# BioWell Breamore Montelukast Chewable Tablet 5mg

VIBRExx-06
BW07UM-YYMMDD

## DESCRIPTION
BioWell Breamore (Montelukast Chewable Tablet 5mg):
10 mm, round, pink mottled uncoated tablet, bevel edged, shallow convex faces, “HD” embossed and scored on the same face.

## COMPOSITION
BioWell Breamore (Montelukast Chewable Tablet 5mg)
Each Chewable tablet contains: Montelukast Sodium which is equivalent to Montelukast 5 mg.

## PHARMACODYNAMICS
Montelukast causes potent inhibition of airway cysteinyl leukotriene receptors as demonstrated by the ability to inihibit bronchoconstriction due to inhaled $LTD_4$ in asthmatic patients. Doses as low as 5-mg cause substantial blockage of $LTD_4$-induced bronchoconstriction.

Montelukast causes bronchodilation within 2 hours of oral administration; these effects were additive to the bronchodilation caused by β-agonist.

## PHARMACOKINETICS
**Absorption**
Montelukast is rapidly absorbed following oral administration. For the 5 mg chewable tablet, the Cmax is achieved 2 hours after administration in adults in the fasted state. The mean oral bioavailability is 73%. Food does not have a clinically important influence with chronic administration.

Safety and efficacy were demonstrated in clinical studies where the 5-mg chewable 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.

**Metabolism**
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, 2A6 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 50mg. 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 patent drug in plasma (~14%).

The comparative pharmacokinetics of montelukast when administered as two 5-mg chewable tablets versus one 10-mg film-coated tablet have not been evaluated. Therefore these two products should not be used interchangeably.

**Characteristics in Patients**
*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. In clinical studies, there do not appear to be any difference in clinically important effects.

*Hepatic Insufficiency*
Patients with mild-to-moderate hepatic insufficiency and clinical evidence of cirrhosis had evidence of decrease metabolism of montelukast resulting in approximately 41% higher mean montelukast area under the plasma concentration curve (AUC) following a single 10-mg dose. The elimination of montelukast is 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. There are no clinical data in patients with severe hepatic insufficiency (Child-Pugh score > 9).

*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.

## INDICATIONS
For the prophylaxis and chronic treatment of asthma in pediatric patients 6 to 14 years of age.

BioWell Breamore is indicated in pediatric patients 6 to 14 years of age for the relief of daytime and nighttime symptoms of seasonal allergic rhinitis.

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

## WARNINGS AND PRECAUTIONS
- The efficacy of oral Breamore for the treatment of acute asthma attacks has not been established. Therefore, oral Breamore 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, Breamore should not be abruptly substituted for inhaled or oral corticosteroids. Neuropsychiatric events have been reported in patients taking Breamore. Since other factors may have contributed to these events, it is not known if they are related to Breamore. 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.
- In rare cases patients receiving anti-asthma agents, including leukotriene receptor antagonists, have experienced 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. 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 Breamore.
- Patients with known aspirin sensitivity should continue avoidance of aspirin or non-steroidal anti-inflammatory agents while taking Breamore.
- Although Breamore 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.

## PREGNANCY AND LACTATION
**Use during pregnancy:** Montelukast should be used during pregnancy only if clearly needed. Available data from published prospective and retrospective cohort studies with montelukast use in pregnant women evaluating major birth defects have not established a drug-associated risk. Available studies have methodologic limitations, including small sample size, in some cases retrospective data collection, and inconsistent comparator groups.

**Use during lactation:** 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.

## DRUG INTERACTIONS
- 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 theophylline, prednisone, prednisolone, oral contraceptives (ethinyl estradiol/ norethindrone 35/1), terfenadine, digoxin and warfarin.
- The area under the plasma concentration-time curve (AUC) for montelukast was decreased approximately 40% in subjects with co-administration of phenobarbital. No dosage adjustment for Breamore is recommended.
- In vitro studies have shown that montelukast is an inhibitor of CYP2C8. However, data from a clinical drug-drug interaction study involving montelukast and rosiglitazone (a probe substrate representative of drugs primarily metabolized by CYP2C8) demonstrated that montelukast does not inhibit CYP2C8 in vivo. Therefore, montelukast is not anticipated to alter the metabolism of drugs metabolized by this enzyme (e.g., paclitaxel, rosiglitazone, repaglinide).
- In vitro studies have shown that montelukast is a substrate of CYP 2C8, 2C9, and 3A4. Data from a clinical drug-drug interaction study involving montelukast and gemfibrozil (an inhibitor of both CYP 2C8 and 2C9) demonstrated that gemfibrozil increased the systemic exposure of montelukast by

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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 other known inhibitors of CYP 2C8 (e.g., trimethoprim) are not anticipated. In addition, co-administration of montelukast with itraconazole alone resulted in no significant increase in the systemic exposure of montelukast.

## SIDE EFFECTS

BioWell Breamire 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 BioWell Breamore was comparable to placebo.

**Postmarketing Experience**
The following side effects have been reported in postmarketing 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, disturbances 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, paraethesia/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, 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

## OVERDOSAGE AND TREATMENT

No specific information is available on the treatment of overdosage with BioWell Breamore.

There were no adverse experiences in the majority of overdosage reports. The most frequently occurring adverse experiences were consistent with the safety profile of BioWell Breamore and included abdominal pain, somnolence, thirst, headache, vomiting, and psychomotor hyperactivity.

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

## DOSAGE AND ADMINISTRATION

BioWell Breamore should be taken once daily. For asthma, the dose should be take 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 6-14 years of age with Asthma and/or Seasonal Allergic Rhinitis:**
The dosage for pediatric patients 6 to 14 years of age is one (1) 5mg chewable tablet daily.

**General Recommendations:**
The therapeutic effect of BioWell Breamore on parameters of asthma control occurs within one day. BioWell Breamore chewable tablets can be taken with or without food. Patients should be advised to continue taking BioWell Breamore 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.

BioWell Breamore 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.

BioWell Breamore is a preventive agent, which should be used in addition to other drugs for the management of asthma.

**Therapy with BioWell Breamore in relation to other treatments for asthma:**
BioWell Breamore can be added to a patient's existing treatment regimen.

Bronchodilator Treatments: BioWell Breamore 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 BioWell Breamore 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. BioWell Breamore should not be abruptly substituted for inhaled corticosteroids.

Note: The information given here is limited. For further information, consult your doctor or pharmacist.

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

Presentation/Packing: Blister of 3 x 10’s

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