BRONKEEZ
(Montelukast Sodium)
B.P

TABLETS
SACHET

DESCRIPTION
BRONKEEZ (Montelukast Sodium) is a selective and orally active leukotriene receptor antagonist that inhibits the cysteinyl leukotriene CysLT 1 receptor. It is thought to play important role in the pathogenesis of asthma. It is described chemically as [R-(E)] -1- [[[1- [3- [2- (7-chloro-2-quinolinyl) ethenyl] phenyl] -3- [2-(1-hydroxy-1 methylethyl) phenyl] propyl] thio] methyl] cyclopropaneacetic acid, monosodium salt.

QUANTITATIVE & QUALITATIVE COMPOSITION
4 mg BRONKEEZ Sachet
Each sachet contains:
Montelukast sodium (B.P) equivalent to Montelukast.....4 mg

4mg chewable BRONKEEZ tablet
Each chewable tablet contains:
Montelukast sodium (B.P) equivalent to Montelukast.....4 mg

5mg chewable BRONKEEZ tablet
Each chewable tablet contains:
Montelukast sodium (B.P) equivalent to Montelukast.....5 mg

10mg BRONKEEZ film coated tablet
Each film-coated tablet contains:
Montelukast sodium (B.P) equivalent to Montelukast.....10 mg

CLINICAL PHARMACOLOGY
MECHANISM OF ACTION: As a result of arachidonic acid metabolism the cysteinyl leukotrienes (LTC 4, LTD 4, LTE 4) are released from various cells, including mast cells and eosinophils. These eicosanoids bind to cysteinyl leukotriene receptors (CysLT) found in the human air way. Binding of cysteinyl leukotrienes and leukotriene receptors has been correlated with the pathogenesis of asthma, including airway oedema, smooth muscle contraction, and altered cellular activity associated with the inflammatory process, factors which contribute towards asthma. Thus, montelukast sodium inhibits physiologic actions of LTD 4 at the CysLT 1 receptor without any agonist activity.

PHARMACOKINETICS
ABSORPTION: After oral administration of 4mg sachet or chewable tablet to pediatric patients in the fasted state, Cmax is achieved 2 hours after administration. The mean Cmax is 66% higher while Cmin is lower than in adults receiving a 10-mg tablet. Montelukast sodium is rapidly absorbed following oral administration. For 5-mg chewable tablet, the mean Cmax is achieved in 2 to 2.5 hours after administration to adults in the fasted state. The mean oral bio-availability is 73% in the fasted state versus 63% when administered with a standard meal in the morning. After oral administration of the 10-mg film-coated tablet to fasted adults, the mean peak plasma concentration is achieved in 3 to 4 hours. The mean oral bio-availability is 64%. The oral bio-availability and C max are not influenced by a standard meal in the morning.
DISTRIBUTION: Montelukast is more than 99% bound to plasma proteins. The steady-state volume of distribution of montelukast averages 8 to 11 liters. The mean plasma half-life of montelukast sodium ranged from 2.7 to 5.5 hours in healthy young adults.

METABOLISM: Extensive metabolism of montelukast sodium occurs in the liver by cytochrome P450 isoenzymes CYP3A4, CYP2A6 and CYP2C9. Therapeutic plasma concentrations of montelukast sodium do not inhibit cytochromes P450, 3A4, 2C9, 1A2, 2C19, or 2D6.

ELIMINATION: The plasma clearance of montelukast averages 45 ml/min in healthy adults. Montelukast sodium and its metabolites are excreted almost exclusively via the bile. The pharmacokinetics of montelukast sodium are nearly linear for oral doses up to 50 mg.

SPECIAL POPULATIONS
Plasma pharmacokinetic profile of elderly, paediatric, males, females, and patients with renal insufficiency is as similar as for young adults.

HEPATIC INSUFFICIENCY
The elimination of montelukast sodium was slightly prolonged in patients with mild to moderate hepatic insufficiency compared with healthy subjects (mean half-life, 7.4 hours). No dosage adjustment is required in such patients.

INDICATIONS
BRONKEEZ is indicated for the prophylaxis and chronic treatment of asthma including: -
- The prevention of day and night time symptoms.
- The treatment of aspirin-sensitive asthmatic patients.
- The prevention of exercise-induced bronchoconstriction.

BRONKEEZ is also indicated for the relief of symptoms of seasonal allergic rhinitis in adults and paediatric patients 2 years of age and older.

CONTRAINDICATIONS
Hypersensitivity to any component of this product.

DOSAGE AND ADMINISTRATION
BRONKEEZ should be taken once daily.

4mg SACHET
1 sachet daily for children 6 months to 6 years of age.

4mg CHEWABLE TABLET
1 tablet daily for children 2-5 years of age.

5mg CHEWABLE TABLET
1 tablet daily for children 6-12 years of age.

10mg TABLET
1 tablet for adult patient **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.

Adults 15 Years of Age and Older with Asthma and/or Seasonal Allergic Rhinitis: The dosage for adults 15 years of age and older is one tablet 10mg daily to be taken in the evening.

Paediatric Patients 6 to 14 Years of Age with Asthma and/or seasonal Allergic Rhinitis: The dosage for paediatric patients 6 to 14 years of age is one chewable tablet 5mg daily to be taken in the evening.

Use of BRONKEEZ in relation to other treatment for asthma:
BRONKEEZ can be added to a patient's existing treatment regimen.

Reduction in concomitant therapy
Bronchodilator treatment: Patients who are not adequately controlled on bronchodilator alone **BRONKEEZ** can be added to the treatment of such patients. 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 **BRONKEEZ** 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. The dose of the inhaled corticosteroids can be tapered off completely with advice of physician. **BRONKEEZ** should not be abruptly substituted for inhaled corticosteroids.

GENERAL RECOMMENDATIONS
The therapeutic effect of **BRONKEEZ** on parameters of asthma control occurs within one day. **BRONKEEZ** sachet, tablets and chewable tablets can be taken with or without food. Patients should be advised to continue taking **BRONKEEZ** while their asthma is controlled, as well as during periods of worsening asthma. **BRONKEEZ** can be added to a patient's existing treatment regimen.

SIDE EFFECTS
Montelukast sodium is generally well tolerated. However, following are the adverse effects reported which usually were mild and did not require discontinuation of therapy: Hypersensitivity reactions such as anaphylaxis, angioedema, rash, pruritis, urticaria and, very rarely, hepatic eosinophilic infiltration. Dream abnormalities, hallucinations, palpitations, drowsiness, irritability, restlessness, insomnia, increased sweating, headache. Nausea, vomiting, dyspepsia, diarrhoea, abdominal pain. Myalgia including muscle cramps. Increased bleeding tendency, bruising oedema. Tremor, dry mouth, vertigo, arthralgia.

PRECAUTIONS
GENERAL
- Montelukast sodium should not be abruptly substituted for inhaled or oral corticosteroids. However the dose of inhaled corticosteroid may be reduced gradually under medical supervision.
- Montelukast sodium 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 (beta)-agonists as prophylaxis and have available for rescue a short-acting inhaled (beta)-agonist.
- Aspirin sensitive patients should continue avoidance of aspirin or non-steroidal anti-inflammatory agents while taking montelukast sodium, because montelukast sodium does not block broncho constrictor response to these agents in aspirin sensitive asthmatic patients.
- Caution should be exercised when using montelukast sodium with bronchodilator therapy. When clinical response is apparent the bronchodilator therapy should be reduced.

PREGNANCY
Montelukast sodium has not been studied in pregnant women. It should be used during pregnancy only if clearly needed.

NURSING MOTHERS
It is not known if montelukast sodium is excreted in human milk. Caution should be exercised when **BRONKEEZ** is given to a nursing mother.

PAEDIATRIC USE
Safety and efficacy of **BRONKEEZ** have been established in adequate and well-controlled studies in paediatric patients 6 to 14 years of age. Safety and efficacy profiles in this age group are similar to those seen in adults.

DRUG INTERACTIONS
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/norethindrone 35/1), terfenadine, digoxin and warfarin. No dose adjustment for **BRONKEEZ** is recommended.

OVER-DOSAGE
No specific information is available in the treatment of over dosage with **BRONKEEZ** in adults. There have been reports of acute over dosage in children in post marketing experience and clinical studies up to at least 150mg/day with **BRONKEEZ.** The clinical and laboratory findings observed were consistent with the safety profile in adults and older paediatric patients. There were no adverse experiences reported in the majority of over dosage reports. The most frequent adverse experiences observed were thirst, somnolence, mydriasis, hyperkinesias, and abdominal pain.

INSTRUCTIONS
Store below 30°C. Protect from heat, light & moisture. Keep all medicines out of the reach of children. To be sold on the prescription of a registered medical practitioner only.

PRESENTATION
BRONKEEZ 4mg sachets are available in foil packing of 14 sachets.
BRONKEEZ 4mg chewable tablets are available in Alu-Alu pack of 2x7's.
BRONKEEZ 5mg chewable tablets are available in Alu-Alu pack of 2x7's.
BRONKEEZ 10mg film coated tablets are available in Alu-Alu pack of 2x7's.

برونکیز ٹیبلیٹس/ساشے
(مونٹی لوکاسٹ سوڈیم) بی پی

ہدایات: دوا کو **30°** سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ گرمی، روشنی اور نمی سے بچائیں۔
تمام دوائیں بچوں کی پہنچ سے دُور رکھیں۔ صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

Manufactured by:
STANDPHARM PAKISTAN (PVT) LTD
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