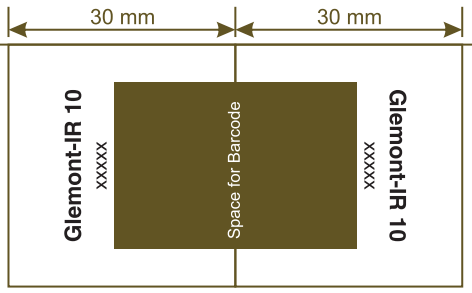

45 and 25 times the AUC for adults and children, respectively, at the maximum recommended daily oral dose.

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.

In fertility studies in female rats, montelukast produced reductions in fertility and fecundity indices at an oral dose of 200 mg/kg (estimated exposure was approximately 70 times the AUC for adults at the maximum recommended daily oral dose). No effects on female fertility or fecundity were observed at an oral dose of 100 mg/kg (estimated exposure was approximately 20 times the AUC for adults at the maximum recommended daily oral dose). Montelukast had no effects on fertility in male rats at oral doses up to 800 mg/kg (estimated exposure was approximately 160 times the AUC for adults at the maximum recommended daily oral dose).

SYMPTOMS AND TREATMENT FOR OVERDOSAGE AND ANTIDOTE (S) 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 SIZES
1. HDPE Bottle of 30 Tablets
2. 10's Alu/Alu Blister X 3
   10's Alu/Alu Blister X 10

SHELF LIFE
24 months
Store below 30°C. Protect from moisture and light.

Product Registration Holder:
Glenmark Pharmaceuticals (Malaysia) Sdn bhd (660397-W)
D-31-2, Menara Suezcap 1, No. 2, Jalan Kerinchi,
59200, Kuala Lumpur, Malaysia.

Glenmont - IR 10 - MAL10120031AZ

Date of Revision: 26.01.2024

MANUFACTURED BY:
glenmark
PHARMACEUTICALS LTD.
B/2, Mahalaxmi Chambers,
22, Bhulabhai Desai Road,
Mumbai - 400 026, (India).
AT: Plot No. S-7,
Colvale Industrial Estate,
Colvale, Bardez, Goa - 403 513.
™ Trade Mark

PE00000 MY

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

Montelukast Tablets 10 mg
Glemont™ - IR 10

Composition:
Each film coated tablet contains:
Montelukast Sodium equivalent to 10 mg Montelukast
Also contains lactose monohydrate and titanium dioxide

THERAPEUTIC CLASS
R03DC03

DESCRIPTION
Round, beige coloured, biconvex film coated tablets engraved with 'G' on one side & '392' on other side.

DOSAGE FORM
Tablet

PHARMACOLOGY
Pharmacodynamics:
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. 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.

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.

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, erythromycin) or 2C9 (e.g., fluconazole) on montelukast pharmacokinetics have not been conducted. Based on further in vitro results in human liver microsomes, therapeutic plasma concentrations of montelukast do not inhibit cytochromes P450 3A4, 2C9, 1A2, 2A6, 2C19, or 2D6. However, in vitro studies have shown that montelukast is a potent inhibitor of cytochrome P450 2C8.

220 mm

170 mm

GLENMARK PHARMACEUTICALS LTD.	DATE: 31.01.2024	PANTONE SHADE NO: Black	
PRODUCT NAME: LEAFLET GLEMONT-IR 10 MY	PKG. DEV.:	Item code, Version, Consistency of Design, overprint area, Pack size, Dimensions & Layout	
ITEM CODE: PE000 VERSION:	RA	Regulatory Text	
PHARMACODE: NA BARCODE: YES	PRODUCTION:	Machine Suitability	
COUNTRY: US	QA:	Entire Text	
LOCATION: Goa	REMARKS: NA		
PACK : folded,gluing:30X32MM			
ACTUAL SIZE: 170X220 MM			
SPECIFICATION: 40 GSM Bible Paper			

FCPDC001/01.00

Glemont-IR 10
XXXXX

Glemont-IR 10
XXXXX

220 mm

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

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

Elderly: 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.

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

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 area under the plasma concentration curve (AUC) following a single 10-mg dose. The elimination of montelukast was slightly prolonged compared with that in healthy subjects (mean half-life, 7.4 hours). No dosage adjustment is required in patients with mild-to-moderate hepatic insufficiency. The pharmacokinetics of montelukast in patients with more
severe hepatic impairment or with hepatitis have not been evaluated.

Renal Insufficiency: Since montelukast and its metabolites are not excreted in the urine, the pharmacokinetics of montelukast were not evaluated in patients with renal insufficiency. No dosage adjustment is recommended in these patients.
Adolescents and Pediatric Patients: 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.

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.

CONTRAINDICATIONS

Hypersensitivity to any component of this product

SIDE EFFECTS / ADVERSE REACTIONS

Cardiovascular rarely can cause allergic granulomatosis angiitis, however this could be severe and might require hospitalization for treatment.
Dermatologic Infrequently maculopopular rash.
Gastrointestinal - Less frequently can cause dyspepsia, gastroenteritis.
Hepatic Can be hepatotoxic. Very rarely causes cholestatic hepatitis.
Neurologic Asthenia, headache, hyperactive behavior, hyperaesthesia, insomnia, parasthesia and tremors.
Psychiatric can rarely cause aggressive behavior, agitation, altered behavior, anxiety, depression, dream, feeling nervous, hallucinations, hyperactive behavior, irritability, nightmares, restlessness, sleep disorder, suicidal thoughts.
Respiratory - Less frequently upper respiratory tract infections, congestion and cough.
Miscellaneous fatigue and malaise

PRECAUTIONS / WARNINGS

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 be 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.

DRUG INTERACTION

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 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 co-administered with montelukast

RECOMMENDED DOSAGE, DOSAGE SCHEDULE AND ROUTE 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. 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
Route of administration: Oral

USE IN SPECIAL POPULATIONS

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.

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 is given to a nursing mother.

CARCINOGENESIS, MUTAGENESIS AND 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 area under the plasma concentration versus time curve (AUC) for adults and children, respectively, at the maximum recommended daily oral dose. The estimated exposure in mice was approximately

PE00000 **MY**

170 mm

GLENMARK PHARMACEUTICALS LTD.	**DATE:** 31.01.2024	**PANTONE SHADE NO:** Black	
PRODUCT NAME: LEAFLET GLEMONT-IR 10 MY	**PKG. DEV.:**	Item code, Version, Consistency of Design, overprint area, Pack size, Dimensions & Layout	
ITEM CODE: PE000 **VERSION:**	**RA**	Regulatory Text	
PHARMACODE: NA **BARCODE:** YES	**PRODUCTION:**	Machine Suitability	
COUNTRY: US	**QA:**	Entire Text	
LOCATION: Goa	**REMARKS:** NA		
PACK : folded,gluing:30X32MM			
ACTUAL SIZE: 170X220 MM			
SPECIFICATION: 40 GSM Bible Paper			

FCPDC001/01.00