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EPAR summary for the public

Arava

leflunomide

This is a summary of the European public assessment report (EPAR) for Arava. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Arava.

What is Arava?

Arava is a medicine that contains the active substance leflunomide. It is available as tablets (10, 20 and 100 mg).

What is Arava used for?

Arava is 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 can only be obtained with a prescription.

How is Arava used?

Arava 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 Arava, and regularly during treatment.

Arava treatment usually starts with a 'loading dose' of 100 mg once a day for three 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 four to six weeks. Its effect may improve further for up to six months.

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How does Arava work?

The active substance in Arava, 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.

How has Arava been studied?

In rheumatoid arthritis, Arava has been studied in four 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 six months, and two lasted a year. The two longer studies were then extended, with patients remaining on the medicines for at least one more year.

In psoriatic arthritis, Arava has been compared with placebo in 186 patients over six months.

In all of the studies, the main measure of effectiveness was the number of patients who responded to treatment, as defined by disease-specific criteria (American College of Rheumatology response rates for rheumatoid arthritis, and the Psoriatic Arthritis treatment Response Criteria for psoriatic arthritis).

What benefit has Arava shown during the studies?

In rheumatoid arthritis, Arava was more effective than placebo and as effective as sulphasalazine. Between 49 and 55% of the patients taking Arava 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, Arava was as effective as methotrexate, but only when it was taken with folate (a type of vitamin B). Arava was not as effective as methotrexate in the extension study.

In psoriatic arthritis, Arava was more effective than placebo, with 59% of the patients taking Arava responding to treatment, compared with 30% of those taking placebo.

What is the risk associated with Arava?

The most common side effects with Arava (seen in between 1 and 10 patients in 100) 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, diarrhoea, nausea (feeling sick), vomiting, inflammation of the mouth such as mouth ulcers, abdominal pain (stomach ache), 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 all side effects reported with Arava, see the package leaflet.

Arava must not be used in people who may be hypersensitive (allergic) to leflunomide, to teriflunomide (a breakdown product of leflunomide) or to any of the other ingredients. Arava 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).

Arava must not be used in pregnant women, in women who can become pregnant and who are not using reliable contraception, or during breastfeeding.

Doctors prescribing Arava 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 Arava, or when switching a patient who is receiving Arava to another treatment.

Why has Arava been approved?

The CHMP decided that Arava's benefits are greater than its risks and recommended that it be given marketing authorisation.

What measures are being taken to ensure the safe use of Arava?

A risk management plan has been developed to ensure that Arava is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Arava, including the appropriate precautions to be followed by healthcare professionals and patients.

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

Other information about Arava

The European Commission granted a marketing authorisation valid throughout the European Union for Arava on 2 September 1999.

The full EPAR for Arava can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports. For more information about treatment with Arava, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 10-2014.