PROPOSED PACKAGE INSERT FOR

LUNAR 10 mg / 20 mg / 100 mg

SCHEDULING STATUS:

S4

PROPRIETARY NAME (AND DOSAGE FORM):

LUNAR 10 mg (Tablets)

LUNAR 20 mg (Tablets)

LUNAR 100 mg (Tablets)

COMPOSITION:

LUNAR 10 mg: Each tablet contains 10 mg of leflunomide.

Inactive ingredients include colloidal anhydrous silica, lactose anhydrous, lactose monohydrate, low substituted hydroxypropyl cellulose, maize starch, magnesium stearate and povidone.

LUNAR 20 mg: Each tablet contains 20 mg of leflunomide.

Inactive ingredients include colloidal anhydrous silica, lactose anhydrous, lactose monohydrate, low substituted hydroxypropyl cellulose, maize starch, magnesium stearate and povidone.

LUNAR 100 mg: Each tablet contains 100 mg of leflunomide.

Inactive ingredients include colloidal anhydrous silica, lactose anhydrous, lactose monohydrate, low substituted hydroxypropyl cellulose, maize starch, magnesium stearate and povidone.

WARNING:

Pregnancy:

Pregnancy must be excluded before the start of treatment with LUNAR. LUNAR is contraindicated in pregnant women, or women of childbearing potential who are not using reliable contraception (see "CONTRAINDICATIONS" and "PREGNANCY AND LACTATION"). Pregnancy must be avoided during LUNAR treatment or prior to the completion of the medicine elimination procedure after LUNAR treatment.

Hepatotoxicity:

Severe liver injury, including fatal liver injury, has been reported in some patients treated with LUNAR. Patients with pre-existing acute or chronic liver disease, or those with serum alanine aminotransferase (AST) > 2 x ULN (Upper Limit of Normal) before initiation of treatment, should not be treated with LUNAR. Use caution when LUNAR is given with other potentially hepatotoxic medicines.

Monitoring of ALT levels is recommended at least monthly for six months after starting LUNAR, and thereafter every 6 – 8 weeks. If ALT elevation > 3-fold ULN occurs, interrupt LUNAR therapy while investigating the probable cause of the ALT elevation by close observation and additional tests. If likely LUNAR-

induced, start cholestyramine washout and monitor liver function tests weekly until normalised. If LUNAR-induced liver injury is unlikely because some other probable cause has been found, resumption of LUNAR therapy may be considered (see "WARNINGS AND SPECIAL PRECAUTIONS").

PHARMACOLOGICAL CLASSIFICATION:

A 3.1 Antirheumatics (anti-inflammatory agents).

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

Leflunomide is an isoxazole immunemodulatory agent which inhibits dihydroorotate dehydrogenase (an enzyme involved in *de novo* pyrimidine synthesis) and which has antiproliferative activity. Several *in vivo* and *in vitro* experimental models have demonstrated an anti-inflammatory effect.

Pharmacokinetic properties:

Following oral administration, leflunomide is metabolised to the active primary metabolite, A771726. Plasma levels of leflunomide are occasionally seen at very low levels. Studies of the pharmacokinetics of leflunomide have primarily examined the plasma concentrations of this active metabolite.

Absorption:

Following oral administration, peak levels of the primary metabolite occurred between 6 to 12 hours after dosing. Due to the very long half-life of the primary metabolite (approximately 2 weeks), a loading dose of 100 mg for 3 days was used

in clinical studies to facilitate the rapid attainment of steady state levels. Without a loading dose, it is estimated that attainment of steady state plasma concentrations would require nearly 2 months of dosing. The plasma concentrations following both loading doses and continued clinical dosing indicate that the primary metabolite levels are dose proportional. Relative to an oral solution, leflunomide tablets are 80 % bioavailable. Co-administration of leflunomide tablets with a high fat meal did not have a significant impact on primary metabolite plasma levels.

Distribution:

The primary metabolite has a low volume of distribution (Vss = 0,13 ℓ/kg) and is extensively bound (> 99,3 %) to albumin. Protein binding has been shown to be linear at therapeutic concentrations. The free fraction of the primary metabolite is slightly higher in patients with rheumatoid arthritis (RA) and approximately doubled in patients with chronic renal failure; the mechanism and significance of these increases are unknown.

Metabolism:

Leflunomide is metabolised to one primary (A771726) and many minor metabolites. Of these minor metabolites, only 4-trifluoromethylaniline (TFMA) is quantifiable, occurring at low levels in the plasma. The parent compound is rarely detectable in plasma. The specific site of leflunomide metabolism is unknown. *In vivo* and *in vitro* studies suggest a role for both the gastrointestinal wall and the liver in medicine metabolism. No specific enzyme has been identified as the primary route of metabolism of leflunomide; however, hepatic cytosolic and microsomal cellular fractions have been identified as sites of medicine metabolism.

Elimination:

The primary metabolite is eliminated by further metabolism and subsequent renal excretion as well as by direct biliary excretion. Studies of both haemodialysis and CAPD (chronic ambulatory peritoneal dialysis) indicate that the primary metabolite cannot be removed by dialysis.

INDICATIONS:

LUNAR is indicated for the treatment of adult patients with active rheumatoid arthritis as a disease-modifying antirheumatic medicine (DMARD), and to improve physical function.

CONTRAINDICATIONS:

LUNAR is contraindicated in:

- Patients with hypersensitivity to leflunomide (especially previous Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme) or to any of the excipients in the tablets.
- Patients with impairment of liver function (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).
- Patients with severe immunodeficiency states, e.g. AIDS.
- Patients with significantly impaired bone marrow function or significant anaemia, leukopenia, neutropenia or thrombocytopenia due to causes other than rheumatoid arthritis (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).
- Patients with serious infections.

- Patients with moderate to severe renal insufficiency, because insufficient clinical experience is available in this patient group.
- Patients with severe hypoproteinaemia, e.g. in nephritic syndrome.
- Pregnant women, or women of childbearing potential who are not using reliable contraception during treatment with **LUNAR** and thereafter as long as the plasma levels of the active metabolite are above 0,02 mg/ℓ. Pregnancy must be excluded before the start of treatment with **LUNAR**. In animal studies leflunomide was teratogenic in rats and rabbits (see **"PREGNANCY AND LACTATION"**). Women must not breastfeed while they are taking **LUNAR**. Male patients should be aware of the possible male-mediated foetal toxicity. Reliable contraception during treatment with **LUNAR** should also be guaranteed.
- Patients under 18 years as safety and efficacy have not been studied in this age group.

WARNINGS AND SPECIAL PRECAUTIONS:

Recent treatment with hepatotoxic or haematotoxic disease-modifying antirheumatic agents may result in increased side-effects; therefore, initiation of **LUNAR** treatment has to be carefully considered against these benefit/risk aspects. Moreover, switching from **LUNAR** to another disease-modifying antirheumatic agent without a washout period may increase the possibility of additive risks of side-effects for a long time after switching.

General:

The active metabolite of LUNAR has a long half-life, usually 1 to 4 weeks. Due to the prolonged half-life of the active metabolite, serious undesirable effects may occur (e.g. hepatotoxicity, haematotoxicity or allergic reactions), or persist even after LUNAR administration has been discontinued. Therefore, when such toxicities occur, or when switching to another disease-modifying antirheumatic agent (e.g. methotrexate) after treatment with LUNAR, or in case of a desired pregnancy, or if for any other reason the primary metabolite needs to be cleared rapidly from the body, a washout procedure (as described under "KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT"), has to be initiated and continued / repeated as clinically necessary. For suspected severe immunologic / allergic reactions, more prolonged cholestyramine or charcoal administration may be necessary to achieve rapid and sufficient clearance.

For washout procedures in case of desired pregnancy, refer to "PREGNANCY AND LACTATION".

Recommendations for monitoring and washout procedures:

Monitoring recommendations:

LUNAR should be administered to patients only under careful medical supervision. ALT (SGPT) must be checked before initiation of treatment and at least at monthly intervals during the first six months of treatment and every 6 – 8 weeks thereafter (see initial boxed "WARNING"). For confirmed ALT (SGPT) elevations between 2- and 3-fold ULN, dose reduction from 20 mg to 10 mg may allow continued administration of LUNAR under close monitoring. If ALT

(SGPT) elevations between 2- and 3-fold ULN persist or if confirmed ALT elevations of more than 3-fold ULN are present, LUNAR should be discontinued. Cholestyramine or activated charcoal should be administered to more rapidly lower the levels of the active metabolite.

Blood pressure must be checked before the start of LUNAR treatment and periodically thereafter, as increases in blood pressure may occur.

A complete blood cell count, including differential white blood cell count and platelets, must be performed before the start of LUNAR treatment as well as monthly for the first 6 months of treatment and every 6 – 8 weeks thereafter.

<u>Combinations with other treatments:</u>

The use of LUNAR with antimalarials used in rheumatic diseases (e.g. chloroquine and hydroxychloroquine), intramuscular or oral gold, D-penicillamine, azathioprine and other immunosuppressive agents (with the exception of methotrexate) has not been studied thus far. The risk associated with combination therapy, in particular in long-term treatment, is unknown. Since such therapy can lead to additive or even synergistic toxicity (e.g. hepato- or haematotoxicity), combination with another disease modifying antirheumatic agent (e.g. methotrexate) is not advisable.

<u>Switching to other treatments:</u>

As LUNAR has a long persistence in the body, switching to another disease modifying antirheumatic agent (e.g. methotrexate) without a washout period

may increase the possibility of additive risks even long after switching (i.e. kinetic interaction, organ toxicity). Similarly, recent treatment with hepatotoxic or haematotoxic medicines (e.g. methotrexate) may result in increased side-effects; therefore, the initiation of LUNAR treatment has to be carefully considered regarding these benefit/risk aspects.

Washout procedure:

Cholestyramine 8 g is administered 3 times daily. Alternatively, 50 g of activated powdered charcoal is administered 4 times daily. The duration of a complete washout is usually 11 days. The duration may be modified depending on clinical or laboratory variables.

Liver reactions:

(See initial boxed "WARNING".)

Rare cases of serious liver injury, including cases with fatal outcome, have been reported during treatment with LUNAR. Most of the cases occurred within the first 6 months of treatment. It is considered essential that monitoring recommendations are closely followed.

Since the active metabolite of LUNAR (the primary metabolite) is highly protein bound and cleared via hepatic metabolism and biliary secretion, free plasma levels of the primary metabolite are expected to be increased in patients with hypoproteinaemia and total serum levels increased in patients with impairment of liver function. LUNAR is contraindicated in patients with severe

hypoproteinaemia or impairment of liver function (see "CONTRAINDICATIONS").

Due to a potential for additive hepatotoxic effects, it is recommended that alcohol consumption be avoided during treatment with LUNAR.

Haematological reactions:

In patients with pre-existing anaemia, leukopenia, and/or thrombocytopenia as well as patients with impaired bone marrow function or those at risk of bone marrow suppression, the risk of haematological disorders is increased. If such effects occur, a washout (see above) to reduce plasma levels of the primary metabolite should be considered.

In case of severe haematological reactions including pancytopenia, LUNAR and any concomitant myelosuppressive medication must be discontinued and a LUNAR washout procedure initiated.

Frequent haematological monitoring (complete blood cell count, including differential white blood cell count and platelet count) should be performed in:

- Patients with recent or concomitant treatment with immunosuppressive or haematotoxic medicines, and when **LUNAR** treatment is followed by such substances without a washout period.
- Patients with a history of relevant haematological abnormalities.
- Patients with relevant haematological abnormalities at baseline due to causes other than rheumatoid arthritis.

Due to the potential for immunosuppression, although there is no clinical experience, **LUNAR** is not recommended in patients with:

- Severe immunodeficiency (e.g. AIDS).
- Significant impairment of bone marrow function.
- Serious infections.

Skin reactions:

In case of ulcerative stomatitis, LUNAR administration should be discontinued. Very rare cases of Stevens-Johnson syndrome or toxic epidermal necrolysis have been reported in patients treated with LUNAR. As soon as skin and/or mucosal reactions are observed which raise the suspicion of such severe reactions, LUNAR and any other possibly associated medication must be discontinued, and a LUNAR washout procedure initiated immediately. A complete washout is essential in such cases. In such cases re-exposure to leflunomide is contraindicated (see "CONTRAINDICATIONS").

Infections:

It is known that medications with immunosuppressive properties may cause patients to be more susceptible to infections, including opportunistic infections (see "SIDE-EFFECTS"). Infections may be more severe in nature and may therefore require early and vigorous treatment. In the event of severe, uncontrolled infections it may be necessary to discontinue LUNAR and administer a washout with cholestyramine as described above. Patients with tuberculin reactivity must be carefully monitored because of the risk of tuberculosis reactivation.

Procreation (recommendation for men):

There is no specific data on the risk of male-mediated foetal toxicity. However, animal studies to evaluate this specific risk have not been conducted. To minimise any possible risk, men wishing to father a child should consider discontinuing use of LUNAR and taking cholestyramine 8 g, three times daily for 11 days, or 50 g of activated charcoal, four times daily for 11 days. In either case the primary metabolite plasma concentration is then measured for the first time. Thereafter, the primary metabolite plasma concentration must be determined again after an interval of at least 14 days. If both plasma concentrations are below 0,02 mg/ℓ and after a waiting period of at least 3 months, the risk of foetal toxicity is very low.

Respiratory:

Interstitial lung disease has been reported rarely during treatment with LUNAR (see "SIDE-EFFECTS"). Interstitial lung disease is a potentially fatal disorder, which may occur acutely during therapy. Patients should be warned to report pulmonary symptoms, such as cough and dyspnoea, which should be further investigated to exclude interstitial lung disease. If interstitial lung disease is suspected, LUNAR should be discontinued and patients should be further investigated as appropriate.

Renal impairment:

At present there is insufficient experience available to make specific dosage recommendations for patients with renal impairment. **LUNAR** is contraindicated in

patients with moderate to severe renal insufficiency (see **"CONTRAINDICATIONS"**). It should be considered that the active metabolite of **LUNAR** is highly protein bound.

Effects on the ability to drive and use machinery:

Patients should be advised to exercise caution when driving or operating machinery. In the case of side-effects such as dizziness the patient's ability to concentrate and to react properly may be impaired.

Lactose:

LUNAR contains lactose. Patients who are lactose intolerant and who take **LUNAR** may experience unwanted side-effects, such as nausea, cramping, bloating, diarrhoea, and flatulence. **LUNAR** should not be administered to patients with hereditary galactose intolerance or with the rare Lapp lactose deficiency.

INTERACTIONS:

Increased side-effects may occur in case of recent or concomitant use of hepatotoxic (including alcohol), haematotoxic or immunosuppressive substances. This is also to be considered when **LUNAR** treatment is followed by such substances without a washout period.

No pharmacokinetic interaction between **LUNAR** (10 mg to 20 mg per day) and methotrexate (10 mg to 25 mg per week) was demonstrated.

In vivo interaction studies have demonstrated a lack of significant interaction between **LUNAR** and triphasic oral contraceptives.

The extent of **LUNAR** absorption is not affected when taken with food.

The enzymes involved in the metabolism of **LUNAR** and its metabolites are not exactly known. An *in vivo* interaction study with cimetidine (non-specific cytochrome P450 inhibitor) has demonstrated a lack of a significant interaction.

Studies have shown that following concomitant administration of a single dose of **LUNAR** with multiple doses of rifampicin (non-specific cytochrome P450 inducer), the primary metabolite peak levels were increased by approximately 40 %, whereas the AUC was not significantly changed. The mechanism of this effect is unclear.

The potential for **LUNAR** primary metabolite levels to continue to increase with multiple dosing may need to be considered if patients are to be taking both **LUNAR** and rifampicin.

Caution is advised when **LUNAR** is given together with medicines, other than NSAIDs, metabolised by CYP2C9, such as phenytoin, warfarin and tolbutamide. Phenytoin, tolbutamide, warfarin and many NSAIDs are metabolised by cytochrome P450 2C9 (CYP2C9). *In vitro* studies indicate that the primary metabolite inhibits CYP2C9 activity. The clinical significance of this finding with regard to phenytoin and tolbutamide is unknown. Caution is advised when these agents are given in combination. In clinical trials no safety concerns were observed when NSAIDs metabolised by CYP2C9 and **LUNAR** were co-administered. There have been case

reports of increased prothrombin time when **LUNAR** and warfarin were co-administered.

No clinical data is available on the efficacy and safety of vaccinations during **LUNAR** treatment. Vaccination with live vaccines is, however, not recommended. The long half-life of **LUNAR** should be considered when contemplating administration of a live vaccine after stopping **LUNAR**.

Administration of cholestyramine or activated charcoal leads to a rapid and significant decrease in plasma primary metabolite concentration. The mechanism is thought to be interruption of enterohepatic recycling and/or gastrointestinal dialysis of the primary metabolite. **LUNAR** should not be given to patients using cholestyramine.

PREGNANCY AND LACTATION:

Pregnancy:

The active metabolite of **LUNAR** is teratogenic in rats and rabbits and it may cause foetal harm in humans. **LUNAR** must not be given to pregnant women or women of childbearing potential who are not using reliable contraception. Women of childbearing potential have to use effective contraception during and up to 2 years after treatment or up to 11 days after a washout procedure (see **"Washout procedure"** below and **"CONTRAINDICATIONS"**). Pregnancy must be excluded before start of treatment with **LUNAR**.

Suspected pregnancy or women deciding to fall pregnant:

Patients must be advised that, if there is any delay in the onset of menses or any other reason to suspect pregnancy, they must notify the medical practitioner immediately for pregnancy testing, and if positive, the doctor and patient must discuss the risk to the pregnancy. It is possible that rapidly lowering the blood level of the active metabolite, by instituting the medicine elimination procedure, at the first delay of menses, may decrease the risk to the foetus from **LUNAR**.

Washout procedure:

For women receiving **LUNAR** treatment and who wish to become pregnant, one of the following procedures is recommended:

- After stopping treatment with **LUNAR**, cholestyramine 8 g is administered three times daily for a period of 11 days.
- After stopping treatment with **LUNAR**, 50 g of activated charcoal is administered four times daily for a period of 11 days.

The 11 days need not be consecutive unless there is a need to lower the primary metabolite plasma level rapidly.

In either case, primary metabolite plasma levels < 0,02 mg/ℓ must be verified by two separate tests at least 14 days apart. Human plasma levels of the active metabolite less than 0,02 mg/ℓ (0,02 µg/mℓ) are expected to have minimal risk based on available data.

Without the **LUNAR** elimination procedure, it may take up to 2 years for the primary metabolite to reach a level of < 0,02 mg/ℓ, due to individual variation in medicine

clearance. However, also after such a waiting period, verification of primary metabolite levels of < 0,02 mg/ℓ by two separate tests at an interval of at least 14 days is required. If a waiting period of up to approximately 2 years under reliable contraception is considered impractical, prophylactic institution of a washout procedure may be advisable. Reliable contraception with oral contraceptives may not be guaranteed during the washout procedure with cholestyramine or activated charcoal. Use of alternative contraceptive methods is recommended.

Lactation:

Animal studies indicate that leflunomide or its metabolites pass into breast milk. Breastfeeding women must therefore not take **LUNAR**.

DOSAGE AND DIRECTIONS FOR USE:

LUNAR treatment should be initiated by medical practitioners experienced in the therapy of rheumatoid diseases. For monitoring recommendations refer to "WARNINGS AND SPECIAL PRECAUTIONS".

LUNAR therapy is started with a loading dose of 100 mg once daily for 3 days. The recommended maintenance dose of **LUNAR** is 10 mg or 20 mg once daily. A therapeutic effect is usually seen after 4 to 6 weeks and further improvement may be seen for up to 4 to 6 months.

There is no dose adjustment recommended in patients with mild renal insufficiency.

No dosage adjustment is required in patients above 65 years of age.

Administration:

LUNAR tablets should be swallowed whole, with sufficient amounts of liquid. The extent of **LUNAR** absorption is not affected if it is taken with food.

SIDE-EFFECTS:

Infections and infestations:

Frequent:	Bronchitis, respiratory tract infection and urinary tract infection.
Less frequent:	Severe infections and sepsis, which may be fatal. Immunosuppressive medicines are known to increase susceptibility to infections, including opportunistic infections and infections with atypical organisms (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).

Neoplasms benign and malignant:

Frequency not known:	The risk of malignancy, particularly lymphoproliferative disorders, is known to be increased with the use of some immunosuppressive medicines, such as **LUNAR**.

Blood and the lymphatic system disorders:

Frequent:	Leukopenia with leucocyte count > 2 x 109/ℓ (> 2 G/ℓ).

Less frequent:	Agranulocytosis, pancytopenia, anaemia, thrombocytopenia with platelet count < 100 x 109/ℓ (< 100 G/ℓ), leukopenia with leucocyte count < 2 x 109/ℓ (< 2 G/ℓ) and eosinophilia. Recent, concomitant or consecutive use of potentially myelotoxic agents may be associated with a higher risk of haematological effects.

Immune system disorders:

Frequent:	Mild allergic reactions (including maculopapular and other rashes).
Less frequent:	Severe anaphylactic / anaphylactoid reactions.

Metabolism and nutrition disorders:

Less frequent:	Hypokalaemia.
Frequency not known:	Hypouricaemia due to a uricosuric effect and mild hyperlipidaemia. Possible further laboratory findings for which a clinical relevance could not be established include small increases in LDH and creatinine kinase (CK) and a small decrease in phosphate.

Psychiatric disorders:

Less frequent:	Anxiety.

Nervous system disorders:

Frequent:	Paraesthesia, headache and dizziness.
Less frequent:	Taste disturbances and peripheral neuropathy.

Eye disorders:

Less frequent:	Conjunctivitis.

Cardiac disorders:

Frequent:	Increase in blood pressure.
Less frequent:	Chest pain, palpitations and tachycardia.

Respiratory, thoracic and mediastinal disorders:

Frequent:	Bronchitis.
Less frequent:	Interstitial lung disease (including interstitial pneumonitis) which may be fatal, dyspnoea, pharyngitis, rhinitis and sinusitis.

Gastrointestinal disorders:

Frequent:	Diarrhoea, nausea and/or vomiting, anorexia, abdominal pain, oral mucosal disorders (e.g. aphthous stomatitis, mouth ulcerations) and dyspepsia.
Less frequent:	Pancreatitis, gastritis, gastroenteritis, constipation, dry mouth and flatulence.

Hepatobiliary disorders:

Frequent:	Hepatotoxicity and elevation of liver parameters (e.g. transaminases, less often gamma-GT, alkaline phosphatase, bilirubin).
Less frequent:	Severe liver injury, such as hepatic failure and acute hepatic necrosis, which may be fatal, hepatitis and jaundice or cholestasis.

Skin and subcutaneous tissue disorders:

Frequent:	Eczema, dry skin, alopecia, skin rash and pruritus. Mild allergic reactions (including maculopapular and other rashes).
Less frequent:	Toxic epidermal necrolysis and Stevens-Johnson syndrome (erythema multiforme of major type), urticaria and vasculitis, including cutaneous necrotising vasculitis.

Musculoskeletal, connective tissue disorders:

Frequent:	Joint disorders and synovitis.
Less frequent:	Tenosynovitis.

Renal and urinary disorders:

Frequency not known:	Renal failure.

General disorders and administrative site conditions:

Frequent: Weight loss, asthenia and back pain.

Less frequent: Malaise and fever.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

See **"SIDE-EFFECTS"**. In the event of relevant overdose or toxicity, cholestyramine or charcoal must be given to accelerate elimination. Cholestyramine given orally at a dose of 8 g three times a day for 24 hours to healthy volunteers decreased plasma levels of the primary metabolite by approximately 40 % in 24 hours and by 49 to 65 % in 48 hours.

Administration of activated charcoal, orally or via a nasogastric tube at a dose of 50 g every six hours for 24 hours, has been shown to reduce plasma concentrations of the active metabolite by 37 % in 24 hours and by 48 % in 48 hours. The washout procedures may be repeated if clinically necessary.

IDENTIFICATION:

LUNAR 10 mg: White, circular, biconvex tablets plain on both sides.

LUNAR 20 mg: Light yellow, triangular, biconvex, film-coated tablets plain on both sides.

LUNAR 100 mg: White-coloured, oval, biconvex, film-coated tablets plain on both sides.

PRESENTATION:

LUNAR 10 mg: Tablets are packed in 50 cc white cylindrical HDPE containers, enclosed by a white opaque polypropylene child resistant cap. The embossing on the cap has the following notations: "WHILE PUSHING DOWN TURN" and "CLOSE TIGHTLY". The liner on the cap has the following notations: "SEALED FOR YOUR PROTECTION" in black colour. Contains one silica gel bag as desiccant.

Pack size: 30s

LUNAR 20 mg: Tablets are packed in 50 cc white cylindrical HDPE containers, enclosed by a white opaque polypropylene child resistant cap. The embossing on the cap has the following notations: "WHILE PUSHING DOWN TURN" and "CLOSE TIGHTLY". The liner on the cap has the following notations: "SEALED FOR YOUR PROTECTION" in black colour. Contains one silica gel bag as desiccant.

Pack size: 30s

LUNAR 100 mg: Tablets are packed in blisters comprised of Alu/Alu blister foil and laminated film. Blisters are packed in an outer carton.

Pack size: 30s

STORAGE INSTRUCTIONS:

Store at or below 25 °C.

Bottles should be kept tightly closed.

Blister packs must be stored in the original package.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS:

LUNAR 10 mg: To be allocated.

LUNAR 20 mg: To be allocated.

LUNAR 100 mg: To be allocated.

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATES OF REGISTRATION:

CIPLA MEDPRO (PTY) LTD

Building 9

Parc du Cap

Mispel Street

Bellville

7530

RSA

DATE OF PUBLICATION OF THIS PACKAGE INSERT:

To be allocated.