OXAIR®

Ingredient(s):
Oxair Chewable Tablet 4mg:
Each tablet contains:
Montelukast Sodium ……..…….. 4.16mg
(eq. to Montelukast 4mg)
Oxair Chewable Tablet 5mg:
Each tablet contains:
Montelukast Sodium ……..…….. 5.2mg
(eq. to Montelukast 5mg)
Oxair Film Coated Tablet 10mg:
Each tablet contains:
Montelukast Sodium ……..…….. 10.4mg
(eq. to Montelukast 10mg)

Pharmacology (Summary of Pharmacodynamics and Pharmacokinetics):
Pharmacodynamics
1. Montelukast sodium is a selective and orally active leukotrine receptor antagonist that specifically inhibits the cysteinyl leukotriene $CysLT_1$ receptor.
2. 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 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.
3. Montelukast is a potent, orally active compound that significantly improves parameters of asthmatic inflammation and causes potent inhibition of airway cysteinyl leukotriene receptors as demonstrated by the ability to inhibit bronchoconstriction due to inhaled LTD_4 in asthmatic patients.
4. It binds with high affinity and selectivity to the $CysLT_1$ receptor. Montelukast potently inhibits physiologic actions of LTC_4, LTD_4, and LTE_4 at the $CysLT_1$ receptor without any agonist activity.
5. Montelukast causes bronchodilation within 2 hours of oral administration and there is no additional clinical benefit to Montelukast doses above 10mg once daily.

Pharmacokinetics
1. Montelukast is rapidly and nearly completely absorbed following oral administration.
   a) Mean peak plasma concentration (C_{max}) is achieved within 2 - 4 hours after administration in the fasted state. The mean oral bioavailability is around 64% to 73%. There is no clinically important influence of standard meal to the oral bioavailability and Cmax of the drug.
2. Distribution:
   a) Montelukast is >99% bound to plasma proteins. The steady state volume of distribution of montelukast averages 8-11 Liter. There is minimal distribution across the blood-brain barrier. Concentration of montelukast at 24 hours post-dose were minimal in all others tissues.
3. Metabolism :
   a) Montelukast is extensively metabolized.
   b) Plasma concentrations of metabolites of Montelukast are undetectable at steady state in adults and pediatric patients.
   c) Cytochrome P-450 3A4 and 2C9 are involved in the metabolism of Montelukast and therapeutic plasma concentrations of montelukast do not inhibit cytochromes P-450 3A4, 2C9, 1A2, 2A6, 2C19 or 2D6.
4. Elimination:
   a) The plasma clearance of Montelukast averages 45ml/min and mean plasma half-life ranged from 2.7 to 5.5 hours in healthy adults.
   b) Montelukast and its metabolites are excreted almost exclusively via the bile.

Indications:
1. For the prophylaxis and chronic treatment of asthma in adults and children ≥ 1 year of age.
2. It is indicated in adults ≥ 15 years of age for the relief of daytime and night-time symptoms of seasonal allergic rhinitis.

Dosage and Administrations:
For asthma patients with or without allergic rhinitis: take one dose in the evening.
For allergic rhinitis patients: the time of administration maybe individualized to suit patient need
Adults ≥ 15 years of age: one 10mg tablet daily.
Children 6-14 years of age: one 5mg tablet daily.
Children 2-5 years of age: one 4mg tablet daily.
General recommendation:
1. The therapeutic effect of this product on parameters of asthma control occurs within 1 day.
2. It may be taken with or without food.
3. Patients should be advised to continue taking Montelukast while their asthma is controlled, as well as during periods of worsening asthma.
4. No dosage adjustment is necessary for pediatric patients, for elderly, for patients with renal insufficiency, or mild to moderate hepatic impairment, or for patients of either gender.
5. Montelukast is a long term controller medication which should not be substituted for short-acting β-agonists. It is effective alone or in combination with other prophylactic agent.
6. Montelukast is a preventive agent, and can be added to the asthma patient's existing treatment regimen. Reduction in existing treatment can be made as tolerated.
7. With administration of montelukast, the dose of inhaled corticosteroids can be reduced gradually or even tapered off completely. However, montelukast should not be abruptly substituted for inhaled corticosteroids.

Orally administration

Contraindications:
Hypersensitivity to any component of this product.

Precautions / Warnings:
1. Montelukast should not be used to treat acute asthma attacks. Patients should be advised to have appropriate rescue medication available.
2. 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.
3. 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.
4. Patients with known aspirin sensitivity should continue avoidance of aspirin or nonsteroidal anti-inflammatory agents while taking Montelukast.
5. Safety and effectiveness in pediatric patients younger than 6 months of age have not been studied.
6. Tablet of 4mg and 5mg contains aspartame therefore it is unsuitable for phenylketourics.

Interaction with Other Medicaments
1. This product may be administered with other therapies routinely used in the prophylaxis and chronic treatment of asthma.
2. The area under the plasma concentration time curve (AUC) for Montelukast was decreased about 40% in subjects with co-administration of phenobarbital. No dosage adjustment is required.

Pregnancy and Lactation:
1. There is no study available for the use of this product in pregnant women. It should be used during pregnancy only if clearly needed.
2. It is not known if Montelukast is excreted in human milk. Caution should be exercised when this product is given to a nursing mother.

Side Effect / Adverse Reactions:
Montelukast has been generally well tolerated. Side effects, which usually were mild, generally did not require discontinuation of therapy. The following side effects have been reported in post-marketing use: blood and lymphatic system disorder (thrombocytopenia), psychiatric disorders (obsessive-compulsive symptoms), hypersensitivity reactions (including anaphylaxis, angioedema, rash, pruritus, urticaria and very rarely, hepatic eosinophilic infiltration); dream abnormalities and hallucinations, drowsiness, irritability, restlessness, insomnia and very rarely seizures; nausea, vomiting, dyspepsia, diarrhea; myalgia including muscle cramps; increased bleeding tendency, bruising; and edema.

Symptoms and Treatment For Overdosage, and Antidotes:
There were no adverse experiences reported in the majority of over-dosage reports. The most frequent adverse experiences observed were thirst, somnolence, mydriasis, hyperkinesia, and abdominal pain.

Shelf-life:
OXT5 and OXT10 = 3 years from date manufacture
OXT4 = 2 years from date manufacture

Storage Conditions:
Store at temperature below 30°C. Protect from light and moisture.

Product description and Packing(s):
Oxair Chewable Tablet 4mg
A light brownish red color, oval tablet. "  "
Blister packing of 10's x 3, 10's x 10 and 10's x 50.
Oxair Chewable Tablet 5mg
A light brownish red color, round tablet." "
Blister packing of 10's x 3, 10's x 10 and 10's x 50.
Oxair Film Coated Tablet 10mg
A beige color film coated square tablet. " "
Blister packing of 10's x 3, 10's x 10 and 10's x 50.

Y. S. P.®
Manufacturer and Product Registration Holder:
Y.S.P. INDUSTRIES (M) SDN. BHD. (199001001034)
Lot 3, 5, 7, 12 & 14 Jalan P/7, Section 13,
Kawasan Perindustrian Bandar Baru Bangi,
43000 Kajang, Selangor, Malaysia.
Ordering Line: 1 800 88 3027
Product Info: 1 800 88 3679