Montelukast sodium

Montiget®

4mg, 5mg, 10mg

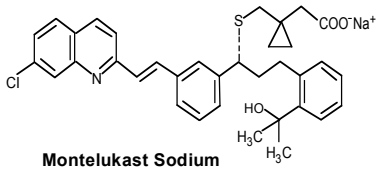
Pediatric Granules, Chewable Tablets, Film-Coated Tablets

Leukotriene Receptor Antagonist

DESCRIPTION

Montelukast sodium (Montiget®) is a selective and orally active leukotriene receptor antagonist that inhibits the cysteinyl leukotriene CysLT1 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

FORMULATION

Montelukast sodium (Montiget®) is available for oral administration as:

1. Montelukast sodium (Montiget®) Pediatric Granules 4mg
   Each sachet contains:
   Montelukast sodium
   equivalent to Montelukast....4mg

2. Montelukast sodium (Montiget®) Chewable Tablets 4mg
   Each chewable tablet contains:
   Montelukast sodium
   equivalent to Montelukast....4mg

3. Montelukast sodium (Montiget®) Chewable Tablets 5mg
   Each chewable tablet contains:
   Montelukast sodium
   equivalent to Montelukast....5mg

4. Montelukast sodium (Montiget®) Film-coated Tablets 10mg
   Each film-coated tablet contains:
   Montelukast sodium
   equivalent to Montelukast....10mg

CLINICAL PHARMACOLOGY

Mechanism of Action

Montelukast sodium (Montiget®) is a competitive, selective and orally active leukotriene D4 (cysteinyl leukotriene CysLT1) receptor antagonist. The cysteinyl leukotrienes (LTC4, LTD4, LTE4) are products of arachidonic acid metabolism and are released from various cells, including mast cells and eosinophils. These eicosanoids bind to cysteinyl leukotriene (CysLT) receptors. 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. Thus, montelukast sodium inhibits physiologic actions of LTD4 at the CysLT1 receptors, without any agonist activity.

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, pediatric, 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 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.

Pediatric 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

- Montelukast sodium (Montiget®) 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.
- Montelukast sodium (Montiget®) is also indicated for the relief of symptoms of seasonal allergic rhinitis in adults and pediatric patients 2 years of age and older.

DOSAGE AND ADMINISTRATION

The therapeutic effect of montelukast sodium on parameters of asthma control occurs within one day. Montelukast sodium (Montiget®) tablets and chewable tablets can be taken with or without food. Patients should be advised to continue taking the drug while their asthma is controlled as well as during periods of worsened asthma.

Montelukast sodium (Montiget®) should be taken once daily. 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 or sachet daily in the evening.

Adults and Adolescents 15 Years of Age and Older with Asthma or Seasonal Allergic Rhinitis:

The dosage for adults and adolescents 15 years of age and older is one 10mg tablet daily.

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

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

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

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

Pediatric Patients 6 Months to 2 Years of Age with Asthma

The dosage for pediatric patients 6 months to 2 years of age is one sachet of pediatric granules 4mg daily to be taken in the evening.

Use of Montelukast sodium (Montiget®) in relation to other treatment for asthma

Montelukast sodium (Montiget®) can be added to a patient's existing treatment regimen.

Reduction in concomitant therapy

- Bronchodilator Treatment: Montelukast sodium (Montiget®) can be added to the treatment 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 sodium (Montiget®) 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 the inhaled corticosteroids can be tapered off completely. Montelukast sodium (Montiget®) should not be abruptly substituted for inhaled corticosteroids.

Administration of Montelukast sodium (Montiget®) Pediatric Granules
Montelukast sodium (Montiget®) pediatric granules 4mg can be administered either directly in the mouth, or mixed with a spoonful of cold or room temperature soft foods. The sachet should not be opened until ready to use. After opening the sachet, the full dose (with or without food) must be adminstered within 15 minutes. If mixed with food, Montelukast sodium (Montiget®) pediatric granules must not be stored for future use. Discard any unused portion. **Montelukast sodium (**Montiget®**) pediatric granules are not intended to be dissolved in liquid for administration.** However, liquids may be taken subsequent to administration.

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 eosinophillic 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.

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.

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 monotherapy 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 ß-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 Montelukast sodium (Montiget®) is given to a nursing mother.

Drug Interactions
It is recommended that clinical monitoring be conducted when potent hepatic enzyme inducers such as phenytoin, phenobarbital, or rifampicin are given with montelukast sodium. No dosage adjustment for Montelukast sodium (Montiget®) is recommended.

STORAGE CONDITIONS
Store at temperatures not exceeding 30°C.
Protect from sunlight & moisture.
The expiration date refers to the product correctly stored at the required conditions.

AVAILABILITY
Montelukast sodium (Montiget®) Pediatric Granules 4mg are available in a pack of 14 sachets.

Montelukast sodium (Montiget®) Chewable tablets 4mg are available in blister packs of 2 x 7's.

Montelukast sodium (Montiget®) Chewable tablets 5mg are available in blister packs of 2 x 7's.

Montelukast sodium (Montiget®) Film-coated tablets 10mg are available in blister packs of 2 x 7's.

CAUTION
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

Keep out of reach of children.

Please read the contents carefully before use.
This package insert is continually updated from time to time.

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