growth and development was observed in rabbits dosed at 200 mg/kg/day, a dose level associated with severe maternal toxicity. Foetal exposure of montelukast was demonstrated in both species. Lukomon has not been studied in pregnant women. Lukomon should be used during pregnancy only if clearly needed.

Use in Lactation
Studies in lactating rats have shown that montelukast is excreted into milk following oral doses of 100 and 200 mg/kg/day, and growth of the pups was slightly inhibited at the higher dose level. It is not known if Lukomon is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Lukomon is given to a nursing mother.

Use in the Elderly
In clinical studies, there were no age-related differences in the efficacy or safety profiles of Lukomon

Interactions with other drugs
Relatively high concentrations of montelukast competitively inhibit the activity of cytochromes P450 3A4 and 2C9. However, these concentrations are at least 15 fold higher than the peak plasma concentrations attained following a 10 mg oral dose of montelukast. Theophylline plasma concentration was not affected by the recommended dose of Lukomon (10 mg once daily). At 20 and 60 fold above the recommended dose, plasma concentration of concomitant theophylline was decreased. Theophylline dose adjustment or a change in the frequency of plasma theophylline monitoring is not necessary at the recommended dose of Lukomon.

Lukomon may be administered with other therapies routinely used in the prophylaxis and chronic treatment of asthma, and in the treatment of allergic rhinitis. In drug-interactions 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 (ethinyl estradiol/ norethisterone 35/1), terfenadine, digoxin and warfarin. The effects of concomitant administration of montelukast and macrolide antimicrobials have not been studied.

ADVERSE REACTIONS

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

DOSAGE AND ADMINISTRATION

Asthma and/or Seasonal Allergic Rhinitis

Use in Children
In asthma :
Lukomon has been studied in paediatric patients six months to 14 years of age). Safety and effectiveness in paediatric patients younger that six months of age have not been studied.

In seasonal allergic rhinitis :
Lukomon has been studied in paediatric patients 2 to 14 years of age. Safety in paediatric patients younger than two years of age has not been studied.

Lukomon should be taken once daily.

For asthma, the dose should be taken in the evening.

For seasonal allergic rhinitis, the time of administration may be individualized to suit patient needs. Patients with both asthma and seasonal allergic rhinitis should take only one tablet daily in the evening.

Age	Dose
6 months - 5 years	one 4 mg sachet daily.
6-14 years	one 5 mg chewable tablet daily.
15 years & older	one 10 mg film coated tablet daily.

General Recommendations
The therapeutic effect of Lukomon on parameters of asthma control occurs within one day. Lukomon may be taken with or without food. Patients should be advised to continue taking Lukomon daily when their asthma is controlled, as well as during periods of worsening asthma.

No dosage adjustment is necessary for paediatric patients, for the elderly, for patients with renal insufficiency, or mild to moderate hepatic impairment, or for patients of either gender.

Therapy with Lukomon in Relation to Other Treatments for Asthma

Lukomon can be added to a patient's existing treatment regimen. Reduction in Concomitant Therapy:

Inhaled Corticosteroids :
Treatment with Lukomon provides additional clinical benefit to patients treated with inhaled corticosteroids. A reduction in the corticosteroid dose can be made as tolerated. The dose should be reduced gradually with medical supervision. In some patients, the dose of inhaled corticosteroids can be tapered off completely. Lukomon should not be abruptly substituted for inhaled corticosteroids.

Bronchodilator Treatments:
Lukomon can be added to the treatment regimen of patients who are not adequately controlled on bronchodilator alone. When a clinical response is evident (usually after the first dose), the patient's bronchodilator therapy can be reduced as tolerated.

OVERDOSAGE

No specific information is available on the treatment of overdosage with Lukomon. In chronic asthma studies, Lukomon 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 one week without clinically important adverse experiences.

There have been reports of acute overdosage in postmarketing experience and clinical studies with Lukomon. 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 paediatric 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 Lukomon and included abdominal pain, somnolence, thirst, headache, vomiting, and psychomotor hyperactivity.

It is not known whether montelukast is dialyzable by peritoneal or hemodialysis.

STORAGE

Store below 30°C in a dry place, protect from light.
To be dispensed on the prescription of a registered medical practitioner only.
Keep out of the reach of children

PRESENTATION

Lukomon 4 mg sachet : Available in sachet 1 x 14's:
Lukomon 5 mg Chewable Tablets : Available in Alu-Alu blister pack of 1 x 14's:
Lukomon 10 mg Film coated Tablets : Available in Alu-Alu blister pack of 1 x 14's:

دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر روشنی سے بچا کر خشک جگہ پر رکھیں۔
صرف مستند معالج کے نسخے پر فروخت کریں۔
بچوں کی پہنچ سے دور رکھیں۔

Manufactured by:
Platinum
Pharmaceuticals (Pvt.) Ltd.
A 20,North Western Industrial Zone,
Bin Qasim, Karachi-75020, Pakistan.

QAR No.AW17-0383

LUKOMON

(Montelukast Sodium)

Tablets & Sachet

لیوکومون

(مونٹیلوکاسٹ سوڈیم)

گولیاں اور ساشے

COMPOSITION

Lukomon sachet 4 mg
Each sachet contains:
Montelukast sodium (U.S.P.)
equivalent to Montelukast ..... 4 mg

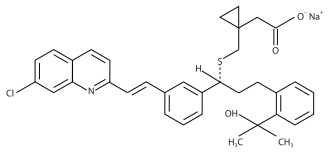
Product Complies U.S.P. Specs.

Lukomon chewable Tablets 5 mg
Each chewable tablet contains:
Montelukast sodium (U.S.P.)
equivalent to Montelukast ..... 5 mg

Product Complies U.S.P. Specs.

Lukomon Tablets 10 mg
Each film coated tablet contains:
Montelukast sodium (U.S.P.)
equivalent to Montelukast ..... 10 mg

Product Complies U.S.P. Specs.



DESCRIPTION

Lukomon (montelukast sodium) is a selective and orally active leukotriene receptor antagonist that specifically inhibits the cysteinyl leukotriene $CysLT_1$ receptor.

PHARMACOLOGY

Pharmacodynamics
The cysteinyl leukotrienes (LTC_4, LTD_4, LTE_4), are potent inflammatory eicosanoids released from various cells including mast cells and eosinophils. These important pro -asthmatic mediators 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 a number of airway actions, including bronchoconstriction, mucous secretion, vascular permeability, and eosinophil recruitment. 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. The clinical relevance of intranasal challenge studies is unknown.

Montelukast is an orally active compound which has been shown in asthmatic patients to reduce peripheral blood eosinophil counts and sputum eosinophils , which are parameters of asthmatic inflammation. The effect of montelukast on reduction of peripheral blood eosinophils was comparable to inhaled corticosteroids. Based on biochemical and pharmacological bioassays, it 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 potently inhibits physiologic actions of LTC_4, LTD_4, and LTE_4 at the $CysLT_1$ receptor without any agonist activity.

In asthmatic patients, montelukast causes potent inhibition of airway cysteinyl leukotriene receptors as demonstrated by the ability to inhibit bronchoconstriction due to inhaled LTD_4. A dose of 5 mg causes substantial blockage of LTD_4-induced bronchoconstriction. Montelukast causes bronchodilation within 2 hours of oral administration. β-agonists caused additive effects when added to montelukast.

Pharmacokinetics

Absorption
Montelukast is rapidly and nearly completely absorbed following oral administration. For the 10 mg film-coated tablet, the mean peak plasma concentration (C_{max}) is achieved 3 hours (Tmax) after administration in adults in the fasted state. The mean oral bioavailability is 64%. The oral bioavailability and Cmax are not influenced by a standard meal.

For the 5 mg chewable tablet, the Cmax is achieved in 2 hours after administration in adults in the fasted state. The mean oral bioavailability is 73% and is decreased to 63% by a standard meal. This is unlikely to have any clinical significance with chronic administration. Efficacy was demonstrated in clinical studies in children where the montelukast 5 mg chewable tablet was administered irrespective of food.

For the 4 mg sachet, Cmax is achieved 2 hours after the administration in paediatric patients 2 to 5 years of age in the fasted state.

Safety and efficacy were demonstrated in clinical studies where the 4 mg sachet , 5 mg chewable tablet, and 10 mg film-coated tablet were administered without regard to the timing of food ingestion.

The 10 mg film coated tablets of montelukast are not bioequivalent to two 5 mg chewable tablets, and these two products should not be used interchangeably.

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 (<20 ng/mL) at steady state in adults and children. Further studies showed that relatively high concentrations of montelukast competitively inhibit the activity of cytochromes P450 3A4 and 2C9. However, these concentrations are at least 15 fold higher than the peak plasma concentrations attained following a 10 mg oral dose of montelukast. Based on these and other in vitro results in human liver microsomes, therapeutic plasma concentrations of montelukast should not be expected to inhibit cytochromes P450, 3A4, 2C9, 1A2, 2A6, 2C19 or 2D6.

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%).

INDICATIONS

- Prophylaxis and treatment of chronic asthma in adults and children 2 years of age and older.
- Symptomatic treatment of seasonal allergic rhinitis.

CONTRAINDICATIONS

Hypersensitivity to any component of this product.

PRECAUTIONS

The efficacy of oral Lukomon for the treatment of acute asthma attacks has not been established. Therefore, oral tablets of Lukomon should not be relied upon to treat acute asthma attacks. Patients should be advised to have appropriate rescue medication available.

Use in Pregnancy (Category B1)
In animal studies, montelukast sodium had no adverse effects on embryofoetal development at oral doses up to 400 mg/kg/day in rats or up to 100 mg/kg/day in rabbits. Retardation of foetal