EMA/319123/2014
EMEA/H/C/002655

EPAR summary for the public

Envarsus

tacrolimus

This is a summary of the European public assessment report (EPAR) for Envarsus. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Envarsus.

For practical information about using Envarsus, patients should read the package leaflet or contact their doctor or pharmacist.

What is Envarsus and what is it used for?

Envarsus is a medicine that contains the active substance tacrolimus. It is used for the long-term treatment of adult patients who have had a kidney or a liver transplant, to prevent rejection (when the immune system attacks the transplanted organ). Envarsus can also be used to treat organ rejection in adult patients when other immunosuppressive medicines (medicines that reduce the activity of the immune system) are not effective.

Envarsus is a 'hybrid medicine'. This means that Envarsus is similar to a 'reference medicine' that contains the same active substance but Envarsus has been formulated in a different way and is available at different doses. The reference medicine for Envarsus is Advagraf.

How is Envarsus used?

Envarsus can only be obtained with a prescription and should only be prescribed by doctors experienced in immunosuppressive medicines and in the management of transplant patients. Switching or changes in immunosuppressive medicines should be started and monitored by experienced transplant doctors.

Envarsus is available as prolonged-released tablets containing tacrolimus (0.75, 1 and 4 mg). These 'prolonged-release' tablets allow tacrolimus to be released slowly from the tablet over several hours and in a form that the body can absorb easily, so that it need be given only once a day.

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Doses of Envarsus are calculated based on the patient's weight. In the prevention of rejection, doses should start at 0.17 mg per kg of body weight daily in patients who have had a kidney transplant, and 0.11 to 0.13 mg per kg daily in those who have had a liver transplant. These starting doses may also be tried for the treatment of rejection. Doctors should monitor the levels of tacrolimus in the blood to check that they stay within certain limits. Treatment is adjusted according to the medicine's blood levels and the patient's response. Lower doses may be needed in patients with reduced liver function. Black patients may require higher doses than white patients.

Because tacrolimus is absorbed into the body differently from Envarsus than from other tacrolimus medicines, when switching patients who are already being treated with any other formulation of tacrolimus they should be given a dose of Envarsus 30% less than their existing dose.

Envarsus should be taken once daily with water, on an empty stomach. Envarsus is often given with other immunosuppressive medicines following the transplant. For further details see the package leaflet.

How does Envarsus work?

Tacrolimus, the active substance in Envarsus, is an immunosuppressive medicine. Tacrolimus reduces the activity of certain cells in the immune system, called T-cells, that are primarily responsible for attacking the transplanted organ (organ rejection).

What benefits of Envarsus have been shown in studies?

Because Envarsus is similar to the reference medicine Advagraf, the applicant provided comparative data on Advagraf.

In addition, because of the formulation/dosage differences between Envarsus and Advagraf, clinical studies in patients were also provided. These studies compared Envarsus with Prograf, a widely used and well-established tacrolimus medicine that releases tacrolimus more quickly.

Envarsus has been shown to be at least as effective as Prograf in two main studies in patients with kidney transplants. The main measure of effectiveness in both studies was the number of patients who had treatment failure (death, failure or rejection of the transplanted organ, or loss of the patient from follow-up) after 12 months.

The first study involved 326 patients who had already had a kidney transplant and were being treated with Prograf and other immunosuppressants to prevent rejection. Patients were either switched to treatment with Envarsus once daily or continued Prograf treatment twice daily. Failure rates were 2.5% in both groups (4 of 162 patients treated with Envarsus, and 4 of 162 treated with Prograf). The second study compared Envarsus with Prograf as part of standard treatment in 543 patients with a newly transplanted kidney. Treatment failure occurred in 18.3% patients treated with Envarsus (49 out of 268), and 19.6% given Prograf (54 out of 275).

The company also provided studies on the levels of tacrolimus in the body after taking Envarsus, which showed that it produced levels of tacrolimus that have been previously shown to be effective in treating and preventing rejection, and reported results in 29 patients who were given Envarsus starting after a liver transplant, none of whom rejected the transplanted organ during the 360 days following transplantation.

What are the risks associated with Envarsus?

The most commonly reported side effects with Envarsus (seen in more than 1 patient in 10) are tremor (shaking), headache, nausea (feeling sick), diarrhoea, kidney problems, hyperglycaemia (raised blood glucose levels), diabetes, hyperkalaemia (raised blood potassium levels), hypertension (high blood pressure) and insomnia (difficulty sleeping). Patients may also have abnormal results in liver function tests. For the full list of all side effects reported with Envarsus see the package leaflet

Envarsus must not be used in patients who are hypersensitive (allergic) to tacrolimus or any of the other ingredients, nor in those who are allergic to substances called macrolides (which include antibiotics such as erythromycin).

Why is Envarsus approved?

The Agency's Committee for Medicinal Products for Human Use (CHMP) decided that the approved doses of Envarsus have been shown to have a comparable quality, safety and effectiveness to Advagraf and Prograf. Therefore, the CHMP's view was that, as for other authorised forms of tacrolimus, the benefit outweighs the identified risk. The Committee recommended that Envarsus be given marketing authorisation.

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

A risk management plan has been developed to ensure that Envarsus 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 Envarsus, including the appropriate precautions to be followed by healthcare professionals and patients.

In addition, the company that markets Envarsus will provide educational material for healthcare professionals who are likely to prescribe or dispense Envarsus, reminding them of its authorised uses and dosage, and the need for care if switching patients between different forms of tacrolimus.

Further information can be found in the summary of the risk management plan.

Other information about Envarsus

The European Commission granted a marketing authorisation valid throughout the European Union for Envarsus on 18 July 2014.

The full EPAR and risk management plan summary for Envarsus 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 Envarsus, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 07-2014.