PROPOSED PROFESSIONAL INFORMATION FOR LEVOMONT

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

LEVOMONT film coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains montelukast sodium equivalent to 10 mg montelukast, and 5 mg levocetirizine dihydrochloride.

Contains sugar (lactose monohydrate, 83,60 mg).

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film coated tablet

Yellow, round, biconvex, film coated tablets plain on both sides.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

LEVOMONT is indicated in adults for the relief of symptoms associated with seasonal allergic rhinitis (SAR).

4.2 Posology and method of administration

Posology:

Adults (≥ 18 years of age):

The recommended dose is one tablet to be taken orally, in the evening. The tablets should be swallowed whole, with or without food.

Paediatric and adolescent patients (≤ 18 years):

LEVOMONT has not been studied in the paediatric and adolescent population and is not recommended for use in this age group.

Special population:

Patients with renal impairment:

No dose adjustment is needed in patients with mild renal impairment (creatinine clearance > 79 mL/min). **LEVOMONT** should be used with caution and under strict medical supervision in patients with moderate to severe renal impairment (creatinine clearance < 79 mL/min to > 10mL/min).

Patients with hepatic impairment:

No dose adjustment is needed in patients with hepatic impairment.

Method of administration:

LEVOMONT is for oral administration.

4.3 Contraindications

LEVOMONT is contraindicated in

- Hypersensitivity to the active substances, or to hydroxyzine, or to any other piperazine derivatives or to any of the excipients (see section 6.1).
- Patients with severe renal impairment at less than 10 mL/min creatinine clearance.

4.4 Special warnings and precautions for use

Montelukast

LEVOMONT is not indicated in the reversal of bronchospasm in acute asthma attacks, including status asthmaticus as the efficacy of **LEVOMONT** has not been established for the treatment of acute asthma attacks.

Eosinophilic Conditions

In some cases, patients on therapy with montelukast, as contained in **LEVOMONT**, may present with systemic eosinophilia, sometimes presenting with clinical features of vasculitis consistent with Churg-Strauss syndrome, a condition which is often treated with systemic corticosteroid therapy. These events usually, but not always, have been associated with the reduction of oral corticosteroid therapy. Medical practitioners should be alert to eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in their patients. Patients who develop these symptoms should be reassessed and their treatment regimens evaluated.

Neuropsychiatric events

Neuropsychiatric events have been reported in adult, adolescent and paediatric patients taking **LEVOMONT**.

Post-marketing reports with **LEVOMONT** use include agitation, aggressive behaviour or hostility, anxiousness, depression, disorientation, disturbance in attention, abnormal dreams, hallucinations, insomnia, irritability, memory impairment, restlessness, somnambulism, suicidal ideation and behaviour (including suicide), tic and tremor.

Patients and medical practitioners should be alert for neuropsychiatric events. Patients should be instructed to notify their medical practitioners if these changes occur. Medical practitioners should carefully evaluate the risks and benefits of continuing treatment with **LEVOMONT** if such events occur.

Hypersensitivity to aspirin

Patients with a known hypersensitivity to aspirin should continue avoiding aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) while taking **LEVOMONT**. Although **LEVOMONT** is effective in improving airway function in asthmatics, it has not been demonstrated to reduce the broncho-constrictor response to aspirin or other NSAIDs in aspirin-sensitive asthmatic patients.

Hepatic impairment

The metabolism of montelukast may be decreased in patients with mild to moderate hepatic impairment and clinical evidence of cirrhosis. The half-life may be slightly prolonged; however, dosage adjustment is not necessary. No data are available for patients with severe hepatic impairment.

Levocetirizine

Alcohol

Precaution is recommended with intake of alcohol (see section 4.5). **LEVOMONT** lacks significant sedative effects. Patients should, however, be warned that a small number of individuals may experience sedation. This effect may be compounded by the simultaneous intake of alcohol or other central nervous system depressants (see section 4.5).

Risk of urinary retention

Caution should be taken in patients with predisposing factors of urinary retention (e.g. spinal cord lesion, prostatic hyperplasia) as levocetirizine may increase the risk of urinary retention.

Risk of seizure aggravation

Caution should be taken in patients with epilepsy and patients at risk of convulsion as levocetirizine may cause seizure aggravation.

Allergy skin tests

Response to allergy skin tests are inhibited by antihistamines and a wash-out period (of 3 days) is required before performing them.

Withdrawal syndrome

Pruritus may occur when levocetirizine is stopped even if those symptoms were not present before treatment initiation. The symptoms may resolve spontaneously. In

some cases, the symptoms may be intense and may require treatment to be restarted. The symptoms should resolve when the treatment is restarted.

Excipient warnings:

LEVOMONT contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicines and other forms of interaction

Pharmacodynamic interactions:

No specific drug-drug interaction studies have been performed with **LEVOMONT**. The data is complied with the available information from the individual components of the fixed dose combination (FDC). Also, since both montelukast and levocetirizine metabolises with different receptors there are no drug-drug interaction anticipated with the use of **LEVOMONT**.

Montelukast

Montelukast may be administered with other therapies routinely used in the prophylaxis and chronic treatment of asthma, and seasonal allergic rhinitis. In medicine-interactions studies, the recommended clinical dose of montelukast did not have clinically important effects on the pharmacokinetics of the following medicines: theophylline, prednisone, prednisolone, oral contraceptives (ethinyl oestradiol/norethindrone 35/1), terfenadine, digoxin and warfarin.

The area under the plasma concentration - time curve (AUC) for montelukast was decreased approximately 40 % in subjects with co-administration of phenobarbital. Since montelukast is metabolised by GYP 3A4, 2C8, and 2C9, caution should be exercised when montelukast is co-administered with inducers of GYP 3A4, 2C8, and 2C9, such as phenytoin, phenobarbital and rifampicin.

In vitro studies have shown that montelukast is a potent inhibitor of CYP 2C8. However, data from an interaction study involving montelukast and rosiglitazone (a probe substrate representative of medicines primarily metabolized by CYP2C8) demonstrated that montelukast did not significantly inhibit CYP2C8 *in vivo*. Therefore, montelukast is not anticipated to alter the metabolism of drugs metabolized by this enzyme (e.g. paclitaxel, rosiglitazone, and repaglinide).

In vitro studies have shown that montelukast is a substrate of GYP2C8, and to a less significant extent, of 2C9, and 3A4. In a medicine-medicine interaction study involving montelukast and gemfibrozil (an inhibitor of both GYP 2C8 and 2C9) gemfibrozil increased the systemic exposure of montelukast by 4,4-fold. No routine dosage adjustment of montelukast is required upon co-administration with gemfibrozil or other potent inhibitors of GYP 2C8, but the doctor 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 GYP2C8 (e.g. trimethoprim) are not anticipated. Co-administration of montelukast with itraconazole, a strong inhibitor of GYP3A4, resulted in no significant increase in the systemic exposure of montelukast.

Levocetirizine

No interaction studies have been performed with levocetirizine (including no studies with CYP3A4 inducers). Studies with the racemate compound cetirizine demonstrated that there were no clinically relevant adverse interactions with phenazone, azithromycin, cimetidine, diazepam, erythromycin, glipizide, ketoconazole and pseudoephedrine.

Theophylline

A decrease in the clearance of cetirizine (16 %) was observed in a multiple dose study with theophylline (400 mg once a day); while the disposition of theophylline was

not altered by concomitant cetirizine administration.

Ritonavir

In a multiple dose study of ritonavir (600 mg twice daily) and cetirizine (10 mg daily), the extent of exposure to cetirizine was increased by about 40 % while the disposition of ritonavir was decreased (-11 %). Ritonavir increased the plasma AUC of cetirizine by about 42 % accompanied by an increase in half-life (53 %) and a decrease in clearance (29 %) of cetirizine. The disposition of ritonavir was not altered by concomitant cetirizine administration.

Food

The extent of absorption of levocetirizine, as contained in **LEVOMONT**, is not reduced with food, although the rate of absorption is decreased.

Alcohol

In sensitive patients the simultaneous administration of levocetirizine and alcohol or other central nervous system (CNS) depressants may have effects on the central nervous system such a reductions in alertness and impairment of performance.

4.6 Fertility, pregnancy and lactation

No specific studies have been performed with **LEVOMONT** on pregnant and lactating women.

The safety of **LEVOMONT** in pregnant and lactating women has not been established.

Pregnancy:

Montelukast:

Animal studies do not indicate harmful effects with respect to effects on pregnancy or embryonal/foetal development. Limited data from available pregnancy databases do not suggest a causal relationship between montelukast and malformations (i.e. limb defects) that have been rarely reported in worldwide post marketing experience.

Levocetirizine:

There are no or limited amount of data (less than 300 pregnancy outcomes) from the use of levocetirizine in pregnant women.

Breastfeeding:

Montelukast:

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

Levocetirizine

Cetirizine, the racemate of levocetirizine, has been shown to be excreted in human. Therefore, the excretion of levocetirizine in human milk is likely. Adverse reactions associated with levocetirizine may be observed in breastfed infants.

Fertility:

No clinical data are available for **LEVOMONT.**

4.7 Effects on ability to drive and use machines

LEVOMONT may cause dizziness, drowsiness, and fatigue. Therefore, patients intending to drive, engage in potentially hazardous activities or operate machinery should take their response to the medicine into account.

4.8 Undesirable effects

Summary of the safety profile

The most frequently reported adverse events were nervous system disorders, gastrointestinal disorders and respiratory disorders. The most common single adverse event reported was headache. Adverse events of fever, urinary tract infection and cough were also common. No serious adverse events were reported.

Tabulated list of adverse reactions:

Montelukast

System Organ Class	**Frequency**	**Side effects**
Infections and infestations	Frequent	Upper respiratory infection
Blood and lymphatic system disorders	Less frequent	Thrombocytopenia, increased bleeding tendency
Immune system disorders	Less frequent	Hypersensitivity reactions including anaphylaxis, hepatic eosinophilic infiltration
Psychiatric disorders	Less frequent	Dream abnormalities including nightmares, insomnia, somnambulism, anxiety, agitation including aggressive behaviour or hostility, depression, psychomotor hyperactivity (including irritability, restlessness, tremor), disturbance in attention, memory impairment, tic, hallucinations, disorientation, suicidal thinking and behaviour (suicidality), obsessive-compulsive

		symptoms, dysphemia
Nervous system disorders	Frequent Less frequent	Headache Dizziness, drowsiness, paraesthesia/hypoesthesia, seizure
Cardiac disorders	Less frequent	Palpitations
Respiratory, thoracic and mediastinal disorders	Less frequent	Epistaxis, Churg-Strauss syndrome, pulmonary eosinophilia
Gastrointestinal disorders	Frequent Less frequent	Abdominal pain, diarrhoea, nausea, vomiting Dry mouth, dyspepsia
Hepato-biliary disorders	Frequent Less frequent	Elevated levels of serum transaminases (ALT, AST) Hepatitis (including cholestatic, hepatocellular, and mixed-pattern liver injury)
Skin and subcutaneous tissue disorders	Frequent Less frequent	Rash Bruising, urticaria, pruritus, angioedema, erythema nodosum, erythema multiforme
Musculoskeletal and connective tissue disorders	Less frequent	Arthralgia, myalgia including muscle cramps
General disorders and	Frequent Less frequent	Pyrexia Asthenia/fatigue, malaise

administration sites conditions		Oedema

Levocetirizine

System Organ Class	**Frequency**	**Side effects**
Immune system disorders	Frequency unknown	Hypersensitivity including anaphylaxis
Metabolism and nutrition disorders	Frequency unknown	Increased appetite
Psychiatric disorders	Frequency unknown	Aggression, agitation, hallucination, depression, insomnia, suicidal ideation, nightmare
Nervous system disorders	Frequent Frequency unknown	Headache, somnolence Convulsions, paraesthesia, dizziness, syncope, tremor, dysgeusia
Eye disorders	Frequency unknown	Visual disturbances, blurred vision
Ear and labyrinth disorders	Frequency unknown	Vertigo
Cardiac disorders	Frequency unknown	Palpitations, tachycardia
Respiratory, thoracic and mediastinal disorders	Frequency unknown	Dyspnoea
Gastrointestinal disorders	Frequent Frequency unknown	Dry mouth Nausea, vomiting, diarrhoea

Hepato-biliary disorders	Frequency unknown	Hepatitis
Skin and subcutaneous tissue disorders	Frequency unknown	Angioedema, fixed drug eruption, pruritus, rash, urticaria
Musculoskeletal and connective tissue disorders	Frequency unknown	Myalgia, arthralgia
Renal and urinary disorders	Frequency unknown	Dysuria, urinary retention
General disorders and administration sites conditions	Frequent Frequency unknown	Fatigue Oedema
Investigations	Frequency unknown	Weight increased, abnormal liver function tests

LEVOMONT:

System Organ Class	**Frequency**	**Side effects**
Infections and infestations	Frequent Frequency unknown	Upper respiratory tract infection, nasopharyngitis, tonsillitis Urinary Tract Infection
Blood and Lymphatic System Disorders	Frequency unknown	Eosinophilia
Psychiatric disorders	Frequency unknown	Restlessness

Nervous system disorders	Frequency unknown	Dizziness, headache, somnolence, hypersomnia
Eye disorders	Frequency unknown	Eye Pain, eyelid oedema
Ear and labyrinth disorders	Frequency unknown	Ear Pain
Respiratory, thoracic and mediastinal disorders	Frequency unknown	Cough, oropharyngeal pain, rhinorrhoea
Gastrointestinal disorders	Frequent Frequency unknown	Gastrointestinal disorder Nausea, dry mouth, constipation, dyspepsia, vomiting
Renal and urinary disorders	Frequency unknown	Pyuria
General disorders and administration sites conditions	Frequency unknown	Fatigue, fever, weakness

Post-marketing experience

Post-marketing reports with **LEVOMONT** use include agitation, aggressive behaviour or hostility, anxiousness, depression, disorientation, disturbance in attention, abnormal dreams, hallucinations, insomnia, irritability, memory impairment, restlessness, somnambulism, suicidal ideation and behaviour (including suicide), tic and tremor.

Reporting of suspected adverse reactions:

Reporting of suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse

reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**",

found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

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

Montelukast:

Symptoms:

The most frequently occurring adverse experiences were consistent with the safety profile of montelukast and included abdominal pain, somnolence, thirst, headache, vomiting, and psychomotor hyperactivity.

Management:

Should overdose occur, symptomatic and supportive treatment is recommended.

Levocetirizine

Symptoms:

Symptoms of overdose may include drowsiness in adults and initially agitation and restlessness, followed by drowsiness in children.

Management:

There is no known specific antidote to levocetirizine.

Should overdose occur, symptomatic or supportive treatment is recommended.

Levocetirizine is not effectively removed by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

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

A 5.7.1 Anti-histaminics (Levocetirizine)

Pharmacotherapeutic group: An agent acting as a leukotriene receptor antagonist and an antihistamine for systemic use, piperazine derivative.

ATC code: R03D C03 (Montelukast)

ATC code: R06A E09 (Levocetirizine)

Montelukast:

Montelukast is a leukotriene receptor antagonist.

The cysteinyl leukotrienes (LTC_4, LTD_4, LTE_4) are potent inflammatory eicosanoids released from various cells, including mast cells and eosinophils. These important pro-asthmatic mediators bind to cysteinyl leukotriene (CysLT) receptors. The CysLT type-1 ($CysLT_1$) receptor is found in the human airway (including airway smooth muscle cells and airway macrophages) and on other pro-inflammatory cells (including eosinophils and certain myeloid stem cells). CysLTs have been correlated with the pathophysiology of asthma and allergic rhinitis. In asthma, leukotriene-mediated effects include a number of airway actions, including bronchoconstriction, mucous secretion, vascular permeability, and eosinophil recruitment. In allergic rhinitis, CysLTs are released from the nasal mucosa after allergen exposure during both early- and late-phase reactions and are associated with symptoms of allergic rhinitis. Intranasal challenge with CysLTs has been shown to increase nasal airway resistance and symptoms of nasal obstruction.

Levocetirizine:

Levocetirizine, the (R) enantiomer of cetirizine, is a potent and selective antagonist of peripheral H1-receptors.

Binding studies revealed that levocetirizine has high affinity for human H1-receptors (Ki = 3.2 nmol/L). Levocetirizine has an affinity 2-fold higher than that of cetirizine (Ki = 6.3 nmol/L). Levocetirizine dissociates from H1-receptors with a half-life of 115 ± 38 min. After single administration, levocetirizine shows a receptor occupancy of

90 % at 4 hours and 57 % at 24 hours.

Pharmacodynamic studies in healthy volunteers demonstrate that, at half the dose, levocetirizine has comparable activity to cetirizine, both in the skin and in the nose.

5.2 Pharmacokinetic Properties

Montelukast:

Absorption:

Montelukast is rapidly absorbed following oral administration. For the 10 mg film-coated tablet, the mean peak plasma concentration (C_{max}) is achieved 3 hours (T_{max}) after administration in adults in the fasted state. The mean oral bioavailability is 64 %. The oral bioavailability and C_{max} are not influenced by a standard meal. Safety and efficacy were demonstrated in clinical trials where the 10 mg film-coated tablet was administered without regard to the timing of food ingestion.

Distribution:

Montelukast is more than 99 % bound to plasma proteins. The steady-state volume of distribution of montelukast averages 8 to 11 litres. Studies in rats with radiolabelled montelukast indicate minimal distribution across the blood-brain barrier. In addition, concentrations of radiolabelled material at 24 hours post-dose were minimal in all other tissues.

Biotransformation:

Montelukast is extensively metabolized. In studies with therapeutic doses, plasma concentrations of metabolites of montelukast are undetectable at steady state in adults and paediatric patients.

Cytochrome (CYP) P450 2C8 is the major enzyme in the metabolism of montelukast. Additionally CYP 3A4 and 2C9 may have a minor contribution, although itraconazole, an inhibitor of CYP 3A4, was shown not to change pharmacokinetic variables of

montelukast in healthy subjects that received 10 mg montelukast daily. Based on in vitro results in human liver microsomes, therapeutic plasma concentrations of montelukast do not inhibit cytochromes P450 3A4, 2C9, 1A2, 2A6, 2C19, or 2D6. The contribution of metabolites to the therapeutic effect of montelukast is minimal.

Elimination:

The plasma clearance of montelukast averages 45 mL/min in healthy adults. Following an oral dose of radiolabelled montelukast, 86 % of the radioactivity was recovered in 5-day faecal collections and less than 0,2 % was recovered in urine. Coupled with estimates of montelukast oral bioavailability, this indicates montelukast and its metabolites are excreted almost exclusively via the bile.

Levocetirizine

Absorption:

The pharmacokinetics of levocetirizine are linear with dose- and time-independent with low inter-subject variability. The pharmacokinetic profile is the same when given as the single enantiomer or when given as cetirizine. No chiral inversion occurs during the process of absorption and elimination.

Levocetirizine is rapidly and extensively absorbed following oral administration. In adults, peak plasma concentrations are achieved 0.9 h after dosing. Steady state is achieved after two days. Peak concentrations are typically 270 ng/mL and 308 ng/mL following a single and a repeated 5 mg o.d. dose, respectively. The extent of absorption is dose-independent and is not altered by food, but the peak concentration is reduced and delayed.

Distribution:

No tissue distribution data are available in humans, neither concerning the passage of levocetirizine through the blood-brain-barrier. In rats and dogs, the highest tissue levels are found in liver and kidneys, the lowest in the CNS (central nervous system)

compartment. In Human, levocetirizine is 90 % bound to plasma proteins. The distribution of levocetirizine is restrictive, as the volume of distribution is 0.4 L/kg.

Biotransformation:

The extent of metabolism of levocetirizine in humans is less than 14 % of the dose and therefore differences resulting from genetic polymorphism or concomitant intake of enzyme inhibitors are expected to be negligible. Metabolic pathways include aromatic oxidation, N- and O- dealkylation and taurine conjugation. Dealkylation pathways are primarily mediated by CYP 3A4 while aromatic oxidation involved multiple and/or unidentified CYP isoforms. Levocetirizine had no effect on the activities of CYP isoenzymes 1A2, 2C9, 2C19, 2D6, 2E1 and 3A4 at concentrations well above peak concentrations achieved following a 5 mg oral dose.
Due to its low metabolism and absence of metabolic inhibition potential, the interaction of levocetirizine with other substances, or vice-versa, is unlikely.

Elimination:

The plasma half-life in adults is 7,9 ± 1,9 hours. The half-life is shorter in small children. The mean apparent total body clearance in adults is 0.63 mL/min/kg. The major route of excretion of levocetirizine and metabolites is via urine, accounting for a mean of 85,4 % of the dose. Excretion via faeces accounts for only 12,9% of the dose. Levocetirizine is excreted both by glomerular filtration and active tubular secretion.

Pharmacokinetics in Special populations

Hepatic impairment:

Montelukast:

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 (Child-Pugh score >9).

Levocetirizine

The pharmacokinetics of levocetirizine in hepatically impaired subjects have not been tested. Patients with chronic liver diseases (hepatocellular, cholestatic, and biliary cirrhosis) given 10 or 20 mg of the racemic compound cetirizine as a single dose had a 50 % increase in half-life along with a 40 % decrease in clearance compared to healthy patients.

Renal impairment:

Montelukast:

Studies in patients with renal impairment have not been undertaken. Because montelukast and its metabolites are eliminated by the biliary route, no dose adjustment is anticipated to be necessary in patients with renal impairment.

Levocetirizine

The apparent body clearance of levocetirizine is correlated to the creatinine clearance. It is therefore recommended to adjust the dosing intervals of levocetirizine, based on creatinine clearance in patients with moderate and severe renal impairment. In anuric end stage renal disease subjects, the total body clearance is decreased by approximately 80 % when compared to normal subjects. The amount of levocetirizine removed during a standard 4-hour hemodialysis procedure was < 10%.

Elderly

Montelukast

No dosage adjustment is necessary for the elderly.

Levocetirizine

Limited pharmacokinetic data are available in elderly subjects. Following once daily repeat oral administration of 30 mg levocetirizine for 6 days in 9 elderly subjects (65–74 years of age), the total body clearance was approximately 33 % lower compared to that in younger adults. The disposition of racemic cetirizine has been shown to be

dependent on renal function rather than on age. This finding would also be applicable for levocetirizine, as levocetirizine and cetirizine are both predominantly excreted in urine. Therefore, the levocetirizine dose should be adjusted in accordance with renal function in elderly patients.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Intragranular part

Anhydrous dibasic calcium phosphate

Croscarmellose sodium

Hydroxypropyl cellulose

Lactose monohydrate

Microcrystalline cellulose

Purified water

Extragranular part

Croscarmellose sodium

Magnesium stearate

Microcrystalline cellulose

Film tablet coating

Opadry Yellow (containing hypromellose, iron oxide yellow, iron oxide red, macrogol, polysorbate and titanium dioxide)

Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 25 °C.

Protect from light and moisture.

6.5 Nature and contents of container

A 10 mL white opaque HDPE round container, containing a silica gel canister, fitted with a polypropylene child resistant cap with an induction seal, packed into an outer carton.

Pack size: 28 or 30 film coated tablets.

6.6 Special precautions for disposal and other handling

No special precautions.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Forrester Pharma (Pty) Ltd

2 Waterford Mews

Waterford Place

Century City

7441

Cape Town

South Africa

8. REGISTRATION NUMBERS

Will be allocated by the SAHPRA upon registration.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of registration: To be allocated by the SAHPRA.

10. DATE OF REVISION OF THE TEXT

PROPOSED PROFESSIONAL INFORMATION FOR LEVOMONT