Package leaflet: Information for the user

Leflunomide 20 mg Film-coated Tablets

leflunomide

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects , talk to your doctor, pharmacist or nurse. This includes side effects not listed in this leaflet.

What is in this leaflet:

1. What Leflunomide Tablets are and what they are used for

Leflunomide belongs to the group of drugs known as anti-rheumatic medicines which are used in the treatment of adult patients with active rheumatoid arthritis or with active psoriatic arthritis. It contains the active substance leflunomide.

Symptoms of Rheumatoid Arthritis include inflammation of joints, swelling, difficulty moving and pain. Other symptoms that affect the entire body include loss of appetite, fever, loss of energy and anaemia (lack of red blood cells).

Symptoms of Active Psoriatic Arthritis include inflammation of joints, swelling, difficulty moving, pain and patches of red, scaly skin (skin lesions).

2. What you need to know before you take Leflunomide Tablets

Do not take Leflunomide Tablets if you

- are **allergic** to leflunomide or any of the other ingredients of this medicine (listed in section 6),
- have decreased **liver function**,
- have moderate to severe decreased **kidney function**,
- have severely low amounts of **protein in your blood** (hypoproteinaemia),
- suffer from any problem which affects your **immune system** (e.g. AIDS),
- 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,
- are suffering from a **serious infection,**
- **are pregnant**, think you may be pregnant or are breast-feeding.

Warnings and Precautions
Talk to your doctor, pharmacist or nurse before taking Leflunomide Tablets

- if you have a history of interstitial lung disease
- 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 are **male** and wish to father a child. As it cannot be excluded that Leflunomide Tablets passes into semen reliable contraception should be used during treatment with Leflunomide Tablets. Men wishing to father a child should contact their doctor who may advise them to stop taking Leflunomide Tablets and take certain medicines to remove Leflunomide Tablets rapidly and sufficiently from their body. You will then need a blood test to make sure that leflunomide has been sufficiently removed from your body, and you should then wait for at least another 3 months before attempting to father a child.
- if you are due to have a specific blood test (calcium level). Falsely low levels of calcium can be detected.
-

Leflunomide Tablets 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. For more information on these, please read section 4 (Possible side effects).

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.

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

Talk to your doctor if you have unexplained chronic diarrhoea. Your doctor may perform additional tests for differential diagnosis.

<u>Children and adolescents</u>
Leflunomide Tablets are not recommended for use in children and adolescents below 18 years of age.

Other medicines and Leflunomide Tablets

Please tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription. This is especially important if you are taking:

- other medicines for rheumatoid arthritis such as antimalarials (e.g. chloroquine and hydroxychloroquine), intramuscular or oral gold, D-penicillamine, azathioprine and other immunosuppressive drugs (e.g. methotrexate) as these combinations are not advisable,
- warfarin and other oral medicines used to thin the blood, as monitoring is necessary to reduce the risk of side effects of this medicine
- teriflunomide for multiple sclerosis
- repaglinide, pioglitazone, nateglinide, or rosiglitazone for diabetes
- daunorubicin, doxorubicin, paclitaxel, or topotecan for cancer
- duloxetine for depression, urinary incontinence or in kidney disease in diabetics
- alosetron for the management of severe diarrhoea
- theophylline for asthma
- tizanidine, a muscle relaxant
- oral contraceptives (containing ethinylestradiol and levonorgestrel)
- cefaclor, benzylpenicillin (penicillin G), ciprofloxacin for infections
- indomethacin, ketoprofen for pain or inflammation
- furosemide for heart disease (diuretic, water pill)
- zidovudine for HIV infection
- rosuvastatin, simvastatin, atorvastatin, pravastatin for hypercholesterolemia (high cholesterol)
- sulfasalazine for inflammatory bowel disease or rheumatoid arthritis

- a medicine called colestyramine (used to reduce high cholesterol) or activated charcoal as these medicines can reduce the amount of leflunomide which is absorbed by the body.

If you are already taking a non-steroidal **anti-inflammatory** drug (NSAID) and/or **corticosteroids**, you may continue to take them after starting Leflunomide Tablets.

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

Leflunomide Tablets with food, drink and alcohol

You may take the tablets with or without food. Alcohol should be avoided whilst taking this medicine as it may increase the risk of side effects on the liver.

Pregnancy and breast-feeding

Pregnancy
Do not take Leflunomide Tablets if you are or think you might be **pregnant.** If you are pregnant or become pregnant whilst taking Leflunomide Tablets, the risk of having a baby with serious birth defects is increased. Women of childbearing potential must not take Leflunomide Tablets without using reliable contraceptive measures. Leflunomide can last for a long time in the body after treatment is stopped. You must not get pregnant while taking leflunomide and for at least two years after treatment has finished. This may be reduced to a few weeks by taking certain medicines which remove Leflunomide Tablets rapidly and sufficiently from your body. In either case it should be confirmed by a blood test that Leflunomide Tablets 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 Leflunomide Tablets or in the two years after you have stopped treatment, you must contact your doctor immediately for a pregnancy test. If the test confirms that you are pregnant, your doctor may suggest treatment with certain medicines to speed up the removal of Leflunomide Tablets from the body, as this may decrease the risk to your baby.

Breast-feeding

Do not take Leflunomide Tablets when you are **breast feeding,** as leflunomide passes into the breast milk.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines
Leflunomide Tablets may cause dizziness and impairs the ability to concentrate and react. Do not drive or use machines if you have such symptoms.

Leflunomide Tablets contain lactose.
If you have been told by your doctor that you have intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take Leflunomide Tablets

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure. The usual starting dosage is one 100 mg tablet once daily for the first three days. After this, most patients need a dose of:

- For rheumatoid arthritis: 10 or 20 mg once daily, depending on the severity of the disease.
- For psoriatic arthritis: 20 mg once daily.

Swallow the tablet **whole** and with plenty of **water**. It may take about 4 weeks or longer until you start to feel an improvement in your condition. Some patients may even still feel further improvements after 4 to 6 months of therapy. You will normally take Leflunomide Tablets over long periods of time.

If you take more Leflunomide Tablets than you should
If you take more of the medicine than you should, a physician or nearest hospital casualty department must be contacted immediately. Take your medicine package to show a doctor.

If you forget to take Leflunomide Tablets

Take the missed dose as soon as you remember, unless it is nearly time for your next dose. Do not take two doses at the same time to make up for forgotten individual doses. If you have any further questions on the use of this product, ask your doctor, pharmacist or nurse.

If you stop taking Leflunomide Tablets

Do not stop taking the tablets unless your doctor tells you to. If you have any further questions on how to take this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Tell your doctor **immediately** and stop taking Leflunomide Tablets:

- if you experience **weakness**, feel lightheaded or dizzy or have **difficulty breathing**, as these may be signs of a serious allergic reaction,
- if you develop a **skin rash** or **ulcers in your mouth**, as these may indicate severe, sometimes life-threatening reactions (e.g. Stevens-Johnson syndrome, toxic epidermal necrolysis, and erythaema multiforme), Drug Reaction with Eosinophilia and Systemic Symptoms [DRESS]), see section 2.

Tell your doctor **immediately** if you experience:

- **pale skin**, **tiredness**, or **bruising**, as these may indicate blood disorders caused by an imbalance in the different types of blood cells which make up blood,
- **tiredness**, **abdominal pain**, or **jaundice** (yellow discolouration of the eyes or skin), as these may indicate serious conditions such as liver failure, which may be fatal,

- 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 life-threatening,
- a **cough** or **breathing problems** as these may indicate problems of the lung (interstitial lung disease or pulmonary hypertension).
- unusual tingling, weakness or pain in your hands or feet as these may indicate problems with your nerves (peripheral neuropathy).

Common side effects (may affect up to 1 in 10 people)
- a slight decrease in the number of white blood cells (leucopoenia),
- mild allergic reactions,
- loss of appetite, weight loss (usually insignificant),
- tiredness (asthenia),
- headache, dizziness,
- abnormal skin sensations like tingling (paraesthesia),
- mild increase in blood pressure,
- colitis,
- diarrhoea,
- nausea, vomiting,
- inflammation of the mouth or mouth ulcers,
- abdominal pain,
- an increase in some liver test results,
- increased hair loss,
- eczema, dry skin, rash, itching,
- tendonitis (pain caused by inflammation in the membrane surrounding the tendons usually in the feet or hands),
- an increase of certain enzymes in the blood (creatine phosphokinase).
- problems in the nerves of the arms or legs (peripheral neuropathy).

Uncommon side effects (may affect up to 1 in 100 people)
- a decrease in the number of red blood cells (anaemia) and a decrease in the number of blood platelets (thrombocytopenia),
- a decrease in the levels of potassium in the blood,
- anxiety,
- taste disturbances,
- urticaria (nettle rash),
- tendon rupture,
- an increase in the levels of fat in the blood (cholesterol and triglycerides),
- a decrease in the levels of phosphate in the blood.

Rare side effects (may affect up to 1 in 1,000 people)
- an increase in the numbers of blood cells called eosinophiles (eosinophilia); mild decrease in the number of white blood cells (leucopoenia); decrease in the number of all blood cells (pancytopaenia),
- severe increase in blood pressure,
- inflammation of the lung (interstitial lung disease),
- an increase in some liver results which may develop into serious conditions such as hepatitis and jaundice,
- severe infections called sepsis which may be fatal,
- an increase of certain enzymes in the blood (lactate dehydrogenase).

Very rare side effects (may affect up to 1 in 10,000 people)
- a marked decrease of some white blood cells (agranulocytosis),
- severe and potentially severe allergic reactions,
- inflammation of the small vessels (vasculitis, including cutaneous necrotizing vasculitis),
- inflammation of the pancreas (pancreatitis),

- severe liver injury such as liver failure or necrosis which may be fatal,
- severe sometimes life-threatening reactions (Stevens-Johnson syndrome, toxic epidermal necrolysis, erythaema multiforme).

Other side effects such as kidney failure, a decrease in the levels of uric acid in your blood, pulmonary hypertension, male infertility (which is reversible once treatment with this medicine is stopped), cutaneous lupus (characterised by rash/erythema on skin areas that are exposed to light), psoriasis (new or worsening) and DRESS may also occur with a not known frequency.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via:

HPRA Pharmacovigilance
Earlsfort Terrace, IRL - Dublin 2
Tel: +353 1 6764971, Fax: +353 1 6762517
Website: www.hpra.ie, e-mail: medsafety@hpra.ie.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Leflunomide Tablets

Keep this medicine out of the sight and reach of children

Do not use this medicine after the expiry date which is stated on the package. The expiry date refers to the last day of that month.

Keep the container tightly closed.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Leflunomide Tablets contain

- The active substance is leflunomide. Each film-coated tablet contains 20 mg of leflunomide.
- The other ingredients are lactose monohydrate, lactose anhydrous, maize starch, hydroxypropyl cellulose, Povidone, colloidal anhydrous silica, magnesium stearate, hypromellose (E464), titanium dioxide (E171), macrogol and iron oxide yellow (E172).

What Leflunomide Tablets look like and contents of the pack

Leflunomide 20 mg Tablets are light yellow, triangular, biconvex film-coated tablets plain on both sides.
Leflunomide 20 mg Tablets are available in containers containing 30 tablets.

Marketing Authorisation Holder
Morningside Healthcare Ltd
Unit C, Harcourt Way
Leicester
LE19 1WP
UK

Manufacturer
Morningside Pharmaceuticals Ltd
5 Pavilion Way
Loughborough
LE11 5GW
UK

This leaflet was last revised in December 2018