Proposed Patient Information Leaflet

Information for the Patient about

LUNAR 10 mg / 20 mg / 100 mg (Tablets)

SCHEDULING STATUS:

S4

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM:

LUNAR 10 mg (Tablets)

LUNAR 20 mg (Tablets)

LUNAR 100 mg (Tablets)

Read all of this leaflet carefully before you start taking LUNAR.

- **Keep this leaflet. You may need to read it again.**
- **If you have further questions, please ask your doctor or your pharmacist.**
- **LUNAR has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.**

WHAT LUNAR CONTAINS:

LUNAR 10 mg: The active substance is 10 mg of leflunomide.

The other ingredients are colloidal anhydrous silica, lactose anhydrous, lactose monohydrate, low substituted hydroxypropyl cellulose, maize starch, magnesium stearate and povidone.

LUNAR 20 mg: The active substance is 20 mg of leflunomide.

The other ingredients are colloidal anhydrous silica, lactose anhydrous, lactose monohydrate, low substituted hydroxypropyl cellulose, maize starch, magnesium stearate and povidone.

LUNAR 100 mg: The active substance is 100 mg of leflunomide.

The other ingredients are 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. If you are pregnant or are able to fall pregnant and are not using reliable contraception you should not take LUNAR. Pregnancy must be avoided during LUNAR treatment or prior to the completion of the medicine elimination procedure after LUNAR treatment.

Liver damage:

Severe liver injury, which may be fatal, has been reported in some patients treated with LUNAR. If you have pre-existing acute or chronic liver disease, or abnormal liver function before initiation of treatment, you should not take LUNAR.

You will have to undergo blood tests to monitor your liver function at least monthly for six months after starting LUNAR, and every 6 – 8 weeks thereafter.

Depending on these results, you may have to undergo additional tests and investigations. Your doctor will decide whether or not it is safe for you to continue with LUNAR treatment and/or whether you require treatment with other medicines.

WHAT LUNAR IS USED FOR:

LUNAR belongs to a group of medicines called antirheumatics (anti-inflammatory agents) and is used to treat adult patients who have been diagnosed with active rheumatoid arthritis to delay progression of rheumatic disease and to improve physical function.

BEFORE YOU TAKE LUNAR:

Do NOT take LUNAR if you:

- Are hypersensitive (allergic) to leflunomide or any of the above ingredients of **LUNAR**, especially if you have had Stevens-Johnson syndrome (a serious allergic skin reaction with blister formation and fever) or toxic epidermal necrolysis (rash in which the outer layers of skin blister and peel off) or erythema multiforme (skin condition characterised by symmetrical, red, raised skin areas all over the body).
- Have impaired liver function or liver disease.
- Have severe suppression of your immune system, e.g. AIDS (Acquired Immune Deficiency Syndrome).
- Have impaired bone marrow function or anaemia (a shortage of red blood cells), abnormally low white blood cell counts (known as leukopenia), neutropenia (reduced levels of a specific type of white blood cell) or

thrombocytopenia (reduced number of platelets). Bone marrow is responsible for producing blood cells and platelets. Red blood cells carry oxygen, white blood cells help to fight infection and platelets play an important role in blood clotting.

- Suffer from a serious infection.
- Have reduced kidney function.
- Have a shortage of proteins in your blood plasma, which, amongst others, may be due to kidney disease.
- Are pregnant, or are able to fall pregnant and are not using reliable contraception. You will have to undergo a pregnancy test to rule out pregnancy before you start treatment with **LUNAR**.
    - If you are male, please discuss possible risks to the developing baby if your spouse/partner should fall pregnant while you are taking **LUNAR**.
- Are breastfeeding.
- Are under 18 years old.

Take special care with LUNAR:

Therapy with **LUNAR** may be toxic to the liver or bone marrow. If you are taking or recently have taken other medicines that may injure the liver or bone marrow, please discuss the use of **LUNAR** with your doctor, since this may increase your risk of experiencing side-effects. If you are switching from another medicine to **LUNAR**, you may have to undergo a washout procedure to lower the concentrations of **LUNAR** in your body to prevent side-effects from occurring. Your doctor will decide whether or not this is necessary.

LUNAR remains in the body for a long time. You may therefore still experience side-effects from LUNAR, even after you have stopped taking it. These may include liver damage, suppression of bone marrow function or allergic reactions. In order to prevent this from happening, you may have to undergo a washout procedure to hasten the elimination of LUNAR from your body. This is especially important when these side-effects should occur, or if you have to switch to another antirheumatic medicine or in case of a desired pregnancy. Your doctor will prescribe the necessary medicines and procedures.

You will be carefully monitored while you are taking LUNAR. You will have to undergo a blood test to monitor your liver and bone marrow function before treatment with LUNAR and at least at monthly intervals during the first six months of treatment. Thereafter such blood tests will be performed every 6 to 8 weeks. Based on these results your doctor will decide whether you qualify for further treatment and at which dose.
If you develop side-effects involving the liver or bone marrow (see "SIDE-EFFECTS"), your doctor may decide to perform a washout procedure to quickly lower the amount of LUNAR in your body.

LUNAR may cause serious liver injury, which has been fatal in cases. Most of these cases occurred within the first six months of treatment with LUNAR. Symptoms of liver injury include loss of appetite, nausea and/or vomiting, pain over the liver area, yellow discolouration of the whites of the eyes or skin and possibly pale stools with dark urine (see "SIDE-EFFECTS"). Please report any of these symptoms to your doctor as a matter of urgency.

LUNAR may cause an increase in blood pressure. Your blood pressure will therefore be checked prior to treatment with LUNAR and periodically thereafter.

Due to a potential for additive toxic effects on the liver, it is recommended that you avoid drinking alcohol while you are taking LUNAR.

Treatment with LUNAR may cause severe and potentially life-threatening allergic skin reactions. If you develop ulcers in the mouth or on the lips, please inform your doctor immediately. You should also report to your doctor as a matter of urgency if you should develop blisters on the skin or a skin rash accompanied by fever (see "SIDE-EFFECTS"). In these instances you should stop taking LUNAR and your doctor will initiate a washout procedure. If you have experienced any of these serious allergic skin reactions to LUNAR, you should never take LUNAR or any other product containing leflunomide ever again.

Medicines, like LUNAR, that suppress the immune system, may make you more susceptible to infections. Infections may be more severe in nature and may therefore require early and vigorous treatment. You should immediately report any symptoms suggestive of a possible infection to your doctor. These include fever, chills, coughing, sneezing, sore throat, skin ulcers, and generally feeling unwell, amongst others (see "SIDE-EFFECTS"). If you

suffered from tuberculosis previously, please inform your doctor as you will require careful monitoring.

If you are wishing to father a child, please check with your doctor first because LUNAR may harm the developing baby. Your doctor will advise you when it is safe to father a child and may perform a washout procedure to clear LUNAR from your body.

If you develop cough or shortness of breath while being treated with LUNAR, you must report this to your doctor immediately, because these may be symptoms of interstitial lung disease. This is a potentially fatal inflammation of the lining of the lungs.

LUNAR should not be used if you have moderate to severe kidney damage.

Taking LUNAR with food and drink:

LUNAR tablets should be swallowed whole, with sufficient amounts of liquid. **LUNAR** may be taken with or without food. You should avoid drinking alcohol while you are taking **LUNAR**, because it increases the risk of liver injury.

Pregnancy and breastfeeding:

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking LUNAR.

LUNAR may harm a developing baby. You must not use **LUNAR** if you are pregnant or if you are able to fall pregnant and are not using reliable contraception. You will have to undergo a pregnancy test to rule out pregnancy before you start taking **LUNAR**. Women who are able to fall pregnant must use reliable contraception during treatment with **LUNAR** and for up to two years after **LUNAR** has been stopped. If you wish to become pregnant, even after you have stopped **LUNAR**, you must check with your doctor first. Your doctor may perform a washout procedure and perform blood tests to ensure that it is safe for you to fall pregnant.

If your period is late or if you suspect that you may be pregnant, please report to your doctor as a matter of urgency.

You must not breastfeed while you are using **LUNAR**.

Driving and using machinery:

LUNAR may cause dizziness. If you experience dizziness, you should refrain from driving a car, operating machinery or performing other tasks where dizziness may lead to accidents.

Important information about some of the ingredients of LUNAR:

LUNAR contains lactose. If you are lactose intolerant, you may experience unwanted side-effects, such as nausea, cramping, bloating, diarrhoea, and flatulence (gas). If you suffer from hereditary galactose intolerance, or the rare Lapp lactase deficiency, you should not take **LUNAR**. Please discuss this with your treating doctor if you are unsure.

Taking other medicines with LUNAR:

Always tell your healthcare professional if you are taking any other medicine. (This includes complementary or traditional medicines.)

In particular, please tell your doctor or pharmacist if you are taking any of the following:

- Other medicines used in rheumatoid diseases (e.g. chloroquine and hydroxychloroquine), intramuscular or oral gold, D-penicillamine, azathioprine, and other immunosuppressive agents (e.g. methotrexate) as combination with **LUNAR** may increase your risk of experiencing side-effects and adverse reactions.
- Rifampicin, an antibiotic for the treatment of tuberculosis.
- Phenytoin (an anti-epileptic medicine), warfarin (a blood-thinning agent) and tolbutamide (for the treatment of diabetes), since **LUNAR** may increase the blood concentrations of these medicines, possibly leading to toxic reactions.
- Cholestyramine for the treatment of high cholesterol levels, since it decreases blood levels of **LUNAR**.

You should not receive vaccinations with live vaccines while you are taking **LUNAR** and for a certain amount of time after stopping treatment. Please discuss this with your treating doctor.

HOW TO TAKE LUNAR:

Do not share medicines prescribed for you with any other person.

Always take LUNAR exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

Your doctor will decide the most appropriate dose for you. The usual dose is a 100 mg once daily for 3 days and then a maintenance dose of 10 mg or 20 mg daily.

LUNAR tablets should be swallowed whole, with sufficient amounts of liquid. It may be taken with or without food.

After starting treatment with **LUNAR** it will take between 4 to 6 weeks for you to experience an improvement in symptoms. You may continue to experience improvement for up to 4 to 6 months.

Your doctor will decide how long treatment with **LUNAR** should last.

If you have the impression that the effect of **LUNAR** is too strong or too weak, talk to your doctor or pharmacist.

If you take more LUNAR than you should:

In the event of an overdosage, or if someone else has taken your medicine by mistake, you, or this other person, may experience any of the side-effects listed below. The most frequent adverse events observed with **LUNAR** overdose were diarrhoea (runny stomach) and stomach pain.

In the event of overdosage, consult your doctor or pharmacist immediately. If neither is available, immediately seek help at the nearest hospital or poison control centre.

If you forget to take LUNAR:

Always take **LUNAR** as prescribed. If you miss a dose, take it as soon as you remember. If you do not remember the missed dose until the next dose is due, skip the missed dose and go back to your regular dosing schedule of one tablet once a day. Do not take a double dose to compensate for the forgotten individual dose.

POSSIBLE SIDE-EFFECTS:

LUNAR can have side-effects.

Not all side-effects reported for LUNAR are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking LUNAR, please consult your doctor, pharmacist or other healthcare professional for advice.

Serious side-effects that you, or a family member, should report to your doctor immediately include:

- Fever, chills, coughing, sneezing, sore throat, skin ulcers and other signs of infection, as this may be due to a low white cell count, which predisposes you to infections. Furthermore, treatment with **LUNAR** may in itself predispose you to infections.
- Pallor accompanied by tiredness, as this may indicate that your red blood cell count is low.

- Pinpoint red spots on the skin, easy bruising or bleeding from the gums, as this may be due to low a platelet count.
- Severe allergic reactions characterised by skin rash, fever, swelling of the lips, tongue, face or whole body, hives and itching, difficulty breathing or shortness of breath, and sometimes blister formation on the skin.
- Abnormal sensation with normal stimulation or pins and needles in the hands and feet as this may indicate nerve damage.
- Coughing or shortness of breath as this may indicate a condition known as interstitial lung disease (see **"Take special care with LUNAR"**).
- Any skin rash with blister formation or any skin rash which involves the mouth, eyes or genitalia as this may indicate the development of toxic epidermal necrolysis or Stevens-Johnson syndrome (see initial boxed **"WARNING"**).
- Yellow discolouration of the skin or the whites of the eyes which may be accompanied by loss of appetite, nausea, pain over the liver area or fever, as this may indicate inflammation of the liver. Severe liver injury, such as liver failure, which may be fatal, have occurred with **LUNAR** use.
- Severe stomach pain accompanied by nausea and/or vomiting, loss of appetite, fever and chills and generally feeling unwell, as this may indicate inflammation of the pancreas.
- Inability to pass urine with swelling of the body, especially the feet and legs, since this may indicate kidney failure.
- Small, solid, red- or purple-coloured skin lesions accompanied by pain and fever, skin ulcers or muscle or joint pain, since this may indicate inflammation of blood vessels.

Other side-effects that you should report to your doctor as soon as possible include:

- Coughing with sputum production, since this may indicate bronchitis or other lung infections.
- Pain with urination, burning urine or pain over the bladder area accompanied by frequent urination or difficulty to pass urine, since this may indicate urinary infection.
- Chest pain, palpitations (increased awareness of the normal heart beat) and tachycardia (rapid heartbeat).
- Hives or any other skin rash other than those mentioned above, including eczema (inflammation of the skin, characterised by redness and itching).
- Pins and needles.
- Teary or watery eyes or red eyes with or without a discharge.
- Sore throat, runny nose or pain over the sinuses with the production of phlegm.
- Runny stomach, nausea and/or vomiting.
- Inflammation of a tendon causing pain, swelling and difficulty moving.
- Fever.

Please report the following side-effects to your doctor if they continue or become bothersome:

- Anxiety.
- Headache, dizziness or taste disturbances.
- Loss of appetite, poor digestion with heartburn, constipation, dry mouth or flatulence.
- Dry skin, hair loss, or itching.

- Weight loss.
- Weakness or generally feeling unwell.
- Back pain.

Other side-effects of **LUNAR** for which you will be monitored include:

- High blood pressure (hypertension).
- The development of certain cancers.
- Abnormal blood cell counts, including white blood cell, red blood cell and platelet counts.
- Low blood levels of potassium.
- High blood lipid levels.
- Decreased blood uric acid levels.
- Abnormal liver and kidney function tests.
- Increased levels of muscle enzymes in the blood.

Not all side-effects of **LUNAR** are included in this leaflet. If you notice any side-effects not mentioned in this leaflet, please inform your doctor or pharmacist.

STORAGE AND DISPOSING OF LUNAR:

Store at or below 25 °C.

Bottles should be kept tightly closed. Blister packs must be stored in the original package (carton).

Do not use after the expiry date stated on the bottle and carton.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

KEEP ALL MEDICINES OUT OF REACH OF CHILDREN.

IDENTIFICATION OF LUNAR:

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 OF LUNAR:

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

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 PATIENT INFORMATION LEAFLET:

To be allocated.