SCHEDULING STATUS: **S4**

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM

Rheumalef 10, 10 mg leflunomide, film-coated tablets

Rheumalef 20, 20 mg leflunomide, film-coated tablets

Rheumalef 100, 100 mg leflunomide, film-coated tablets

Read all of this leaflet carefully before you start taking Rheumalef

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- **Rheumalef** 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.

1. WHAT *RHEUMALEF* CONTAINS

The active substance is leflunomide.

Each film-coated tablet contains 10 mg, 20 mg or 100 mg of leflunomide.

The other ingredients are:

Rheumalef 10: Colloidal silicon dioxide, crospovidone, hypromellose (3cP, 15cP and 50cP), macrogol/peg 4000, magnesium stearate, maize starch 1500, microcrystalline cellulose, povidone, titanium dioxide.

Contains sugar: Lactose monohydrate 19,20 mg

Rheumalef 20: Colloidal silicon dioxide, crospovidone, hypromellose (5cP), iron oxide yellow, macrogol/peg 6000, magnesium stearate, maize starch 1500, microcrystalline cellulose, povidone, talc, titanium dioxide.

Contains sugar: Lactose monohydrate 38,40 mg

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Rheumalef 100: Colloidal silicon dioxide, crospovidone, hypromellose (3cP, 15cP and 50cP), macrogol/peg 4000, magnesium stearate, maize starch 1500, microcrystalline cellulose, povidone, titanium dioxide.

Contains sugar: Lactose monohydrate 192,0 mg

2. WHAT *RHEUMALEF* IS USED FOR

Rheumalef belongs to a group of medicines called anti-rheumatic medicines.

Rheumalef is used to treat adult patients with active rheumatoid arthritis.

3. BEFORE YOU TAKE *RHEUMALEF*

Do not take Rheumalef:

- If you have ever had an allergic reaction to leflunomide (especially a serious skin reaction, often accompanied by fever, joint pain, red skin stains, or blisters e.g. Steven-Johnson syndrome) or to any of the other ingredients of **Rheumalef**,
- If you have any liver problems,
- If you have moderate to severe kidney problems,
- If you have severely low numbers of proteins in your blood (hypoproteinaemia),
- If you suffer from any problems which affect 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 are pregnant or breast-feeding (see **Pregnancy and Breast-feeding**),
- If you are a male patient, you should be aware of the possibility that **Rheumalef** may harm your unborn baby (see **Take special care with Rheumalef**).

Take special care with Rheumalef:

- If you have ever suffered from tuberculosis (a lung disease),
- If you are male and wish to father a child, as **Rheumalef** can cause birth defects in new born infants. To minimise any possible risk, if you wish to father a child you should contact your

doctor who may advise you to stop taking **Rheumalef** and take certain medicines to speed up the removal of **Rheumalef** from your body. You will then need a blood test to make sure that **Rheumalef** has been sufficiently removed from your body, and you should then wait for at least another 3 months.

Rheumalef can occasionally cause some problems with your blood, liver, lungs (see below) or or nerves in your arms or legs. It may also cause some serious allergic reactions or increase the chance of a severe infection. For more information on these, please read the Possible Side Effects section.

Blood problems:

Rheumalef can cause a drop in the number of white blood cells, which are needed to fight infection. It can also cause a drop in the number of platelets, which help to stop bleeding. Your doctor will carry out blood tests at regular intervals, before and during treatment with **Rheumalef**, to monitor your blood cells.

Your doctor will also check your blood pressure regularly as **Rheumalef** can cause an increase in blood pressure.

Liver problems:

Rheumalef may increase some liver enzyme levels (e.g. alanine transaminase). Your doctor will carry out blood tests, before initiation of treatment with **Rheumalef** and thereafter at regular intervals during treatment, to check these liver enzyme levels. If they stay high, your doctor may lower your dose or stop the use **Rheumalef**.

Lung problems:

Rheumalef can cause interstitial lung disease (disease causing progressive thickening of lung tissue). The thickening can be due to inflammation, scarring, or extra fluid. The thickening associated with interstitial lung disease eventually affects your ability to breathe and get enough oxygen into your bloodstream.

Rheumalef is not recommended for use in children and adolescents below 18 years of age.

Taking Rheumalef with food and drink:

Rheumalef may be taken with or without food.

It is not recommended to drink alcohol during treatment with **Rheumalef**. Drinking alcohol while taking **Rheumalef** may increase the chance of liver damage.

Pregnancy and breast-feeding:

Do not take **Rheumalef** if you are or think you may be pregnant. Woman of childbearing potential must not take **Rheumalef** without using reliable contraceptives measures.

Tell your doctor if you plan to become pregnant after stopping treatment with **Rheumalef**, as you need to ensure that all traces of **Rheumalef** 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 **Rheumalef** from your body.

In either case it should be confirmed by a blood test that **Rheumalef** 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 **Rheumalef** 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 **Rheumalef** from the body, as this may decrease the risk to your baby.

Do not take **Rheumalef** when you are breast-feeding, as **Rheumalef** passes into the breast milk.

If you are pregnant or breast-feeding your baby while taking Rheumalef, please consult your doctor, pharmacist or other health care professional for advice.

Driving and using machinery:

Rheumalef can make you feel dizzy which may impair your ability to concentrate and react. If you are affected, do not drive, or use machines.

Important information about some of the ingredients of Rheumalef:

Rheumalef contains lactose. If you have been told by your doctor that you have intolerance to some sugars, contact your doctor before taking **Rheumalef**.

Taking other medicines with Rheumalef:

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

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, Tumor-Necrosis-Factor alpha inhibitors (e.g. adalimumab) and other immunosuppressive medicines (e.g. methotrexate) as these combinations are not advisable,
- a medicine called cholestyramine (used to reduce high cholesterol) or activated charcoal as these medicines can reduce the amount of **Rheumalef** which is absorbed by the body.
- Phenytoin (used to treat epilepsy), warfarin (used to thin the blood), medicines containing rifampicin (an antibiotic used to treat and prevent infections such as tuberculosis (TB)) or tolbutamide (used to treat type 2 diabetes). Your doctor may need to change the doses of your medications or monitor you carefully for side effects.

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

Vaccinations

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

4. HOW TO TAKE *RHEUMALEF*

Always take Rheumalef exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

The usual dose is:

For rheumatoid arthritis: 10 or 20 mg **Rheumalef** once daily depending on the severity of the disease.

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 improvement after 4 to 6 months of therapy.

You will normally take **Rheumalef** over long periods of time.

If you take more Rheumalef than you should:

If you take more **Rheumalef** than you should, contact you doctor or get other medical advice. If possible, take your tablets or the box with you to show the doctor.

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

If you forget to take Rheumalef:

If you forgot to take a dose, take it as soon as you remember, unless it is nearly time for your next dose. Do not take a double dose to make up for a forgotten dose. If you have any further questions on the use of **Rheumalef**, ask your doctor or pharmacist.

5. POSSIBLE SIDE EFFECTS

Not all side effects reported for Rheumalef are included in this leaflet. Should your general health worsen while taking Rheumalef, please consult your doctor, pharmacist or other healthcare professional for advice.

Rheumalef can cause side effects, although not everybody gets them.

Tell your doctor immediately and stop taking Rheumalef:

- if you experience weakness, feel light headed 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, erythema multiforme).

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 a liver failure, which may be fatal,
- any symptoms of an infection such as fever, sore throat or cough, as **Rheumalef** may increase the chance of severe infection which may be life-threatening,
- A cough or breathing problems as these may indicate inflammation of the lungs (interstitial lung disease).

Frequent side effects:

- a slight decrease in the number of white blood cells (leucopenia),
- mild allergic reactions,
- loss of appetite, weight loss (usually insignificant),
- tiredness (asthenia),
- headaches, dizziness,
- abnormal skin sensations like tingling (paraesthesia),
- mild increase in blood pressure,
- 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).

Less Frequent side effects:

- a decrease in the number of red blood cells (anaemia) and a decrease in the number of blood platelets (thromobocytopenia),
- 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,
- an increase in the numbers of blood cells called eosinophiles (eosinophilia); mild decrease in the number of white blood cells (leucopenia); decrease in the number of all blood cells (pancytopenia),
- 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),

- a marked decrease of some white blood cells (agranulocytosis),
- severe and potentially severe allergic reactions,
- inflammation of the small vessels (vasculitis, including cutaneous necrotising vasculitis),
- problems in the nerves of the arms or legs (peripheral neuropathy),
- inflammation of the pancreas (pancreatitis),
- severe liver injury such as liver failure or necrosis which may be fatal,
- Severe sometimes such as life-threatening reactions (Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme).

Other side effects such as kidney failure, a decrease in the levels of uric acid in your blood, male infertility (which is reversible once treatment with **Rheumalef** is stopped) may also occur with an unknown frequency.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

6. STORING AND DISPOSING OF *RHEUMALEF*

Store at or below 25 °C.

KEEP OUT OF REACH OF CHILDREN.

Store in original package.

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

Medicines should not be disposed of via wastewater or household waste. Ask your doctor or pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

7. PRESENTATION OF *RHEUMALEF*

Rheumalef 10 and Rheumalef 20 film-coated tablets are packed in a white opaque polyethylene high density container, with a tamper-evident polypropylene cap, containing either 30 tablets in a 30 ml container or 100 tablets in a 40 ml container. Each HD Polyethylene container also contains a desiccant and is stored in an outer unit carton.

Rheumalef 100 film-coated tablets are packed in Aluminium foil /PVC blisters of 3 tablets per blister, contained in an outer unit carton.

8. IDENTIFICATION *OF RHEUMALEF*

Rheumalef 10 film-coated tablets are white, round biconvex tablets.

Rheumalef 20 film-coated tablets are yellow, round biconvex with a scoreline on one side of the tablet.

Rheumalef 100 film-coated tablets are white, oblong biconvex with a scoreline on one side of the tablet.

9. REGISTRATION NUMBER/REFERENCE NUMBER

RHEUMALEF 10: 45/3.1/0404

RHEUMALEF 20: 45/3.1/0405

RHEUMALEF 100: 45/3.1/0406

10. NAME AND ADDRESS OF REGISTARTION HOLDER

ADCOCK INGRAM LIMITED

1 New Road

Erand Gardens

Midrand

1685

Gauteng, South Africa

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adcock ingram

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