**Floaid**

(Montelukast Sodium)

**10mg Tablets**

5mg Chewable Tablets

4mg Paediatric Dry Powder Sachet

**COMPOSITION**

Floaid 10 mg tablets: Each film coated tablet contains 10.4 mg Montelukast Sodium U.S.P. equivalent to 10 mg Montelukast Acid.

Floaid 5 mg chewable tablets: Each film coated tablet contains 5.2 mg Montelukast Sodium U.S.P. equivalent to 5 mg Montelukast Acid.

Floaid 4 mg Paediatric Dry Powder sachet: Oral use. Each sachet of Floaid contains 4.75 mg Montelukast Sodium U.S.P. equivalent to 4 mg Montelukast Acid.

**DESCRIPTION**

(a) Mode of Action:

Montelukast Sodium is a selective leukotriene receptor antagonist that specifically inhibits the pathway leukotriene Cys LTR receptors.

(b) Pharmacokinetic properties

Absorption: Montelukast is rapidly absorbed following oral administration. For the 10 mg film coated tablet, the mean peak plasma concentration (Cmax) is attained 3 hours (Tmax) after administration in adults in the fasted state. The mean oral bioavailability is 64%. The oral bioavailability and Cmax are not influenced by a standard meal.

For the 5 mg chewable tablet, the Cmax is achieved in 2 hours after administration in adults in the fasted state. The mean oral bioavailability is 73% and is decreased to 65% by a standard meal. After administration of the 4 mg paediatric dry powder to paediatric patients 2 to 5 years of age in the fasted state, Cmax achieved 2 hours after administration. The mean Cmax is 65% higher when montelukast is given in adults receiving a 10 mg tablet.

Distribution: Montelukast is more than 95% bound to plasma proteins. The steady-state volume of distribution of montelukast averages 8-11 litres.

Biotransformation: Montelukast is extensively metabolized in the liver. In studies with therapeutic doses, plasma concentrations of metabolites of montelukast are undetectable at steady state in adults and children.

Cytosplastic (P450) 2C9 is the major enzyme in the metabolism of montelukast. Additionally CYP 3A4 and UGT may have minor contribution.

Elimination: The plasma clearance of montelukast averages 45-55 ml/min in healthy adults. Montelukast and its metabolites are exclusively excreted via the urine.

Characteristics in patients:

No dosage adjustment is necessary for the elderly or mild to moderate hepatic insufficiency. There are no data on the pharmacokinetics of montelukast in patients with severe hepatic insufficiency.

In patients with severe hepatic insufficiency (Child-Pugh score >9), no dosage adjustment is necessary. There are no data on the pharmacokinetics in patients with severe renal insufficiency.

With high doses of montelukast (20-60 fold the recommended adult dose), a decrease in plasma theophylline concentration was observed. This effect was not seen at the recommended dose of 10 mg daily.

**Therapeutic Indications**

1. Asthma: Floaid 5 mg chewable tablet may also be an alternative treatment option to low-dose inhaled corticosteroids for 2 to 5 year old patients with mild to moderate persistent asthma who are inadequately controlled on inhaled corticosteroids and in whom "as needed" short acting β agonists provide inadequate clinical control.

Floaid 4 mg dry powder may be an alternative treatment option to low-dose inhaled corticosteroids for 2 to 5 year old patients with mild persistent asthma who do not have a recent history of serious asthma attacks that required inhaled corticosteroids use, and who have demonstrated that they are not capable of using inhaled corticosteroids.

Floaid 4 mg dry powder is also indicated in the prophylaxis of asthma from 2 years of age and older with the predominant component is exercise-induced bronchoconstriction.

1.1. Floaid 5 mg chewable tablet may also be an alternative treatment option to low-dose inhaled corticosteroids for 6 to 16 year old patients with mild persistent asthma who do not have a recent history of serious asthma attacks that required inhaled corticosteroids use, and who have demonstrated that they are not capable of using inhaled corticosteroids.

Floaid 5 mg dry powder is also indicated in the prophylaxis of asthma in those 6 to 14 years of age with the predominant component is exercise-induced bronchoconstriction.

1.2. Floaid 10 tablet is indicated in the treatment of asthma as add-on therapy in patients 15 years and older with mild to moderate persistent asthma who are inadequately controlled on inhaled corticosteroids and in whom "as needed" short acting β agonists provide inadequate clinical control. In those asthmatics in whom Floaid 10 mg tablet is indicated in asthma, Floaid 10 mg tablet can also provide symptomatic relief of seasonal allergic rhinitis.

10 mg tablet is also indicated in the prophylaxis of asthma in which the predominant component is exercise-induced bronchoconstriction in patients 15 years and older.

2. Pollen Allergic Rhinitis (PAR) in patients 6 months of age and older:

Acute prevention of exercise-induced bronchoconstriction (EIB) in patients 6 years of age and older.

3. Relief of symptoms of allergic rhinitis (SAR): seasonal allergic rhinitis (SAR) in patients 2 years of age and older, and perennial allergic rhinitis (PAR) in patients 4 months of age and older.

**Dosage and Administration**

**Fluid 4 Dry Powder:**

The dosage for paediatric patients 2-5 years of age is one 4 mg dry powder sachet daily.

Floaid 4 mg dry powder can be administered either directly in the mouth, or mixed with a tablespoon of soft food or a liquid mixture containing food (e.g. applesauce, ice cream or tea). The sachet should not be opened until ready to use. After opening the sachet, the full dose of powder must be administered immediately within 15 minutes. It is mixed with food. Floaid powder must not be stored for future use.

Floaid powder is not intended to be dissolved in liquid for administration. However, this may be subsequently added to soft food. Floaid powder can be administered without regard to the timing of food ingestion.

**Fluid 5 mg chewable tablet:**

The dosage for paediatric patients 6-14 years of age is one 5 mg chewable tablet daily to be taken in the evening. The tablets are to be chewed before swallowing. It is taken in conjunction with food. Floaid 5 mg chewable tablet should be taken 1 hour before or 2 hours after food. No dosage adjustment within this age group is necessary.

**General recommendations:**

The therapeutic effect of Fluid 5 mg chewable tablet on parameters of asthma control occurs within one day. Patients should be advised to continue taking Fluid 5 mg chewable tablet even if their asthma is under control, as well as during periods of worsening asthma.

No dosage adjustment is necessary for patients with renal insufficiency, or mild to moderate hepatic impairment. The dosage is the same for both male and female patients.

Floaid 5 mg chewable tablet is an alternative treatment option to low-dose inhaled corticosteroids for mild persistent asthmatics.

**Therapy with Fluid 5 mg chewable tablet:**

When treatment with Floaid 5 mg chewable tablet is used as an add-on therapy to inhaled corticosteroids, Floaid 5 mg chewable tablet should not be abruptly substituted for inhaled corticosteroids.

**Fluid 10 mg tablet:**

10 mg Floaid film coated tablets are available for adults and adolescents 15 years of age and older.

The dosage for adults and adolescents 15 years of age and older, with asthma or concomitant seasonal allergic rhinitis is one 10 mg tablet daily to be taken in the evening.

**General recommendations:**

The therapeutic effect of Fluid 10 mg tablet on parameters of asthma control occurs within one day. Patients should be advised to continue taking Floaid 10 mg tablet even if their asthma is under control, as well as during periods of worsening asthma.

No dosage adjustment is necessary for the elderly or for patients with renal insufficiency, or mild to moderate hepatic impairment. There are no data on the pharmacokinetics in patients with severe renal insufficiency.

Montelukast should be deeply swallowed with liquids or food.

**Contraindications**

Hypersensitivity to any component of this product.

**Special warnings and precautions for use**

Patients should be advised never to use montelukast to treat acute asthma attacks and to keep their usual appropriate rescue medication for this purpose readily available. If an acute attack occurs, a short acting β-agonist should be used. Patients should seek their doctor's advice before they need more inhalations of short-acting β-agonists than usual.

Montelukast should be deeply swallowed with liquids or food.

There are no data demonstrating that oral corticosteroids can be reduced when montelukast is given concurrently.

In rare cases, patients on therapy with anti-asthma agents including montelukast may present with systemic eosinophilia, sometimes presenting with clinical features of vasculitis consistent with Churg Strauss syndrome. In such cases, montelukast should be stopped immediately, and corticosteroids initiated. There are no data on the pharmacokinetics of montelukast in patients with severe renal insufficiency.

Therapy should be stopped immediately should symptoms of vasculitis consistent with Churg Strauss syndrome develop and montelukast should be stopped immediately, and corticosteroids initiated. There are no data on the pharmacokinetics of montelukast in patients with severe renal insufficiency.

The dosage for patients with aspirin-sensitivae allergic asthma is 10 mg tablet daily to be taken in the evening.

Treatment with montelukast does not alter the need for patients with aspirin-sensitive asthma to avoid taking aspirin and other non-steroidal anti-inflammatory drugs.

Patient and physician should be alert for neuropsychiatric events. Patients should be instructed to notify their health care practitioner if any such changes occur.

**Interaction with other medicinal products and other forms of interaction**

Montelukast may be administered with other therapies routinely used in the chronic and chronic treatment of asthma. In drug interaction studies, the recommended clinical doses of montelukast did not have clinically important effects on the pharmacokinetics of the following medicinal products: theophylline, prednisone, prednisolone, oral contraceptives (ethinyl estradiol/ norethindrone), lasix/ hydrochlorothiazide (315), terbinafine, digoxin and warfarin.

The area under the plasma concentration curve (AUC) for montelukast was reduced by approximately 25% when montelukast was administered with rifampicin. There are no data on the pharmacokinetics in patients with severe hepatic insufficiency.

Montelukast should be stopped immediately and montelukast should be stopped immediately, and corticosteroids initiated. There are no data on the pharmacokinetics in patients with severe renal insufficiency.

In vitro studies have shown that montelukast is a potent inhibitor of CYP 2C8, CYP 2C9 and CYP 2C19, caution should be exercised, particularly in children, when montelukast is co-administered with CYP 3A4, 2C9 and 2C19, such as phenytoin, phenobarbital and rifampicin.

There are no data on the pharmacokinetics in patients with severe hepatic insufficiency.

Montelukast may be administered with other therapies routinely used in the chronic and chronic treatment of asthma. In drug interaction studies, the recommended clinical doses of montelukast did not have clinically important effects on the pharmacokinetics of the following medicinal products: theophylline, prednisone, prednisolone, oral contraceptives (ethinyl estradiol/ norethindrone (315), terbinafine, digoxin and warfarin.

The area under the plasma concentration curve (AUC) for montelukast was decreased approximately 40% in subjects co-administered of phenobarbital. Since montelukast is metabolized by CYP 2C9, 2C8 and 2C19, caution should be exercised, particularly in children, when montelukast is co-administered with CYP 3A4, 2C9 and 2C19, such as phenytoin, phenobarbital and rifampicin.
In vitro studies have shown that montelukast is a substrate of CYP 2C8, and to a less significant extent, of 2C9 and 3A4. In a clinical drug-drug interaction study involving montelukast and gemfibrozil (an inhibitor of both CYP 2C8 and 2C9) gemfibrozil increased the systemic exposure of montelukast by 4.4-fold. No notable change in the pharmacokinetics of montelukast was observed on co-administration with gemfibrozil or other potent inhibitors of CYP 2C8, but the physician should be aware of the potential for an increase in adverse reactions. Based on in vitro data, clinically important drug interactions with less potent inhibitors of CYP 2C8, e.g., trimethoprim were not anticipated. Co-administration of montelukast with trimethoprim, a strong inhibitor of CYP 3A4, resulted in no significant change in the systemic exposure of montelukast.

Facility, pregnancy and lactation

Use during pregnancy

Animal studies do not indicate harmful effects with respect to effects on pregnancy or embryo/fetal development. Limited data from available pregnancy databases do not suggest a causal relationship between montelukast and malformations (i.e. birth defects) that have been rarely reported in worldwide post marketing experience. Flunis may be used during pregnancy only if it is considered to be clearly essential.

Use during lactation

Studies in rats have shown that montelukast is excreted in milk. It is not known if montelukast is excreted in human milk.

Effects on ability to drive and use machines

Montelukast is not expected to affect a patient’s ability to drive a car or operate machinery. However, in very rare cases, individuals have reported drowsiness or dizziness.

Geriatric use

In clinical studies, there were no age-related differences in the efficacy or safety profile of Montelukast Sodium.

Undesirable effects

Montelukast has been evaluated in a clinical study in patients with intermittent asthma as follows:

- 4 mg tablets and chewable tablets in 1,038 pediatric patients 6 months to 5 years of age.

The following drug-related adverse reactions in clinical studies were reported commonly (≥1/100 to <1/10) in patients treated with montelukast and at a greater incidence than in patients treated with placebo:

- Asthma: rhinitis, sinusitis, URT infection, sinus headache, cough
- Nasal congestion, rash, ALT & AST increased, Pyuria
- Fever, trauma, dyspepsia, dental pain, gastroenteritis, dizziness, influenza, cough, road congestion, rash, ALT & AST increased, Pyuria
- Asthma: Asthenia / fatigue, fever, trauma, dyspepsia, dental pain, gastroenteritis, dizziness, influenza, cough, road congestion, rash, ALT & AST increased, Pyuria

Other reported adverse events include thrombocytopenia, pancreatitis and Steven Johnson Syndrome toxic epidermal necrolysis.

Floaid 5 mg chewable tablet:

Montelukast has been evaluated in clinical studies as follows:

- 5 mg chewable tablets in approximately 1,750 pediatric patients 6 to 14 years of age

The following drug-related adverse reactions in clinical studies were reported commonly (≥1/100 to <1/10) in patients treated with montelukast and at a greater incidence than in patients treated with placebo:

- Asthma: Asthenia / fatigue, fever, trauma, dyspepsia, dental pain, gastroenteritis, dizziness, influenza, cough, road congestion, rash, ALT & AST increased, Pyuria

Other included Allergic reactions including anaphylaxis, skin eruptions, sensory disturbances, cardiovascular, dermatologic, and conjunctivitis.

Post-marketing Experience

Adverse reactions reported in post-marketing use are listed, by System Organ Class and specific adverse experience term, in the table below. Frequency Categories were estimated based on relevant clinical trials.

Other reported adverse events include thrombocytopenia, pancreatitis and Steven Johnson Syndrome toxic epidermal necrolysis.

Floaid 10 mg tablets:

Montelukast has been evaluated in clinical studies as follows:

- 10 mg film-coated tablets in approximately 4,000 adult and adolescent asthmatic patients 15 years of age and older
- 10 mg film-coated tablets in approximately 4,000 adult and adolescent asthmatic patients with seasonal allergic rhinitis 15 years of age and older

The following drug-related adverse reactions in clinical studies were reported commonly (≥1/100 to <1/10) in patients treated with montelukast and at a greater incidence than in patients treated with placebo:

- Asthma: Asthenia / fatigue, fever, trauma, dyspepsia, dental pain, gastroenteritis, dizziness, influenza, cough, road congestion, rash, ALT & AST increased, Pyuria

Other included Allergic reactions including anaphylaxis, skin eruptions, sensory disturbances, cardiovascular, dermatologic, and conjunctivitis.

OVERDOSE

No specific information is available on the treatment of overdose with montelukast.

STORAGE

Store below 25°C and protect from light and moisture.

PRESENTATION

1. Floaid 5 mg tablets: Blister pack of 14 tablets.
2. Floaid 10 mg tablets: Blister pack of 14 chewable tablets.
3. Floaid 4 mg Pediatric Dry Powder sachet for oral use: Carton of 24 sachets.

To be sold on the prescription of a registered medical practitioner only.

Keep all medicines out of the reach of children.

Manufactured by:
Highview Laboratories Ltd.
17.5 K.M. Multan Road, Lahore-Pakistan.

Marketed by:
Abbott Laboratories (Pakistan) Ltd.
Lahore, Karachi.