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Leflunomide Zentiva[1] (*leflunomide*)

An overview of Leflunomide Zentiva and why it is authorised in the EU

What is Leflunomide Zentiva and what is it used for?

Leflunomide Zentiva is a medicine used to treat adults with active rheumatoid arthritis (an immune system disease causing inflammation of the joints) or active psoriatic arthritis (a disease causing red, scaly patches on the skin and inflammation of the joints). The medicine contains the active substance leflunomide.

How is Leflunomide Zentiva used?

Leflunomide Zentiva is available as tablets (10 mg, 20 mg and 100 mg). It can only be obtained with a prescription and treatment should be started and supervised by a specialist who has experience in the treatment of rheumatoid arthritis and psoriatic arthritis. The doctor should carry out blood tests to check the patient's liver, white blood cell counts and platelet counts before prescribing Leflunomide Zentiva, and regularly during treatment.

Leflunomide Zentiva treatment usually starts with a 'loading dose' of 100 mg once a day for 3 days, followed by a maintenance dose. The recommended maintenance dose is 10 to 20 mg once a day in patients with rheumatoid arthritis, and 20 mg once a day in patients with psoriatic arthritis. The medicine usually starts to have an effect after 4 to 6 weeks. Its effect may improve further for up to 6 months.

For more information about using Leflunomide Zentiva, see the package leaflet or contact your doctor or pharmacist.

How does Leflunomide Zentiva work?

The active substance in Leflunomide Zentiva, leflunomide, is an immunosuppressant. It reduces inflammation by reducing the production of immune cells called 'lymphocytes', which are responsible for inflammation. Leflunomide does this by blocking an enzyme called 'dihydroorotate dehydrogenase', which is necessary for the lymphocytes to multiply. With fewer lymphocytes, there is less inflammation, helping to control the symptoms of arthritis.

[1] Previously known as Leflunomide Winthrop.

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What benefits of Leflunomide Zentiva have been shown in the studies?

Rheumatoid arthritis

In rheumatoid arthritis, Leflunomide Zentiva has been studied in 4 main studies involving over 2,000 patients, in which it was compared with placebo (a dummy treatment), or with methotrexate or sulphasalazine (other medicines used to treat rheumatoid arthritis). Two of the studies lasted 6 months, and two lasted 1 year. The two longer studies were then extended, with patients remaining on the medicines for at least 1 more year.

Results showed that Leflunomide Zentiva was more effective than placebo and as effective as sulphasalazine. Between 49 and 55% of the patients taking Leflunomide Zentiva responded to treatment, compared with 26 to 28% of those taking placebo, and 54% of those taking sulphasalazine. These results were maintained in the extension studies. Over the first year of treatment, Leflunomide Zentiva was as effective as methotrexate, but only when it was taken with folate (a type of vitamin B). Leflunomide Zentiva was not as effective as methotrexate in the extension study.

Psoriatic arthritis

In psoriatic arthritis, a study in 186 patients showed that Leflunomide Zentiva was more effective than placebo over 6 months: 59% of the patients taking Leflunomide Zentiva responded to treatment, compared with 30% of those taking placebo.

What are the risks associated with Leflunomide Zentiva?

The most common side effects with Leflunomide Zentiva (which may affect up to 1 in 10 people) are leucopenia (low white blood cell counts), mild allergic reactions, increased creatine phosphokinase levels (a marker of muscle damage), paraesthesia (abnormal sensations like pins and needles), peripheral neuropathy (nerve damage in hands and feet), headache, dizziness, mild increases in blood pressure, colitis (inflammation in the large bowel), diarrhoea, nausea (feeling sick), vomiting, inflammation of the mouth such as mouth ulcers, abdominal (belly) pain, increased liver enzyme levels, hair loss, eczema, rash, pruritus (itching), dry skin, tenosynovitis (inflammation of the sheath surrounding the tendons), loss of appetite, weight loss and asthenia (weakness). For the full list of side effects with Leflunomide Zentiva, see the package leaflet.

Leflunomide Zentiva must not be used in patients with:

- liver disease;
- severe immunodeficiency states, such as acquired immune deficiency syndrome (AIDS);
- poor bone marrow function or low blood cell counts (red cells, white cells or platelets) caused by conditions other than rheumatoid or psoriatic arthritis;
- serious infections;
- moderate to severely impaired kidney function;
- severe hypoproteinaemia (low blood protein levels).

Leflunomide Zentiva must not be used in pregnant women, in women who can become pregnant and who are not using reliable contraception or during breast-feeding.

For the full list of restrictions, see the package leaflet.

Doctors prescribing Leflunomide Zentiva need to be aware of the risk of liver problems associated with the medicine. They also need to take special care when switching a patient to Leflunomide Zentiva, or when switching a patient who is receiving Leflunomide Zentiva to another treatment.

Why is Leflunomide Zentiva authorised in the EU?

The European Medicines Agency decided that Leflunomide Zentiva's benefits are greater than its risks and it can be authorised for use in the EU.

What measures are being taken to ensure the safe and effective use of Leflunomide Zentiva?

The company that markets Leflunomide Zentiva will ensure that doctors who are expected to prescribe the medicine receive an information pack containing important information on the risks with Leflunomide Zentiva and the monitoring that should be carried out in patients.

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Leflunomide Zentiva have been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Leflunomide Zentiva are continuously monitored. Side effects reported with Leflunomide Zentiva are carefully evaluated and any necessary action taken to protect patients.

Other information about Leflunomide Zentiva

Leflunomide Zentiva received a marketing authorisation valid throughout the EU on 8 January 2010. This authorisation was based on the authorisation granted to Arava in 1999 ('informed consent').

Further information on Leflunomide Zentiva can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/leflunomide-zentiva.

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