Indokast
(Montelukast Sodium)BP

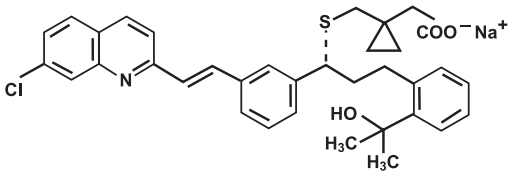
COMPOSITION
Indokast (Montelukast Sodium) is available for oral administration as:

1. **Indokast Sachets 4mg**
   Each sachet contains:
   Montelukast BP..... 4mg (as Montelukast Sodium)
   Product Specification: BP

2. **Indokast Tablets 5mg**
   Each chewable tablet contains:
   Montelukast BP ..... 5mg (as Montelukast Sodium)
   Product Specification: BP

3. **Indokast Tablets 10mg**
   Each film coated tablet contains:
   Montelukast BP..... 10mg (as Montelukast Sodium)
   Product Specification: BP

DESCRIPTION
Indokast (Montelukast sodium) is a selective and orally active leukotriene receptor antagonist that inhibits the cysteinyl leukotriene $CysLT_1$ receptor, stimulation of which by circulating leukotrienes is thought to play a role in the pathogenesis of asthma. It suppresses both early and late bronchoconstrictor responses to inhaled antigens or irritants, but is not suitable for the management of acute attacks of asthma. Montelukast sodium 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. The molecular formula is $C_{35}H_{35}ClNNaO_3S$ and the structural formula is:



Montelukast Sodium

CLINICAL PHARMACOLOGY
Mechanism of Action
Montelukast selectively antagonizes leukotriene D4 (LTD4) at the cysteinyl leukotriene receptor, $CysLT_1$, in the human airway. Montelukast inhibits the actions of LTD4 at the $CysLT_1$ receptor, preventing airway edema smooth muscle contraction and enhanced secretion of thick, viscous mucus.

Pharmacokinetics
Absorption:
Montelukast sodium is rapidly absorbed following oral administration. Peak plasma concentrations of montelukast sodium are achieved in 2 to 4 hours after oral administration. The mean oral bioavailability is 64%.
Distribution:
Montelukast sodium is more than 99% bound to plasma proteins. The mean plasma half-life of montelukast sodium ranged from 2.7 to 5.5 hours in healthy young adults. The pharmacokinetics of montelukast sodium is nearly linear for oral doses up to 50mg.
Metabolism:
Montelukast sodium is extensively metabolized 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, 2A6, 2C19, or 2D6.
Elimination:
The plasma clearance of montelukast sodium averages 45mL/min in healthy adults. Montelukast sodium and its metabolites are excreted principally in the feces via the bile.

Special Populations:
Elderly, paediatric, males, females, and patients with renal insufficiency have similar plasma pharmacokinetic profiles as young adults.
Hepatic Insufficiency:
Patients with mild-to-moderate hepatic insufficiency and clinical evidence of cirrhosis has evidence of decreased metabolism and prolonged elimination half life of montelukast sodium resulting in 41% higher mean montelukast sodium area under the plasma concentration curve (AUC) following a single 10mg dose. No dosage adjustment is required in patients with mild-to-moderate hepatic insufficiency.
Paediatric Patients:
In children 6 to 11 months of age, the systemic exposure to montelukast and the variability of plasma montelukast concentrations were higher than those observed in adults. Safety and tolerability of montelukast in a single-dose pharmacokinetic study in children 6 to 23 months of age were similar to that of patients two years and above.

THERAPEUTIC INDICATIONS
- **Indokast** (Montelukast sodium) is indicated in adult and paediatric patients 6 months of age and older 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.
- **Indokast** (Montelukast sodium) is also indicated for the relief of symptoms of allergic rhinitis:
- Seasonal allergic rhinitis in adults and paediatric patients 2 years of age and older.
- Perennial allergic rhinitis in adults and paediatric patients 6 months of age and older.

DOSAGE AND ADMINISTRATION
Indokast (Montelukast sodium) 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.

Adults and Adolescents 15 Years of Age and Older with Asthma and/or Allergic Rhinitis
The dosage for adults and adolescents 15 years of age and older is one 10mg tablet daily.

Paediatric patients 6 to 14 Years of Age with Asthma and / or Allergic Rhinitis
The dosage for Paediatric patients 6 to 14 years of age is 5mg chewable tablet daily. No dosage adjustment within this age group is necessary.

Paediatric Patients 2 to 5 Years of Age with Asthma and/or Allergic Rhinitis
The dosage for paediatric patients 2 to 5 years of age is one packet of 4mg oral granules daily.

Paediatric Patients 12 to 23 Months of Age with Asthma
The dosage for paediatric patients 12 to 23 months of age is one packet of 4mg oral granules daily to be taken in the evening.

Paediatric Patients 6 to 23 Months of Age with Perennial Allergic Rhinitis
The dosage for paediatric patients 6 to 23 months of age is one packet of 4mg oral granules daily.

Safety and effectiveness in paediatric patients younger than 6 months of age with perennial allergic rhinitis and in patients less than 12 months of age with asthma have not been established.

Exercise-Induced Bronchoconstriction (EIB) in Patients 15 Years of Age and Older
For Prevention of EIB, a single dose of **Indokast** tablets should be taken at least 2 hours before exercise. An additional dose of **Indokast** tablets should not be taken within 24 hours of a previous dose. Patients already taking one tablet daily for another indication (including chronic asthma) should not take an additional dose to prevent EIB. All patients should have available for rescue a short-acting (beta)-agonist. Safety and effectiveness in patients younger than 15 years of age have not been established. Daily administration of **Indokast** tablets for the chronic treatment of asthma has not been established to prevent acute episodes of exercise-induced bronchoconstriction.

Administration of Indokast oral granules

Indokast oral granules 4mg can be administered either directly in the mouth, dissolved in 1 teaspoonful (5mL) of cold or room temperature baby formula or breast milk, or mixed with a spoonful of cold or room temperature soft foods like rice or ice cream. The packet should not be opened until ready to use. After opening the packet, the full dose (with or without mixing with baby formula, breast milk, or food) must be administered within 15 minutes. If mixed with baby formula, breast milk, or food, **Indokast** oral granules must not be stored for future use. Discard any unused portion.

Indokast oral granules are not intended to be dissolved in any liquid other than baby formula or breast milk for administration. However, liquids may be taken subsequent to administration. **Indokast** oral granules can be administered without regard to the time of meals.

CONTRAINDICATIONS

Montelukast sodium is contraindicated in a patient who has shown hypersensitivity to the drug or any of its components. Montelukast sodium is not indicated for use in acute asthma attacks including status asthmaticus.

ADVERSE 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 (including anaphylaxis, angioedema, rash, pruritus, urticaria and very rarely, hepatic eosinophilic infiltration).
- Dream abnormalities, hallucinations, palpitations, drowsiness, irritability, restlessness, insomnia, increased sweating, headache;
- Nausea, vomiting, dyspepsia, diarrhea, abdominal pain;
- Myalgia including muscle cramps;
- Increased bleeding tendency, bruising edema;
- Tremor, dry mouth, vertigo, arthralgia.

DRUG INTERACTIONS

It is recommended that clinical monitoring, particularly in children, be conducted when potent hepatic enzyme inducers such as phenytoin, phenobarbital, or rifampicin are given with montelukast sodium. No dosage adjustment for **Indokast** (Montelukast sodium) is recommended.

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.
- Although a casual relationship with leukotriene receptor antagonism has not been established, caution and appropriate clinical monitoring is recommended when systemic corticosteroid reduction is considered in patients receiving montelukast sodium.
- Montelukast sodium should not be used as mono-therapy for the treatment and management of exercise-induced asthma. Patients who have exacerbations of asthma after exercise should continue to use their usual regimen of inhaled β-agonists as prophylaxis and should have it available as and when required.
- Montelukast sodium does not block bronchoconstrictor response to aspirin or non-steroidal anti-inflammatory drugs in aspirin sensitive asthmatic patients.Such patients should continue to avoid aspirin and other non-steroidal anti-inflammatory drugs.
- 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 Because many drugs are excreted in human milk, caution should be exercised when **Indokast** is given to a nursing mother.

STORAGE CONDITIONS:

- Store below 30°C.
- Protect from heat, light and moisture.

PRESENTATION

- **Indokast** 4mg Sachet : Pack of 14 sachets.
- **Indokast** 5mg Tablet : Pack of 14 chewable tablets.
- **Indokast** 10mg Tablet : Pack of 14 film coated tablets.

Keep all medicines out of the reach of children.

Manufactured by :
Indus Pharma (Pvt.) Ltd.
65/27, Korangi Industrial Area,
Karachi-74900, Pakistan.

0201140026R2