PACKAGE INSERT FOR LUMONT

SCHEDULING STATUS

S3

PROPRIETARY NAME AND DOSAGE FORM

LUMONT 4 mg chewable tablets

LUMONT 5 mg chewable tablets

LUMONT 10 mg film coated tablets

COMPOSITION

LUMONT 4 mg: Each tablet contains montelukast sodium, equivalent to 4 mg montelukast.

LUMONT 5 mg: Each tablet contains montelukast sodium, equivalent to 5 mg montelukast.

LUMONT 10 mg: Each tablet contains montelukast sodium, equivalent to 10 mg montelukast.

LUMONT 4 mg and **5 mg** contain mannitol and aspartame.

LUMONT 10 mg contains lactose.

Inactive ingredients for LUMONT 4 mg and LUMONT 5 mg:

Mannitol, microcrystalline cellulose, ferric oxide red, croscarmellose sodium, hydroxypropyl cellulose, purified water, ethanol anhydrous, crospovidone, cherry dry flavour, aspartame, magnesium stearate.

Inactive ingredients for LUMONT 10 mg:

Microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, crospovidone, magnesium stearate, Opadry Yellow (20A82772) (containing hypromellose 6 cP, hydroxypropyl cellulose, titanium dioxide, iron oxide yellow, iron oxide red, purified water).

PHARMACOLOGICAL CLASSIFICATION

A.10.2.2 Other anti-asthmatics (Leukotriene receptor antagonist)

PHARMACOLOGICAL ACTION

Montelukast is a selective leukotriene receptor antagonist of the cysteinyl leukotriene Cys-LT_1 receptor. The cysteinyl leukotrienes (LTC_4, LTD_4, LTE_4) are products of arachidonic acid metabolism that are released from various cells including mast cells and eosinophills. They bind to cysteinyl leukotriene receptors (Cys-LT_1) found in the human airway. All the cysteinyl leukotrienes are potent constrictors of the bronchial smooth muscle (and are also correlated with effects such as mucous secretion, vascular permeability and eosinophil recruitment).

On a molar basis LTD_4 is approximately 1000 times more potent than histamine as a bronchoconstrictor. The receptor responsible for the bronchoconstrictor effect of leukotrienes is the Cys-LT_1 receptor. Although each of the cysteinyl leukotrienes are agonists at the Cys-LT_1 receptor, LTE_4 is less potent than either LCT_4 or LTD_4. Montelukast is a selective, high affinity competitive antagonist of the Cys-LT_1 receptor and inhibits the physiological actions of LTC_4, LTE_4 and LTD_4. This has been demonstrated by the ability of montelukast to inhibit bronchoconstriction due to inhaled LTD_4 in asthmatic patients. Doses as low as 5 mg cause substantial blockage of LTD_4-induced bronchoconstriction.

Pharmacokinetics

Absorption:

Peak plasma concentrations of montelukast are achieved in 2 hours with the 4 and 5 mg tablets and 3 hours after oral doses of the 10 mg tablet. The mean oral bioavailability is 64 % and 73 % for the 10 mg and the 5 mg tablets respectively. Food does not have a clinically important influence with chronic administration of the 5 mg tablet.

Distribution:

Montelukast is more than 99 % bound to plasma proteins.

Metabolism:

It is extensively metabolised in the liver by cytochrome P450 isoenzymes CYP3A and CYP2C9. In studies with therapeutic doses, plasma concentrations of metabolites of montelukast are undetectable at steady state in adults and paediatric patients. Based on *in vitro* studies of human liver microsomes, therapeutic concentrations of montelukast do not inhibit cytochromes P450, 3A4, 2C9, 2A6, 2C19 or 2D6.

Elimination:

The plasma clearance of montelukast averages 45 ml/min in healthy adults. The half-life of montelukast is approximately 3 to 6 hours in healthy adults.

It is mainly excreted in the faeces via the bile (86 %).

The pharmacokinetics of montelukast are nearly linear at doses up to 50 mg.

Hepatic insufficiency:

Patients with mild to moderate hepatic insufficiency and clinical evidence of cirrhosis had evidence of decreased 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 greater than 9).

INDICATIONS

LUMONT 4 mg chewable tablets are indicated in paediatric patients 2 to 5 years of age for the prophylaxis and chronic treatment of atopic asthma.

LUMONT 5 mg chewable tablets are indicated in paediatric patients 6 to 14 years of age for the prophylaxis and chronic treatment of atopic asthma.

LUMONT 10 mg film coated tablets are indicated in adults and children 15 years of age and older for the prophylaxis and chronic treatment of atopic asthma.

CONTRAINDICATIONS

- Hypersensitivity to montelukast or any other component of **LUMONT**.
- Pregnancy and lactation.
- **LUMONT 4 mg:** Safety and efficacy have not been established in children under the age of 2 years.
- **LUMONT 5 mg:** Safety and efficacy have not been established in children under the age of 6 years.
- **LUMONT 10 mg** should not be used in children under the age of 15 years.

WARNINGS AND SPECIAL PRECAUTIONS:

Asthma:

LUMONT is not indicated for the use in the reversal of bronchospasm in acute asthma attacks, including status asthmaticus. Patients should be advised to have appropriate rescue medication available.

The efficacy of **LUMONT** has not been established for the treatment of acute asthma attacks. Therapy with **LUMONT** may be continued during acute exacerbations of asthma.

LUMONT should not be used as monotherapy for the treatment or management of exercise-induced bronchospasm. Patients should be advised to continue with the usual regimen of an inhaled beta-agonist for prophylaxis of exercise-induced bronchospasm and to have a short-acting inhaled beta-agonist available for rescue treatment.

Patients should be advised to take **LUMONT** exactly as prescribed, even if they are asymptomatic. **LUMONT** should also be used during periods of worsening asthma and patients should contact their healthcare practitioner if their asthma is not well controlled. Medical attention should be

sought if more than the prescribed maximum number of inhalations of short-acting bronchodilator treatment for a 24 hour period are needed.

LUMONT should not be abruptly substituted for inhaled or oral corticosteroids. If appropriate, the dose of corticosteroids should be tapered gradually under medical supervision. To ensure safe and appropriate use, patients should be advised to read the precautions section in the patient information leaflet.

Eosinophilic conditions:

In rare cases, the reduction of systemic corticosteroids in patients on another leukotriene antagonist has been followed by the occurrences of eosinophilia, vasculitis rash, worsening pulmonary symptoms, cardiac complications and/or neuropathy sometimes presenting as Churg-Strauss syndrome (a systemic eosinophilic vasculitis). These events usually, but not always, have been associated with the reduction of oral corticosteroid therapy. Healthcare practitioners should be aware of eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications and/or neuropathy presenting in their patients. **LUMONT** should be withdrawn in these patients.

Neuropsychiatric events:

Neuropsychiatric events have been reported in some patients taking **LUMONT**. These include agitation, aggression, anxiousness, dream abnormalities, hallucinations, depression, insomnia, irritability, restlessness, suicidal thinking and behaviour (including suicide), and tremor. Patients and healthcare professionals should be aware of the potential for neuropsychiatric events. Patients should be instructed to inform their healthcare professionals if these events occur. Healthcare professionals should carefully evaluate the risks and benefits of continuing treatment with **LUMONT** if such events occur.

Hypersensitivity to aspirin:

Patients with a known hypersensitivity to aspirin should continue avoiding aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) while taking **LUMONT**. Although **LUMONT** is effective in

improving airway function in asthmatics, it has not been shown to reduce the bronchoconstrictor response to aspirin or other NSAIDs in aspirin-sensitive asthmatic patients.

Hepatic function impairment:

The metabolism of montelukast may be decreased in patients with mild to moderate hepatic function impairment and clinical evidence of cirrhosis. The half-life may be slightly prolonged however, dosage adjustment is not necessary. Data are not available in patients with severe hepatic function impairment.

Other:

LUMONT 4 mg and **5 mg** chewable tablets contain aspartame, which is metabolised to phenylalanine (1,360 mg phenylalanine for the 4 mg chewable tablets, and 2,423 mg phenylalanine for the 5 mg chewable tablets). **LUMONT** should be used with caution in patients with phenylketonuria.

LUMONT 10 mg tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency, or glucose-galactose malabsorption should not take **LUMONT 10 mg**.

Effects on the ability to drive or operate machinery

LUMONT may cause side effects such as dizziness or drowsiness, which may affect the ability to drive. Patients should therefore be advised not to drive or operate machinery until their individual susceptibility is known.

INTERACTIONS

LUMONT may be used with other medicines used in the prophylaxis and chronic treatment of asthma. Montelukast does not significantly change the pharmacokinetics of theophylline, warfarin, digoxin, fexofenadine, oral contraceptives (containing 1 mg norethindrone and 35 µg ethinyl estradiol), prednisone or prednisolone.

Concurrent use of **LUMONT** and phenobarbital results in significant decreases (approximately 40 %) in the area under the curve for montelukast, as a result of induction of hepatic metabolism. No dosage adjustment is necessary. However, clinical monitoring is required when potent hepatic enzyme inducers such as phenytoin, phenobarbital or rifampicin are given with montelukast.

PREGNANCY AND LACTATION

The safety of the use of **LUMONT** in pregnant and lactating women has not yet been established. It is not known if **LUMONT** is excreted in human milk.

LUMONT should not be used during pregnancy or lactation.

DOSAGE AND DIRECTIONS FOR USE

- **LUMONT** should be taken once daily in the evening.
- **LUMONT** tablets may be taken with or without food.
- The therapeutic effect of **LUMONT** occurs within one day on parameters of asthma control.
- Patients should be advised to continue taking **LUMONT** while their asthma is controlled, as well as during periods of worsening asthma.
- No dosage adjustment is necessary for paediatric patients, the elderly, patients with renal insufficiency, mild to moderate hepatic impairment, or for patients of either gender.

Treatment for atopic asthma

Paediatric patients 2 to 5 years: One **LUMONT 4 mg** chewable tablet daily.

Paediatric patients 6 to 14 years: One **LUMONT 5 mg** chewable tablet daily.

Adults and children 15 years of age and older: One **LUMONT 10 mg** tablet daily.

Therapy with LUMONT in relation to other treatments of asthma

LUMONT can be added to a patient's existing treatment regimen.

SIDE EFFECTS

Blood and lymphatic system disorders

Less frequent: Churg-Strauss syndrome (see **WARNINGS AND SPECIAL PRECAUTIONS**).

Frequency unknown: Increased bleeding tendency, agranulocytosis.

Immune system disorders

Less frequent: Anaphylaxis, angioedema, allergy, hypersensitivity reactions, and hepatic eosinophilic infiltration.

Endocrine disorders

Frequency unknown: Pancreatitis.

Psychiatric disorders

Frequency unknown: Aggressive behaviour or hostility, agitation, hallucinations, dream abnormalities, depression, restlessness, anxiety, irritability, suicidal thinking and behaviour.

Nervous system disorders

Frequent: Headache, dizziness, insomnia.

Frequency unknown: Paraesthesia, hypoesthesia, seizures, tremor, drowsiness.

Cardiac disorders

Frequency unknown: Palpitations.

Respiratory, thoracic and mediastinal disorders

Less frequent: Nasal congestion, cough, influenza, epistaxis.

Gastrointestinal disorders

Frequent: Abdominal pain.

Less frequent: Dyspepsia, gastroenteritis.

Frequency unknown: Diarrhoea, nausea, vomiting, dry mouth.

Hepato-biliary disorders

Less frequent: Elevated hepatic enzymes (AST, ALT).

Frequency unknown: Cholestatic hepatitis, hyperbilirubinaemia, hepatitis.

Skin and subcutaneous tissue disorders

Less frequent: Skin rash.

Frequency unknown: Pruritus, urticaria, bruising, erythema nodosum.

Musculoskeletal, connective tissue and bone disorders

Frequency unknown: Arthralgia, myalgia

Renal and urinary disorders

Frequency unknown: Pyuria.

General disorders and administrative site conditions

Less frequent: Asthenia, fatigue, dental pain, fever.

Frequency unknown: Oedema, generalised pain.

KNOWN SYMPTOMS OF OVERDOSE AND PARTICULARS OF ITS TREATMENT

Symptoms which have been observed are abdominal pain, hyperkinesia, mydriasis, somnolence and thirst. Treatment is symptomatic and supportive and may include clinical monitoring. It is not known whether montelukast is dialysable by peritoneal or haemodialysis.

IDENTIFICATION

LUMONT 4 mg: Pink coloured, oval shaped, uncoated tablets plain on both sides, having a mottled surface.

LUMONT 5 mg: Pink coloured, round shaped, uncoated tablets plain on both sides, having a mottled surface.

LUMONT 10 mg: Yellow coloured, round shaped, bevel edged, film coated tablet debossed with "285" on one side and plain on other side.

PRESENTATION

LUMONT 4 mg: Silver aluminium / aluminium blister strips containing either 14 or 10 tablets each. Each carton contains 28 or 30 tablets.

LUMONT 5 mg: Silver aluminium / aluminium blister strips containing either 7 or 10 tablets each. Each carton contains 28 or 30 tablets.

LUMONT 10 mg: Silver aluminium / aluminium blister strips containing either 7 or 10 tablets each. Each carton contains 28 or 30 tablets.

STORAGE INSTRUCTIONS

LUMONT 4 mg and **5 mg:** Store at or below 25 °C.

LUMONT 10 mg: Store at or below 30 °C.

Protect from moisture and light.

Keep in outer carton until required for use.

KEEP OUT OF REACH OF CHILDREN

REGISTRATION NUMBERS

LUMONT 4 mg: 44/10.2.2/0823

LUMONT 5 mg: 44/10.2.2/0824

LUMONT 10 mg: 44/10.2.2/0792

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

Zydus Healthcare SA (Pty) Ltd.

Southdowns Office Park

Building B, Ground Floor

22 Karee Street

Centurion

0157

DATE OF PUBLICATION OF THE PACKAGE INSERT

June 2012