PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

LEFUNAR 10, film-coated tablets

LEFUNAR 20, film-coated tablets

Leflunomide

Contains sugar (lactose monohydrate, 80,00 mg per 10 mg film-coated tablet and 160,00 mg per 20 mg film-coated tablet)

Contains lecithin (derived from soybeans, 0,06 mg per 10 mg film-coated tablet and 0,12 mg per 20 mg film-coated tablet)

Read all of this leaflet carefully before you start taking LEFUNAR

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor, pharmacist nurse or other healthcare provider.
- LEFUNAR 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 is in this leaflet

1. What LEFUNAR is and what it is used for
2. What you need to know before you take LEFUNAR
3. How to take LEFUNAR
4. Possible side effects
5. How to store LEFUNAR
6. Contents of the pack and other information

1. What LEFUNAR is and what it is used for

LEFUNAR tablets contain a medicine called leflunomide. It belongs to a group of medicines called anti-rheumatic medicines.

LEFUNAR is used to treat adult patients with active rheumatoid arthritis and to improve physical function.

It works by slowing down the process of joint damage and relieves the symptoms of the disease, such as inflammation of joints, swelling, difficulty moving and pain

2. What you need to know before you take LEFUNAR

Do not take LEFUNAR if:

- you are allergic (hypersensitive) to leflunomide or any of the other ingredients of LEFUNAR listed in section 6 (especially a serious skin reaction, often accompanied by fever, joint pain, red skin stains, or blisters e.g. Stevens-Johnson syndrome)
- if you have any liver problems
- if you suffer from any problem which affects your immune system (e.g. AIDS)
- if you have any problem with your bone marrow, or if you have low numbers of red or white cells in your blood or a reduced number of blood platelets
- if you are suffering from a serious infection
- if you have moderate to severe kidney problems
- if you have severely low numbers of proteins in your blood (hypoproteinaemia)
- if you are pregnant, think you may be pregnant, or are breastfeeding
- if you are under 18 years of age.

Warnings and Precautions

Take special care with LEFUNAR if:

- if you are taking other anti-rheumatic medicines or your doctor want to switch your anti-rheumatic medicines (refer to Other medicines with LEFUNAR). This can cause an increase in side effects.
- if your doctor determines that LEFUNAR is damaging your liver, you may be given treatment to quickly eliminate LEFUNAR from your body.
- if you have ever had tuberculosis or if you have been in close contact with someone who has or has had tuberculosis. Your doctor may perform tests to see if you have tuberculosis.
- if you have ever suffered from inflammation of the lung (interstitial lung disease).
- if you are male and wish to father a child. As it cannot be excluded that LEFUNAR passes into semen, reliable contraception should be used during treatment with LEFUNAR. Men wishing to father a child should contact their doctor who may advise them to stop taking LEFUNAR and take certain medicines to remove LEFUNAR rapidly and sufficiently from their body. You will then need a blood test to make sure that LEFUNAR has been sufficiently removed from your body, and you should then wait for at least another 3 months before attempting to father a child.
- LEFUNAR can interfere with the blood test used to determine calcium levels. Tell your doctor that you are taking LEFUNAR before performing blood tests.

LEFUNAR can occasionally cause some problems with your blood, liver, lungs, or nerves in your arms or legs. It may also cause some serious allergic reactions (including Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)) or increase the chance of a severe infection (see section 4).

DRESS appears initially as flu-like symptoms and a rash on the face then an extended rash with a high temperature, increased levels of liver enzymes seen in blood tests and an increase in a type of white blood cell (eosinophilia) and enlarged lymph nodes.

Tell your doctor if you have unexplained chronic diarrhoea. Your doctor may perform additional tests to determine the cause of the diarrhoea.

Your doctor will carry out blood tests at regular intervals, before and during treatment with LEFUNAR, to monitor your blood cells and liver. Your doctor will also check your blood pressure regularly as LEFUNAR can cause an increase in blood pressure.

Other medicines and LEFUNAR

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

LEFUNAR may affect or be affected by some other medicines. Medicines which may have an effect on LEFUNAR:

- Other medicines for rheumatoid arthritis such as antimalarials (e.g. chloroquine and hydroxychloroquine), intramuscular or oral gold, D-penicillamine, azathioprine and other immunosuppressive medicines (e.g. methotrexate). These combinations are not advisable, as it may lead to increased risk for blood or liver side effects
- warfarin and other oral medicines used to prevent blood clots, close monitoring of your blood clotting is necessary as LEFUNAR may reduce the effect of these medicines
- a medicine called cholestyramine (used to reduce high cholesterol) or activated charcoal as these medicines can reduce the amount of LEFUNAR which is absorbed by the body
- rifampicin, for tuberculosis as it may increase the levels of LEFUNAR
- repaglinide or pioglitazone, for diabetes. LEFUNAR may increase the effect of these medicines
- daunorubicin, doxorubicin, paclitaxel, or topotecan for cancer. LEFUNAR may increase the effect of these medicines
- duloxetine for depression and anxiety as LEFUNAR may reduce the effect of these medicines
- theophylline for asthma, chronic bronchitis and other lung diseases as LEFUNAR may reduce the effect of these medicines

- oral contraceptives containing ethinylestradiol and levonorgestrel as LEFUNAR may increase the levels of these medicines
- cefaclor, benzylpenicillin, ciprofloxacin for infections as LEFUNAR may increase the levels of these medicines
- cimetidine, for stomach and intestinal ulcers as LEFUNAR may increase the levels of this medicine
- indomethacin, ketoprofen for pain or inflammation as LEFUNAR may increase the levels of these medicines
- furosemide, a diuretic (water pill) as LEFUNAR may increase the levels of this medicine
- zidovudine for HIV infection as LEFUNAR may increase the levels of this medicines
- rosuvastatin, simvastatin, atorvastatin, pravastatin for high cholesterol. LEFUNAR may increase the effect of these medicines
- sulfasalazine for inflammatory bowel disease or rheumatoid arthritis. LEFUNAR may increase the effect of this medicine.

If you are already taking a nonsteroidal anti-inflammatory drug (NSAID) and/or corticosteroids, you may continue to take them after starting LEFUNAR.

Vaccinations:

If you have to be vaccinated, ask your doctor for advice. Certain vaccinations should not be given while taking LEFUNAR, and for a certain amount of time after stopping treatment.

LEFUNAR with food, drink and alcohol

You should avoid consuming alcohol while on treatment with LEFUNAR as the risk of side effects are increased.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before taking LEFUNAR.

LEFUNAR may cause serious birth defects when taken while pregnant. Do not take LEFUNAR if you are pregnant.

If you are pregnant or become pregnant while taking LEFUNAR, the risk of having a baby with serious birth defects is increased. Women of childbearing potential must not take LEFUNAR without using reliable contraceptive measures.

Tell your doctor if you plan to become pregnant after stopping treatment with LEFUNAR, as you need to ensure that all traces of LEFUNAR have left your body before trying to become pregnant. This may take up to 2 years. This may be reduced to a few weeks by taking certain medicines which speed up removal of LEFUNAR from your body.

In either case it should be confirmed by a blood test that LEFUNAR has been sufficiently removed from your body and you should then wait for at least another month before you become pregnant.

For further information on the laboratory testing please contact your doctor.

If you suspect that you are pregnant while taking LEFUNAR or in the two years after you have stopped treatment, you must contact your doctor **immediately** for a pregnancy test.

LEFUNAR passes into breast milk. Women should not breastfeed their babies while taking LEFUNAR.

Driving and using machines

LEFUNAR can make you feel dizzy which may impair your ability to concentrate and react. If this happens to you, do not drive or use any tools or machines.

It is not always possible to predict to what extent LEFUNAR may interfere with the daily activities of a patient. You should ensure that you do not engage in driving a vehicle or using machines until you are aware of the measure to which LEFUNAR affects you.

LEFUNAR contains lactose monohydrate and lecithin

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking LEFUNAR.

LEFUNAR contains lecithin, derived from soybeans. If you are allergic to peanut or soya, do not use this medicine.

3. How to take LEFUNAR

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

Always take LEFUNAR exactly as your doctor or pharmacist has instructed you. Check with your doctor or pharmacist if you are not sure.

Your doctor will tell you how long your treatment with LEFUNAR will last. Do not stop treatment early because your symptoms have cleared up. If you have the impression that the effect of LEFUNAR is too strong or too weak, talk to your doctor or pharmacist.

The usual starting dose of LEFUNAR is one 100 mg tablet once daily for the first three days.

After this, the maintenance dose is: 10 or 20 mg LEFUNAR once daily.

Your doctor will tell you how many tablets to take.

It may take about 4 weeks or longer until you start to feel an improvement in your condition. Some patients may even feel further improvements after 4 to 6 months of therapy.

LEFUNAR should only be prescribed by specialists experienced in the treatment of rheumatoid diseases.

Swallow the tablet whole with a glass of water. You may take LEFUNAR with or without food.

If you take more LEFUNAR than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

Always take the box, this leaflet and any tablets that are left over with you, if you can. Signs of an overdose may include abdominal pain, nausea, diarrhoea and rash.

If you forget to take LEFUNAR

If you forget to take your tablets, take them as soon as you remember. If it is nearly time for the next dose, take the dose as usual. Do not take a double dose to make up for forgotten individual doses.

If you stop taking LEFUNAR

Do not stop taking LEFUNAR tablets without first discussing it with your doctor.

After stopping treatment with LEFUNAR, traces of LEFUNAR will remain in your body for up to 2 years. If your treatment was stopped due to serious side effects or pregnancy, or planned pregnancy (both male and female patients), your doctor may reduce the levels of LEFUNAR in your body within a few days to weeks by giving you certain medicines which speed up the removal of LEFUNAR from your body. Speak to your doctor or healthcare provider if this is applicable to you.

4. Possible side effects

LEFUNAR can have side effects.

Not all side effects reported for LEFUNAR are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking LEFUNAR, please consult your healthcare provider for advice.

If any of the following happens, stop taking LEFUNAR and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing and fainting
- severe rash or itching, may include blistering and peeling of your skin, bleeding under the skin, accompanied by fever and joint stiffness

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to LEFUNAR.

You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- any symptoms of an infection such as fever, sore throat or cough, as this medicine may increase the chance of a severe infection which may be fatal
- pale skin, tiredness, or bruising, as these may indicate blood disorders caused by an imbalance in the different types of cells which make up blood
- severe increase in blood pressure
- cough or breathing problems as these may indicate problems of the lung (interstitial lung disease or pulmonary hypertension), which may be fatal
- yellowing of the skin and eyes, also called jaundice, accompanied by fever, fatigue, loss of appetite, nausea, vomiting, abdominal pain, dark urine. This may indicate liver damage.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent side effects:

- dizziness, headache
- abnormal skin sensations like tingling (paraesthesia)
- unusual tingling, weakness or pain in your hands or feet as these may indicate problems with your nerves (peripheral neuropathy)
- mild increase in blood pressure
- colitis (inflammation of the colon) – you may notice blood in your stool, abdominal pain and cramps
- diarrhoea
- feeling sick (nausea)

- being sick (vomiting)
- inflammation of the mouth or mouth ulcers
- stomach pain
- increased hair loss
- eczema, dry skin
- inflammation of a tendon – you may experience pain, swelling and difficulty moving the affected joint
- loss of appetite, weight loss
- tiredness (asthenia)

Less frequent side effects:

- nervousness, worrying
- taste disturbances
- inflammation of the pancreas – you may experience upper abdominal pain, nausea and vomiting
- severe liver injury such as liver failure or necrosis which may be fatal
- hives
- tendon rupture, which will cause immediate bruising and severe pain which gets worse with tendon use.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor or, pharmacist or nurse. You can also report side effects to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of LEFUNAR.

5. How to store LEFUNAR

Store at or below 25 °C. Store in the original container until required for use.

Do not use after the expiry date printed on the label/ carton.

Return all unused medicine to your pharmacist.

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

STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

6. Contents of the pack and other information

What LEFUNAR contains

The active substance is leflunomide.

The other ingredients are:

Tablet core: Low-substituted hydroxypropyl cellulose, lactose monohydrate, magnesium stearate, sodium laurilsulfate, tartaric acid.

Film coating: Opadry AMB white consisting of lecithin, poly (vinyl alcohol), talc, titanium dioxide, xanthan gum.

What LEFUNAR looks like and contents of the pack

LEFUNAR 10 mg: White to off-white, round, biconvex film-coated tablets.

LEFUNAR 20 mg: White to off-white, round, biconvex film-coated tablets with one-sided break-mark.

LEFUNAR 10 and LEFUNAR 20 are packed in white round or square HDPE bottles closed with white PP closures with desiccant insert.

Pack size: 30 or 100 tablets.

Holder of Certificate of Registration

Biotech Laboratories (Pty) Ltd.

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