Package Insert

MONTAS
(Montelukast Paediatric Chewable Tablets 4 mg / 5 mg)

- **Name and strength of active ingredient**

MONTAS 4:
Each uncoated tablet contains:
Montelukast Sodium Ph.Eur. 4.16 mg eq. to Montelukast 4 mg

MONTAS 5:
Each uncoated tablet contains:
Montelukast Sodium Ph.Eur. 5.20 mg eq. to Montelukast 5 mg

- **Product Description**

MONTAS 4: Pink coloured, mottled, oval, biconvex, uncoated tablet, debossed "M4" on one side and plain on other side.
MONTAS 5: Pink coloured, mottled, round, biconvex, uncoated tablet, debossed "M5" on one side and plain on other side.

- **Pharmacodynamics & Pharmacokinetics**

Pharmacodynamic effects
Montelukast is a selective and active leukotriene receptor antagonist. Montelukast inhibits bronchoconstriction due to antigen challenge. Montelukast is a selective leukotriene receptor antagonist of the cysteinyl leukotriene CysLT 1 receptor. The cysteinyl leukotrienes (LTC 4, LTD 4, LTE 4) are products of arachidonic acid metabolism that are released from various cells, including mast cells and eosinophils. They bind to cysteinyl leukotriene receptors (CysLT) found in the human airway. Binding of cysteinyl leukotrienes to leukotriene receptors has been correlated with the pathophysiology of asthma, including airway edema, smooth muscle contraction, and altered cellular activity associated with the inflammatory process, factors that contribute to the signs and symptoms of asthma.

It binds to cysteinyl leukotrienes (CysLT) type-1 receptors found in human airway (smooth muscle cells and macrophages), which prevents airway edema, smooth muscle contraction and other respiratory inflammation. The leukotrienes are also released from the nasal mucosa after allergen exposure where montelukast sodium may inhibit symptoms of allergic rhinitis.

Montelukast binding to the CysLT1 receptor is high-affinity and selective, preferring the CysLT1 receptor to other pharmacologically important airway receptors, such as the prostanoid, cholinergic, or beta-adrenergic receptor. Montelukast inhibits physiologic actions of LTD4 at the CysLT1 receptors, without any agonist activity.
Montelukast causes bronchodilation within 2 hours of oral administration; these effects were additive to the bronchodilation caused by a β-agonist.

Pharmacokinetic properties

Absorption

Montelukast is rapidly and nearly completely absorbed following oral administration. Peak plasma concentrations of montelukast occur 2 to 4 hours after oral doses. The mean oral bioavailability is 64% to 73%. The oral bioavailability and Cmax are not influenced by a standard meal.

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.

Metabolism

Montelukast is extensively metabolized in the liver by cytochrome P450 isoenzymes, mainly by CYP2C8 and to a lesser extent by CYP3A4 and CYP2C9. 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.
Montelukast and its metabolites are excreted principally in the faeces via the bile.
Elimination Half-life: 2.7 to 5.5 hours

- **Indication**

Montelukast chewable tablet is indicated in pediatric patients 2 to 14 years of age for:
- the prophylaxis and chronic treatment of asthma
- the relief of daytime and nighttime symptoms of seasonal allergic rhinitis.

- **Recommended Dosage**

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.

Pediatric Patients 6 to 14 Years of Age with Asthma and/or Seasonal Allergic Rhinitis

The dosage for pediatric patients 6 to 14 years of age is one 5-mg chewable tablet daily.

Pediatric Patients 2 to 5 Years of Age with Asthma and/or Seasonal Allergic Rhinitis

The dosage for pediatric patients 2 to 5 years of age is one 4-mg chewable tablet daily.

General Recommendations

The therapeutic effect of montelukast on parameters of asthma control occurs within one day. Montelukast chewable tablets can be taken with or without food. Patients should be advised to continue taking Montelukast while their asthma is controlled, as well as during periods of worsening asthma.

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

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.

Therapy with Montelukast in Relation to Other Treatments for Asthma
Montelukast can be added to a patient's existing treatment regimen.

Reduction in Concomitant Therapy:
Bronchodilator Treatments: Montelukast 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 Montelukast 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. Montelukast should not be abruptly substituted for inhaled corticosteroids.

- **Route of Administration**

Oral

- **Contraindications**

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

- **Warnings & Precautions**

The efficacy of oral Montelukast for the treatment of acute asthma attacks has not been established. Therefore, oral Montelukast should not be used to treat acute asthma attacks. Patients should be advised to have appropriate rescue medication available.
While the dose of concomitant inhaled corticosteroid may be reduced gradually under medical supervision, Montelukast should not be abruptly substituted for inhaled or oral corticosteroids. Neuropsychiatric events (eg, agitation, aggression, anxiousness, dream abnormalities, hallucinations, depression, disorientation, insomnia, irritability, restlessness, suicidal thinking and behavior (including suicide), tremor) have occurred. Since other factors may have contributed to these events, it is not known if they are related to Montelukast. Physicians should discuss these adverse experiences with their patients and/or caregivers. Patients and/or caregivers should be instructed to notify their physician if these changes occur.

The reduction in systemic corticosteroid dose in patients receiving anti-asthma agents including leukotriene receptor antagonists has been followed in rare cases by the occurrence of 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 eosinophilic vasculitis. Although a casual relationship with leukotriene receptor antagonism has not been established, caution and appropriate clinical monitoring are recommended when systemic corticosteroid reduction is considered in patients receiving Montelukast.

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 documented aspirin sensitivity.

Effects on Ability to Drive and Use Machines
Montelukast is not expected to affect a patient's ability to drive a car or operate machinery. However, in very rare cases, individuals have reported drowsiness or dizziness.

5 mg Chewable tablet:
Montelukast contains aspartame, a source of phenylalanine. Unsuitable for phenylketonurics. Each 5 mg chewable tablet contains phenylalanine in an amount equivalent to 0.842 mg phenylalanine per dose.

4 mg Chewable tablet:
Safety and efficacy of 4 mg chewable tablets have not been established in the paediatric population below 2 years of age.
Montelukast Paediatric chewable tablet contains aspartame, a source of phenylalanine. Unsuitable for phenylketonurics. Each 4 mg chewable tablet contains phenylalanine in an amount equivalent to 0.674 mg phenylalanine per dose.

- **Interaction with other medicaments**

Montelukast may be administered with other therapies routinely used in the prophylaxis and chronic treatment of asthma, and in the treatment of allergic rhinitis.

Montelukast is not anticipated to alter the metabolism of drugs metabolized by this enzyme (e.g., paclitaxel, rosiglitazone, repaglinide).

Concurrent use of gemfibrozil and montelukast may result in elevated montelukast plasma concentrations montelukast.

Concurrent use of prednisone and montelukast may result in severe peripheral edema.

Concurrent use of montelukast and repaglinide may result in increased repaglinide plasma concentrations.

Montelukast is metabolised by CYP 3A4, caution should be exercised, particularly in children, when montelukast is co-administered with inducers of CYP 3A4, such as phenytoin, phenobarbital and rifampicin.

Concurrent use of montelukast and phenobarbital may result in decreased bioavailability of montelukast.
Concurrent use of montelukast and rifampin may result in decreased bioavailability of montelukast.

- **Statement on usage during pregnancy and lactation**

Use during pregnancy: Animal studies do not indicate harmful effects with respect to effects on pregnancy or embryonal/foetal development.
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.
Use during lactation: Studies in rats have shown that montelukast is excreted in milk. It is not known if montelukast is excreted in human milk.
Montelukast may be used in breast-feeding only if it is considered to be clearly essential.

- **Adverse Effects/ Undesirable Effects**

Montelukast has been generally well tolerated. Side effects, which usually were mild, generally did not require discontinuation of therapy.

Cardiovascular Effects: palpitations, allergic granulomatosis angiitis (Systemic eosinophilia with vasculitis and a clinical presentation consistent with Churg-Strauss . Symptoms may include eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications and/or neuropathy)

Skin and subcutaneous tissue disorders: angioedema, bruising, erythema nodosum, atopic dermatitis , eczema, infection of skin and/or subcutaneous tissue, rash, urticaria

Gastrointestinal Effects: abdominal pain, dental pain, diarrhea, gastroenteritis, indigestion, infection of tooth, nausea, pancreatitis, tonsillitis, vomiting

Hematologic Effects: blood coagulation disorder (increased bleeding tendency)

Hepatic Effects: ALT/ AST levels raised, cholestatic hepatitis

Immunologic Effects: hypersensitivity reactions, including anaphylaxis, varicella, and viral infection *Neurologic Effects:* asthenia, disorientated, dizziness, headache, hyperactive behavior, hypesthesia, insomnia, paresthesia, seizure, sinus headache, drowsiness, and tremor

Ophthalmic Effects: conjunctivitis, myopia

Otic Effects: Otalgia, Otitis, Otitis media

Psychiatric Effects: aggressive behavior, agitation, altered behavior, anxiety, depression, dream disorder, feeling nervous, hallucinations, irritability, nightmares, restlessness, sleep disorder, somnambulism,suicidal thinking and behavior (including suicide)

Renal Effects: pyuria

Respiratory Effects: bronchitis, acute, cough, epistaxis, laryngitis, nasal congestion, nasal discharge, pharyngitis, pneumonia, respiratory tract infection, rhinitis, sinusitis, upper respiratory infection, wheezing

Musculoskeletal and connective tissue disorders: arthralgia, myalgia including muscle cramps

Other: fatigue, fever, influenza, malaise, traumatic injury

Postmarketing Experience
Blood and lymphatic system disorders: thrombocytopenia

- **Overdose and Treatment**

Symptoms
Symptoms included abdominal pain, somnolence, thirst, headache, vomiting, and psychomotor hyperactivity.

Treatment
Treatment is symptomatic and supportive. Treatment may include removal of unabsorbed material from the gastrointestinal tract, clinical monitoring and supportive therapy if required.
It is not known if montelukast can be removed by peritoneal dialysis or hemodylasis.

- **Storage Conditions**

Do not store above 30°C.
Store in the original package in order to protect from light and moisture.
Keep out of the reach and sight of children.

- **Dosage forms and packaging**

MONTAS 4/5 is available in Aluminium-Aluminium blister pack. 14 Tablets of MONTAS 4/5 are packed in each blister and 2 such blisters are packed in 1 carton.

- **Name and address of manufacturer**

Intas Pharmaceuticals Limited.
Camp road, Selaqui-248197,
Dehradun, Uttarakhand (India).

- **Name and Address of Marketing Authorization Holder**

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Bandar Tun Razak, 56000 Kuala Lumpur, Malaysia

- **Date of revision of PI**

18th April, 2023