Pharmacode position may change as per Supplier's m/c requirement & additional small pharma code may appear on the front / back panel

SUMMARY OF PRODUCT CHARACTERISTICS

M-KAST 10

Montelukast Tablets 10 mg

Rx Only

NAME OF DRUG PRODUCT: Montelukast Tablets 10 mg.

(TRADE) NAME OF PRODUCT: M-KAST 10

STRENGTH: 10 mg.

PHARMACEUTICAL DOSAGE FORM: Tablet.

QUALITATIVE AND QUANTITATIVE COMPOSITIONS:
Montelukast Tablets 10 mg:
Each film coated tablet contains Montelukast Sodium is equivalent to Montelukast 10 mg.

PHARMACEUTICAL FORM:
Montelukast Tablets 10 mg: Beige, rounded square shaped, film coated tablets debossed with 'X' on one side and '54' on other side.

CLINICAL PARTICULARS:
Therapeutic indications
Montelukast is indicated in adult for the prophylaxis and chronic treatment of asthma, including the prevention of day- and nighttime symptoms, the treatment of aspirin-sensitive asthmatic patients, and the prevention of exercise-induced bronchoconstriction.

Montelukast is indicated for the relief of daytime and nighttime symptoms of allergic rhinitis (seasonal allergic rhinitis in adults). Because the benefits of Montelukast may not outweigh the risk of neuropsychiatric symptoms in patients with allergic rhinitis, reserve use for patients who have an inadequate response or intolerance to alternative therapies.

Posology and method of administration
The recommended dose for adults and adolescents 15 years of age and older with asthma, or with asthma and concomitant seasonal allergic rhinitis, is one 10 mg tablet daily to be taken in the evening.

General recommendations. The therapeutic effect of Montelukast on parameters of asthma control occurs within one day. Montelukast may be taken with or without food. Patients should be advised to continue taking Montelukast even if their asthma is under control, as well as during periods of worsening asthma. Montelukast should not be used concomitantly with other products containing the same active ingredient, Montelukast.

No dosage adjustment is necessary for the elderly, or for patients with renal insufficiency, or mild to moderate hepatic impairment. There are no data on patients with severe hepatic impairment. The dosage is the same for both male and female patients.

Therapy with Montelukast in relation to other treatments for asthma
M-KAST 10 can be added to a patient's existing treatment regimen.

Bronchodilator Treatments: M-KAST-10 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.

Inhaled corticosteroids: Treatment with M-KAST-10 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.

Paediatric population
Do not give M-KAST 10 tablets to children less than 15 years of age. The safety and efficacy of M-KAST 10 tablets in children less than 15 years has not been established.
5 mg chewable tablets are available for paediatric patients 6 to 14 years of age.
4 mg chewable tablets are available for paediatric patients 2 to 5 years of age.
4 mg granules are available for paediatric patients 6 months to 5 years of age.

Method of administration
Oral use.

Contraindications
Hypersensitivity to the active substance or to any of the excipients.

Special warnings and precautions for use
Patients should be advised never to use oral Montelukast to treat acute asthma attacks and to keep their usual appropriate rescue medication for this purpose readily available. If an acute attack occurs, a short-acting inhaled β-agonist should be used. Patients should seek their doctor's advice as soon as possible if they need more inhalations of short-acting β-agonists than usual.

Montelukast should not be substituted for inhaled or oral corticosteroids.

In rare cases, patients on therapy with anti-asthma agents including montelukast may present with one or more of the following: eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications and/or neuropathy sometimes diagnosed as Churg- Strauss syndrome, a systemic eosinophillic vasculitis. These cases have been sometimes associated with the reduction or withdrawal of oral corticosteroid therapy.

Although a causal relationship with leukotriene receptor antagonism has not been established, caution and appropriate clinical monitoring are recommended in patients receiving montelukast .

Neuropsychiatric events have been reported in patients taking Montelukast (see SIDE EFFECTS). Post-marketing reports with Montelukast use include agitation including aggressive behavior or hostility, anxiousness, depression, disorientation, disturbance in attention, dream abnormalities, dysphemia (stuttering), hallucinations, insomnia, memory impairment, obsessive-compulsive symptoms, psychomotor hyperactivity (including irritability, restlessness and tremor), somnambulism, suicidal thinking and behavior (suicidality) and tic. The clinical details of some post-marketing reports involving Montelukast appear consistent with a drug-induced effect.

These neuropsychiatric events have been reported in patients with and without a previous history of psychiatric disorder. Neuropsychiatric events have been reported mostly during Montelukast treatment, but some were reported after Montelukast discontinuation. Based upon the available data, it is difficult to identify risk factors for or quantify the risk of neuropsychiatric events with Montelukast use.

Physicians should discuss the benefits and risks of Montelukast use with patients and caregivers when prescribing Montelukast. Patients and/or caregivers should be advised to be alert for changes in behavior or for new neuropsychiatric symptoms when taking Montelukast. If changes in behavior are observed, or if new neuropsychiatric symptoms or suicidal thoughts and/or behavior occur, patients should be advised to contact a healthcare provider immediately. In many cases, symptoms resolved after stopping Montelukast therapy; however, in some cases symptoms persisted after discontinuation of Montelukast. Therefore, patients should be monitored and provided supportive care until symptoms resolve.

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 β-agonists as prophylaxis and have available for rescue a short-acting inhaled β-agonist.

Treatment with Montelukast does not alter the need for patients with aspirin- sensitive asthma to avoid taking aspirin and other non-steroidal anti-inflammatory drugs.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose galactose mal absorption should not take this medicine.

Prescribers should carefully evaluate the risks and benefits of continuing treatment with Montelukast if such events occur.

Interaction with other medicinal products and other forms of interaction
Montelukast may be administered with other therapies routinely used in the prophylaxis and chronic treatment of asthma. In drug-interactions studies, the recommended clinical dose of montelukast did not have clinically important effects on the pharmacokinetics of the following medicinal products: theophylline, prednisone, prednisolone, oral contraceptives (ethinyl estradiol/norethindrone 35/1), terfenadine, digoxin and warfarin.

The area under the plasma concentration curve (AUC) for montelukast was decreased approximately 40% in subjects with co-administration of phenobarbital. No dosage adjustment for M-Kast is recommended.

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

In vitro studies have shown that montelukast is a substrate of CYP 2C8, 2C9, and 3A4. In a clinical drug-drug interaction study involving montelukast and gemfibrozil (an inhibitor of both CYP 2C8 and 2C9) gemfibrozil increased the systemic exposure of montelukast by 4.4-fold. Co-administration of itraconazole, a strong CYP 3A4 inhibitor, with gemfibrozil and montelukast did not further increase the systemic exposure of montelukast. The effect of gemfibrozil on systemic exposure of montelukast is not considered to be clinically meaningful based on clinical safety data with doses greater than the 10 mg approved dose in adults (e.g., 200 mg/day to adult patients for 22 weeks, and up to 900 mg/day to patients for approximately one week) where clinically important adverse experiences were not observed. Therefore, no dosage adjustment of montelukast is required upon co-administration with gemfibrozil.

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

Fertility, Pregnancy and lactation.
Pregnancy
Limited data from available pregnancy databases do not suggest a causal relationship between Montelukast and malformations (i.e. limb defects) that have been rarely reported in worldwide post-marketing experience.

Montelukast may be used during pregnancy only if it is considered to be clearly essential.

Breast feeding

It is unknown whether montelukast/metabolites are excreted in human milk.

Montelukast may be used in breast-feeding only if it is considered to be clearly essential.

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

Undesirable effects
Montelukast 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 Montelukast was comparable 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 only 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 at least 6 months, 253 for one year and 21 for 2 years in clinical studies. With prolonged treatment, the adverse experience profile did not change.

Adults 15 Years of Age and Older with Seasonal Allergic Rhinitis
Montelukast has been evaluated in 2199 adult patients 15 years of age and older for the treatment of seasonal allergic rhinitis in clinical studies. Montelukast administered once daily in the morning or in the evening was generally well tolerated with a safety profile similar to that of placebo. In placebo-controlled, clinical studies, no 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 observed. 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.

Adults 15 Years of Age and Older with Asthma and Seasonal Allergic Rhinitis
Montelukast 10-mg film-coated tablets have been evaluated in approximately 400 asthmatic patients 15 years of age and older with seasonal allergic rhinitis. The safety profile in asthmatic patients with seasonal allergic rhinitis was consistent with that observed in patients with asthma.

Adults 15 Years of Age and Older with Perennial Allergic Rhinitis
Montelukast has been evaluated in 3235 adult and adolescent patients 15 years of age and older with perennial allergic rhinitis in two, 6-week, placebo-controlled, clinical studies. Montelukast administered once daily was generally well tolerated, with a safety profile consistent with that observed in patients with seasonal allergic rhinitis and similar to that of placebo. In these two studies, no 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 observed. The incidence of somnolence was similar to that of placebo.

Post-Marketing Experience
The following side effects have been reported in post-marketing use:
Infections and infestations: upper respiratory infection
Blood and lymphatic system disorders: increased bleeding tendency, thrombocytopenia
Immune system disorders: hypersensitivity reactions including anaphylaxis, very rarely hepatic eosinophilic infiltration
Psychiatric disorders: agitation including aggressive behavior or hostility, anxiousness, depression, disorientation, disturbance in attention, dream abnormalities, dysphemia (stuttering), hallucinations, insomnia, memory impairment, obsessive-compulsive symptoms, psychomotor hyperactivity (including irritability, restlessness and tremor), somnambulism, suicidal thinking and behavior (suicidality), tic
Nervous system disorders: dizziness, drowsiness, paraesthesia/hypoesthesia, very rarely seizure
Cardiac disorders: palpitations
Respiratory, thoracic and mediastinal disorders: epistaxis; pulmonary eosinophilia
Gastrointestinal disorders: diarrhea, dyspepsia, nausea, vomiting
Hepatobiliary disorders: increased ALT and AST, very rarely hepatitis (including cholestatic, hepatocellular, and mixed-pattern liver injury)
Skin and subcutaneous tissue disorders: angioedema, bruising, erythema multiforme, erythema nodosum, pruritus, rash, Steven 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: asthenia/fatigue, edema, pyrexia

Over dosage
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 one week without clinically important adverse experiences.

There have been reports of acute overdose in post-marketing experience and clinical studies with montelukast. These include reports in adults and children with a dose as high as 1,000 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 overdose reports.

Symptoms of overdose
The most frequently occurring adverse experiences were consistent with the safety profile of montelukast and included abdominal pain, somnolence, thirst, headache, vomiting, and psychomotor hyperactivity.

Management of overdose
No specific information is available on the treatment of overdose with montelukast. It is not known whether Montelukast is dialysable by peritoneal- or haemodialysis

PHARMACOLOGICAL PROPERTIES

Pharmacological Properties:

Pharmacotherapeutic group: Leukotriene receptor antagonist

ATC-Code: R03D C03

Mechanism of action
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 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

A/s: 210 x 360 mm ■ Black

AUROBINDO Packaging Development	Product Name: M-KAST 10 mg	Component: Leaflet	Item Code: P1523922	Date & Time: 11.10.2021 & 02.30 pm
	Customer / Country: Singapore_Unit 7	Version No.: 06	Reason Of Issue: Submission	Reviewed / Approved by
Team Leader: Kiran K	Dimensions: 210 x 360 mm	No. of Colours : 01		
Initiator: Shirisha N		23922		
Artist: SC Designers	Pharmacode: 23922			
Additional Information : Dimension changed 15-09-2021				Sign / Date

allergic rhinitis. Intranasal challenge with CysLTs has been shown to increase nasal airway resistance and symptoms of nasal obstruction.

Pharmacodynamic effects

Montelukast is a potent, orally active compound with anti-inflammatory properties which significantly improves parameters of asthmatic inflammation. Based on biochemical and pharmacological bioassays, it binds with high affinity and selectivity to the CysLT1 receptor (in preference to other pharmacologically important airway receptors such as the prostanoid, cholinergic, or β-adrenergic receptor). Montelukast potently inhibits physiologic actions of LTC4, LTD4, and LTE4 at the CysLT1 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 LTD4. Doses as low as 5 mg cause substantial blockage of LTD4-induced bronchoconstriction. Montelukast causes bronchodilation within 2 hours of oral administration; these effects were additive to the bronchodilation caused by a β-agonist.

Clinical Studies - Asthma

In clinical studies, MONTELUKAST is effective in adult and pediatric patients for the prophylaxis and chronic treatment of asthma, including the prevention of day- and night time symptoms, the treatment of aspirin-sensitive asthmatic patients, and the prevention of exercise-induced bronchoconstriction. MONTELUKAST is effective alone or in combination with other agents used in the maintenance treatment of chronic asthma. MONTELUKAST and inhaled corticosteroid may be used concomitantly with additive effects to control asthma or to reduce the inhaled corticosteroid dose while maintaining clinical stability.

Adults 15 years of age and older

In two similarly-designed 12-week double-blind placebo-controlled studies in adult asthmatic patients 15 years of age and older, MONTELUKAST, 10 mg once daily in the evening, demonstrated significant improvements in parameters of asthma control measuring asthma symptoms, asthma-related outcomes, respiratory function and “as-needed” β-agonist use.

MONTELUKAST significantly improved patient-reported daytime symptoms and nocturnal awakenings, compared with placebo. Asthma-specific outcomes, including asthma attacks, corticosteroid rescue, discontinuations due to worsening asthma, asthma exacerbations and asthma-free days were also significantly better than placebo. Physicians’ and patients’ global asthma evaluations and asthma-specific quality-of-life evaluations (in all domains, including normal daily activity and asthma symptoms) were significantly better than placebo. MONTELUKAST caused significant improvements in morning forced expiratory volume in 1 second (FEV1), AM and PM peak expiratory flow rate (PEFR) and significantly decreased the use of “as-needed” β-agonist, compared with placebo.

The treatment effect was achieved after the first dose and was maintained throughout the 24-hour dosing interval. Treatment effect also remained constant during continuous once-daily administration in extension studies for up to one year. Withdrawal of MONTELUKAST after 12 weeks of use did not cause rebound worsening of asthma.

Compared with inhaled beclomethasone (200 µg twice daily with a spacer device), MONTELUKAST demonstrated a more rapid initial response although over the full duration of the 12-week study, beclomethasone provided a greater average treatment effect. However, a high percentage of patients treated with MONTELUKAST achieved similar clinical responses compared with inhaled beclomethasone.

Effects in patients on concomitant inhaled corticosteroids

Separate studies in adults demonstrated the ability of MONTELUKAST to add to the clinical effect of inhaled corticosteroid and allow steroid tapering when used concomitantly. In a placebo-controlled study, patients taking initial inhaled corticosteroid doses of approximately 1600 µg per day reduced their steroid use by approximately 37% during a placebo run-in period. MONTELUKAST allowed a further 47% reduction of the inhaled corticosteroid dose, compared with 30% for placebo. In another study, MONTELUKAST provided additional clinical benefit to a similar population of patients maintained but not adequately controlled on inhaled corticosteroid (beclomethasone 400 µg per day). Complete abrupt removal of beclomethasone in patients receiving both MONTELUKAST and beclomethasone caused clinical deterioration in some patients, suggesting that tapering as tolerated rather than abrupt removal is preferred. In aspirin-sensitive patients, nearly all of whom were receiving concomitant inhaled and/or oral corticosteroids, MONTELUKAST resulted in significant improvement in the parameters of asthma control.

Effects on exercise-induced bronchoconstriction

MONTELUKAST, 10 mg once daily, prevented exercise-induced bronchoconstriction (EIB) in adults 15 years of age and older. In a 12-week study, MONTELUKAST significantly inhibited the extent and duration of fall in FEV1 over 60 minutes after exercise, the maximal percent fall in FEV1 after exercise, and the time to recovery to within 5% of the pre-exercise FEV1. Protection was consistent through the treatment period indicating that tolerance did not occur. In a separate cross-over study, protection was observed after two once-daily doses. In pediatric patients 6 to 14 years of age, using the 5-mg chewable tablet, a similarly designed cross-over study demonstrated similar protection and the protection was maintained throughout the dosing interval (24 hours).

Effects on asthmatic inflammation

In clinical studies MONTELUKAST inhibited both early- and late-phase bronchoconstriction due to antigen challenge. Because inflammatory cell (eosinophil) infiltration is an important feature of asthma, the effects of MONTELUKAST on eosinophils in the peripheral blood and airway were examined. In Phase IIb/III clinical studies, MONTELUKAST significantly decreased peripheral blood eosinophils approximately 15% from baseline, compared with placebo. In pediatric patients 6 to 14 years of age, MONTELUKAST decreased peripheral blood eosinophils 13% over the 8-week treatment period, compared with placebo. MONTELUKAST also significantly decreased airway eosinophils in sputum, compared with placebo. In this study, peripheral blood eosinophils decreased and clinical asthma endpoints improved with treatment with MONTELUKAST.

Effects in Patients with Asthma and Seasonal Allergic Rhinitis

In a clinical study in adult asthmatic patients 15 years of age and older with concomitant seasonal allergic rhinitis, montelukast 10-mg tablets administered once daily demonstrated a statistically significant improvement in the primary variable, Daily Rhinitis Symptoms score (average of the Daytime Nasal Symptoms score [mean of nasal congestion, rhinorrhea, sneezing, nasal itching] and the Night time Symptoms score [mean of nasal congestion upon awakening, difficulty going to sleep, and night time awakenings scores]), compared with placebo. Global evaluations of allergic rhinitis by patients and physicians, and global evaluations of asthma by patients and physicians, were also significantly improved, compared with placebo.

Clinical Studies - Allergic Rhinitis

The efficacy of MONTELUKAST for the treatment of seasonal allergic rhinitis was investigated in similarly designed randomized, 2-week, double-blind, placebo-controlled trials including 4924 patients (1751 patients were treated with MONTELUKAST). Patients were 15 years of age and older with a history of seasonal allergic rhinitis, a positive skin test to at least one relevant seasonal allergen, and active symptoms of seasonal allergic rhinitis at study initiation.

In a combined analysis of three pivotal studies, MONTELUKAST 10-mg tablets administered to 1189 patients once daily in the evening resulted in a statistically significant improvement in the primary endpoint, daytime nasal symptoms score, and its individual components (nasal congestion, rhinorrhea, nasal itching and sneezing); night time symptoms score, and its individual components (nasal congestion upon awakening, difficulty going to sleep, and night time awakenings); composite symptoms score (composed of the daytime nasal and night time symptoms scores); and global evaluations of allergic rhinitis by patients and by physicians, compared with placebo.

In a separate 4-week study in which MONTELUKAST was administered once daily in the morning, the efficacy over the initial 2 weeks was significantly different from placebo and consistent with the effect observed in studies using evening dosing. Additionally, the effect over the entire 4 weeks was consistent with the 2-week results.

In patients with seasonal allergic rhinitis aged 15 years and older who received MONTELUKAST, a median decrease of 13% in peripheral blood eosinophil counts was noted, compared with placebo, over the double-blind treatment periods.

The efficacy of MONTELUKAST for the treatment of perennial allergic rhinitis was investigated in two, similarly designed randomized, 6-week, double-blind, placebo-controlled studies including 3235 patients (1632 patients were treated with MONTELUKAST). Patients were 15 to 82 years of age with a history of perennial allergic rhinitis, positive skin test results to relevant perennial allergens (including dust mites, animal dander, and mold spores), and active symptoms of perennial allergic rhinitis at study initiation.

In one study, MONTELUKAST 10-mg tablets administered to 1000 patients once daily resulted in a statistically significant improvement in the primary endpoint, Daytime Nasal Symptoms score, and its individual components (nasal congestion, rhinorrhea, and sneezing), compared with placebo. MONTELUKAST also demonstrated patient-perceived improvement of allergic rhinitis as assessed by the secondary endpoints of Global Evaluation of Allergic Rhinitis by Patient, and Rhinoconjunctivitis Quality-of-Life overall score (average of scores for the 7 domains of activity, sleep, non-nose/non-eye symptoms, practical problems, nasal symptoms, eye symptoms, and emotions), compared with placebo.

Pharmacokinetic properties

Absorption: Montelukast is rapidly absorbed following oral administration. For the 10 mg film-coated tablet, the mean peak plasma concentration (Cmax) is achieved three 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. Safety and efficacy were demonstrated in clinical trials where the 10 mg film-coated tablet was administered without regard to the timing of food ingestion.

Distribution: Montelukast is more than 99% bound to plasma proteins. The steady-state volume of distribution of montelukast averages 8-11 litres. Studies in rats with radiolabelled montelukast indicate minimal distribution across the blood-brain barrier. In addition, concentrations of radiolabelled material at 24 hours post-dose were minimal in all other tissues.

Biotransformation

Montelukast is extensively metabolised. In studies with therapeutic doses, plasma concentrations of metabolites of montelukast are undetectable at steady state in adults and children.

In vitro studies using human liver microsomes indicate that cytochrome P450 3A4, 2C8, and 2C9 are involved in the metabolism of montelukast. 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.

Elimination:

The plasma clearance of montelukast averages 45 ml/min in healthy adults. . Following an oral dose of radiolabelled montelukast, 86% of the radioactivity was recovered in 5-day faecal 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. No difference in pharmacokinetics was noted between dosing in the morning or in the evening. During once-daily dosing with 10-mg montelukast, there is little accumulation of the parent drug in plasma (~14%).

Characteristics in patients: No dosage adjustment is necessary for the elderly or mild to moderate hepatic insufficiency. Studies in patients with renal impairment have not been undertaken. There are no data on the pharmacokinetics of montelukast in patients with severe hepatic insufficiency.

The safety and effectiveness in pediatric patients younger than 1 year of age with perennial allergic rhinitis and in patients below the age of 12 months with asthma have not been established.

PHARMACEUTICAL PARTICULARS

List of excipients

Lactose Monohydrate, Cellulose Microcrystalline, Croscarmellose Sodium, Magnesium Stearate. Hydroxy Propyl Cellulose.

Film coating: Hypromellose, Hydroxy propyl cellulose, Titanium dioxide (E 171), Red and yellow ferric oxide (E 172), Carnauba wax.

Incompatibilities

Not applicable.

Shelf life

24 months

Special precautions for storage

Store below 30 ºC. Protect from light and moisture.

Nature and contents of container

M-KAST 10mg tablets packed in a carton of 30 tablets [30’s (10’s Blister x3)].

DISTRIBUTED IN SINGAPORE BY:

Apotheca Marketing Pte. Ltd.,
63 Hillview Avenue #09-16,
Lam Soon Industrial Building,
Singapore 669569.

DATE OF PREPARATION OF THIS TEXT: 10/2021

P1523922