phenobarbital, which induces hepatic metabolism, decreased the AUC of Montelukast approximately 40% following a single 10-mg dose of Montelukast. No dosage adjustment for Montelukast is recommended. It is reasonable to employ appropriate clinical monitoring when potent cytochrome P450 enzyme inducers, such as phenobarbital or rifampin, are coadministered with Montelukast.

DOSAGE AND METHOD OF ADMINISTRATION

Montelukast is a long term-controller medication which should not be substituted for short acting beta-agonists. It is effective alone or in combination with other prophylactic agent. Montelukast is a preventive agent, which should be used in addition to other drugs for the management of asthma should be taken once daily. Montelukast should be taken once daily. For asthma, the dose should be taken in the evening. For allergic rhinitis the time of administration may be individualized to suit patient needs. Patients with both asthma and allergic rhinitis should take only one tablet daily in the evening.

Adults and Adolescents 15 Years of Age and Older with Asthma or Allergic Rhinitis
The dosage for adults and adolescents 15 years of age and older is 1 0-mg daily.

Pediatric Patients 6 to 14 Years of Age with Asthma or Allergic Rhinitis
The dosage for pediatric patients 6 to 14 years of age is one 5-mg chewable tablet daily. No dosage adjustment within this age group is necessary.

Pediatric Patients 2 to 5 Years o f Age with Asthma or Allergic Rhinitis
The dosage for pediatric patients 2 to 5 years of age is one 4-mg chewable tablet daily.

Route of Administration: Oral

OVERDOSE

No mortality occurred following single oral doses of Montelukast up to 5000 mg/kg in mice (estimated exposure was approximately 335 and 210 times the AUC for adults and children, respectively, at the maximum recommended daily oral dose) and rats (estimated exposure was approximately 230 and 145 times the AUC for adults and children. respectively, at the maximum recommended daily oral dose).

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 pediatric patients in post-marketing experience and clinical studies of up to at least 150 mg/day with Montelukast. 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, mydriasis, hyperkinesia. and abdominal pain.

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

PACKING / PACK SIZE
HDPE bottle of 30 tablets

SHELF-LIFE
24 months

SPECIAL PRECAUTIONS FOR STORAGE
Store below 30°C. Protect from moisture and light

Date of Revision: 27/05/2022

Product Registration Holder
Glenmark Pharmaceuticals (Malaysia)
Sdn Bhd (660397-W)
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Manufactured by:
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Colvale, Bardez, Goa - 403 513.
® Registered Trade Mark

PE00000 MY

For the use only of a Registered Medical Practitioner or a Hospital or a laboratory

Glemont®-CT 4/5

Montelukast Chewable Tablets 4/5 mg

COMPOSITION
Each uncoated tablet contains:
Montelukast sodium equivalent to 4 mg Montelukast
Also includes mannitol and aspartame equivalent to 0.674 mg of phenylalanine.

DESCRIPTION
Oval, white to off white coloured, biconvex uncoated tablets engraved with “G” on one side and “390” on other side.

GLEMONT CT5
(MONTELUKAST CHEWABLE TABLETS 5MG)

COMPOSITION
Each uncoated tablet contains:
Montelukast sodium equivalent to 5 mg Montelukast
Also includes mannitol and aspartame equivalent to 0.842 mg of phenylalanine.

DESCRIPTION
Round, white to off white coloured, biconvex uncoated tablets engraved with “G” on one side and “391” on other side.

PHARMACOLOGY
Pharmacodynamic
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 (CysLT1) receptor is found in the human airway (including airway smooth muscle cells and airway macrophages) and on other pro- inflammatory cells (including eosinophils and certain myeloid stem cells). CysLTs have been correlated with the pathophysiology of asthma and allergic rhinitis. 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- late-phase reactions and are associated with symptoms of allergic rhinitis. Intranasal challenge with CysLTs has been shown to increase nasal airway resistance and symptoms of nasal obstruction. Montelukast has not been assessed in intranasal challenge studies. The clinical relevance of intranasal challenge studies is unknown.

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.

Pharmacokinetic properties
Absorption: Montelukast is rapidly absorbed following oral administration. The oral bioavailability
and Cmax are not influenced by a standard meal in the morning.

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

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 and 2C9 are involved in the metabolism of Montelukast. Clinical studies investigating the effect of known inhibitors of cytochromes P450 3A4 (e.g., ketoconazole, erythrornycin) 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.

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 rnontelukasl oral bioavailability, this indicates that Montelukast and its metabolites are excreted almost exclusively via the bile.

ICONGRAPHICS CODE:

PANTONE SHADE
PANTONE BLACK PROCESS C
Supersedes Artwork Code

PHARMACODE:

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Glemont-CT 4/5

SPACE FOR PHARMACODE

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Glemont-CT 4/5

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.

SPECIAL POPULATIONS

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

Elderly: The plasma half-life of Montelukast is slightly longer in the elderly. No dosage adjustment in the elderly is required.

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

Hepatic insufficiency: 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.

Adolescents and Pediatric Patients: The mean systemic exposure of 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.

INDICATIONS

Montelukast is indicated for the prophylaxis & chronic treatment of asthma in adults & pediatric patients 12 months of age & older. Montelukast is indicated in adults & pediatric patients 2 years of age & older for the relief of daytime & nighttime symptoms of seasonal allergic rhinitis.

CONTRA-INDICATIONS

Hypersensitivity to any component of this product

UNDESIRABLE EFFECTS

Gelmont has been generally well tolerated. Side effects which were usually mild generally did not require discontinuation of therapy. The overall incidence of side effects reported with Glemont was similar to placebo.

Adults 15 years of age and older with Asthma

Montelukast has been evaluated in approximately 2600 adult patients 15 years of age and older in clinical studies. In two similarly designed 12 week placebo controlled clinical studies, the adverse experiences reported as drug related in ≥ 1% of patients treated with Montelukast and at a greater incidence than in patients treated with placebo were abdominal pain and headache. The incidences of these events were not significantly different in the two treatment groups.

Cumulatively 544 patients were treated with Montelukast for atleast 6 months, 253 for 1 year and 21 for 2 years in clinical studies. With prolonged treatment, the adverse experience profile did not change.

Pediatric Patients 6 to 14 Years of Age with Asthma

Montelukast has been evaluated for safety in 476 pediatric patients 6 to 14 years of age. Cumulatively, 289 pediatric patients were treated with SINGULAIR for at least 6 months, and 241 for one year or longer in clinical trials. The safety profile of Montelukast in the 8-week, doubleblind, 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 frequency of less common adverse events was comparable between Montelukast and placebo. With prolonged treatment, the adverse experience profile did not significantly change.

In studies evaluating growth rate, the safety profile in these pediatric patients was consistent with the safety profile previously described for Montelukast.

Cumulatively, 263 patients 6 to 14 years of age were treated with Montelukast for at least 3 months and 164 for 6 months or longer. With prolonged treatment, the adverse event profile didn't change.

Pediatric Patients 2 to 5 Years of Age with Asthma

Montelukast has been evaluated for safety in 573 pediatric patients 2 to 5 years of age in singleand multiple-dose studies. In a 12 week placebo controlled clinical study, the only adverse experience reported as drug related in > 1% of patients treated with Montelukast and at a greater incidence than in patients treated with placebo thirst. The incidence of thirst was not significantly different in the two treatment groups.

In a 12 month, placebo controlled clinical study (PREvention of Viral Induced Asthma - PREVIA), the safety profile was consistent with the safety profile previously described for Montelukast.

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. With prolonged treatment the adverse effect profile did not change.

Pediatric Patients 6 to 2 years of age with asthma

Montelukast has been evaluated for safety in 175 pediatric patients 6 to 2 years of age. In a 6- week, placebo-controlled clinical study the adverse experiences reported as drug related in > 1% of patients treated with Montelukast and at a greater incidence than in patients treated with pacebo were diarrhoea, hyperkinesia, asthma, eczematous dermatitis and rash. The incidence of these adverse experiences were not significantly different in the two treatment groups.

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

Montelukast has been evaluated for safety in 2199 adult and adolescent patients 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.

Pediatric Patients 2 to 14 Years of Age with Seasonal Allergic Rhinitis

Montelukast has been evaluated in 280 pediatric patients 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.

Adults and Adolescents 15 Years of Age and Older with 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 SINGULAIR 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 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. 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

Psychiatric disorders

obsessive-compulsive symptoms

Blood and lymphatic system disorders: thrombocytopenia

SPECIAL WARNING AND PRECAUTIONS FOR USE

Montelukast is not indicated for use in the reversal of bronchospasm in acute asthma attacks, including status asthmaticus. Patients should be advised to have appropriate rescue medication available.

Therapy with Montelukast can be continued during acute exacerbations of asthma.

While the dose of inhaled corticosteroid may he reduced gradually under medical supervision.

Montelukast should not be abruptly substituted for inhaled or oral corticosteroids.

Montelukast should not be used as monotherapy for the treatment and management of exercise induced bronchospasm. Patients who have exacerbations of asthma after exercise should continue to use their usual regimen of inhaled (beta)-agonists as prophylaxis and have available for rescue a short-acting inhaled (beta)-agonist.

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

In rare cases, 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.

Phenylketonurics

Aspartame is unsuitable for Phenylketonurics.

Pregnancy

Category B : No teratogenicity was observed in rats at oral doses up to 400 mg/kg/day (estimated exposure was approximately 100 times the AUC for adults at the maximum recommended daily oral dose) and in rabbits at oral doses up to 300 mg/kg/day (estimated exposure was approximately 110 times the AUC for adults at the maximum recommended daily oral dose). Montelukast crosses the placenta following oral dosing in rats and rabbits. There are, however, 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.

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.

Effects on ability to drive and use machine.

Montelukast has no or negligible influence on the ability to drive and use machines. However, individuals have reported drowsiness or dizziness.

INTERACTION WITH OTHER DRUGS, OTHER FORM OF INTERACTIONS

Montelukast 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

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Supersedes Artwork Code

PHARMACODE: