European Medicines Agency

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EUROPEAN PUBLIC ASSESSMENT REPORT (EPAR)

MODIGRAF

EPAR summary for the public

This document is a summary of the European Public Assessment Report (EPAR). It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the studies performed, to reach their recommendations on how to use the medicine.
If you need more information about your medical condition or your treatment, read the Package Leaflet (also part of the EPAR) or contact your doctor or pharmacist. If you want more information on the basis of the CHMP recommendations, read the Scientific Discussion (also part of the EPAR).

What is Modigraf?

Modigraf is a medicine that contains the active substance tacrolimus. It is available as sachets (0.2 mg and 1 mg) containing granules that are made up into an oral suspension.

What is Modigraf used for?

Modigraf is used in adults and children who have had a kidney, liver or heart transplant, to prevent rejection (when the immune system attacks the transplanted organ). Modigraf can also be used to treat organ rejection when other immunosuppressive medicines are not effective.
The medicine can only be obtained with a prescription.

How is Modigraf used?

Treatment with Modigraf should only be prescribed by doctors who have experience in the management of transplant patients.
Modigraf is for long-term use. Doses are calculated based on the patient's weight. Doctors should monitor the levels of tacrolimus in the blood to check that they stay within predefined ranges.
In the prevention of rejection, the dose of Modigraf to use depends on the type of transplant the patient has received. In kidney transplant patients, the starting daily dose is 0.2 to 0.3 mg per kilogram body weight for adults and 0.3 mg/kg for children. In liver transplant patients, the starting daily dose is 0.1 to 0.2 mg/kg for adults and 0.3 mg/kg for children. The starting daily dose for heart transplant patients is 0.075 mg/kg for adults and 0.3 mg/kg for children.
When treating rejection, the same doses may be used in kidney and liver transplants. For heart transplants the dose is 0.15 mg/kg/day for adults and 0.2 to 0.3 mg/kg for children.
Modigraf is taken twice a day, usually in the morning and evening.

How does Modigraf work?

Tacrolimus, the active substance in Modigraf, is an immunosuppressive agent. This means that it reduces the activity of the immune system (the body's natural defences). Tacrolimus acts on some special cells in the immune system called T-cells that are primarily responsible for attacking the transplanted organ (organ rejection).
Tacrolimus has been available in the European Union (EU) for preventing organ rejection since the mid-1990's. Modigraf is similar to another tacrolimus-containing medicine, Prograf or Prograft, which

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is available as capsules. Because Modigraf contains granules, it allows for making fine adjustments in dosing and provides an alternative for young children and others unable to swallow capsules.

How has Modigraf been studied?
Because tacrolimus has been in use for many years, the company presented results of studies from the scientific literature on the effectiveness of tacrolimus in organ transplantation.
Modigraft was studied in two main studies in children who had had a liver transplant. One study involved 28 children who were given the medicine for up to one year. Modigraf was not compared with any other medicine. The main measure of effectiveness was based on the number of patients who did not have organ rejection. The second study involved 185 children who were given either Modigraf with corticosteroids (a group of immunosuppressant medicine) or a combination of other immunosuppressant medicines (cicosporin, azathioprine and corticosteroids) for one year. The main measure of effectiveness in this study was based on the number of patients who did not have organ rejection. It also looked at the number of organ rejections in patients that did not respond to corticosteroids.

What benefit has Modigraf shown during the studies?
Modigraf was effective at preventing organ rejection in children who had had a liver transplant. In the first study, 79% of patients given Modigraf (22 out of 28) did not have organ rejection. In the second study, the difference between the total number of rejections for the two medicine combinations was not considered to be relevant. However, the Modigraf combination was more effective than the other combination at preventing organ rejections that could not be treated by corticosteroids.

What is the risk associated with Modigraf?
The most common side effects with Modigraf (seen in more than 1 patient in 10) are diabetes, hyperglycaemia (high blood glucose), hyperkalaemia (high blood potassium), insomnia (difficulty sleeping), headache, tremor (shaking), hypertension (high blood pressure), diarrhoea, nausea (feeling sick), abnormal liver function test (abnormal level of liver enzymes), and kidney problems. For the full list of all side effects reported with Modigraf, see the Package Leaflet.
Modigraf should not be used in people who may be hypersensitive (allergic) to tacrolimus or any of the other ingredients or to other macrolides (medicines with a similar structure to tacrolimus).

Why has Modigraf been approved?
The Committee for Medicinal Products for Human Use (CHMP) was of the opinion that in terms of effectiveness and safety, Modigraf was similar to other tacrolimus medicines available as capsules. Modigraf also offered the possibility of giving more exact doses and may be more easily administered to young children. The CHMP decided that Modigraf's benefits are greater than its risks for prophylaxis of transplant rejection in kidney, liver and heart recipients, and in the treatment of rejection resistant to treatment with other immunosuppressive medicinal products. The Committee recommended that Modigraf be given marketing authorisation.

Other information about Modigraf:
The European Commission granted a marketing authorisation valid throughout the European Union for Modigraf to Astellas Pharma Europe B.V. on 15 May 2009.

The full EPAR for Modigraf can be found here.

This summary was last updated in 04-2009.