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Rapamune (*sirolimus*)

An overview of Rapamune and why it is authorised in the EU

What is Rapamune and what is it used for?

Rapamune is a medicine used to prevent the body from rejecting a newly transplanted kidney. It is used in adults who are at a low to moderate risk of rejection. It is recommended that Rapamune is used with ciclosporin and corticosteroids (other medicines to prevent organ rejection) for two to three months. Rapamune can then be used for continuing treatment with corticosteroids, but only if ciclosporin treatment can be stopped.

Rapamune is also used for treating patients with sporadic lymphangioleiomyomatosis (S-LAM) with moderate lung disease or worsening lung function. S-LAM is a rare lung disease that causes worsening symptoms such as shortage of breath and occurs mainly in women who are at an age when they can have children.

Rapamune contains the active substance sirolimus.

How is Rapamune used?

Rapamune treatment should be started by and remain under the guidance of a doctor who is a qualified specialist in transplantation. The medicine can only be obtained with a prescription.

Rapamune is available as an oral solution (1 mg/ml) and tablets (0.5, 1 and 2 mg).

To prevent organ rejection, the first dose is usually 6 mg given soon after the transplantation followed by 2 mg once a day. The doctor will adjust the dose to achieve appropriate levels of sirolimus in the patient's blood.

To treat patients with S-LAM, the dose of Rapamune is 2 mg daily and after 10 to 20 days the doctor will adjust the dose to achieve appropriate levels of sirolimus in the patient's blood.

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

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How does Rapamune work?

The active substance in Rapamune, sirolimus, is an immunosuppressant (a medicine that reduces the activity of the immune system). In the body, sirolimus attaches to a protein inside cells to make a 'complex'. This complex then blocks another protein called 'mammalian target of rapamycin' (mTOR). Since mTOR is involved in the multiplication of activated T-lymphocytes (white blood cells that are responsible for attacking the transplanted organ), Rapamune reduces the number of these cells, reducing the risk of organ rejection.

In S-LAM, mTOR is overactive, causing excessive multiplication of cells that cause the disease. By blocking mTOR, Rapamune reduces the multiplication of these cells.

What benefits of Rapamune have been shown in studies?

Prevention of rejection

Rapamune was more effective than placebo (a dummy treatment) or azathioprine (another immunosuppressive medicine) in two main studies involving a total of 1,295 patients who were having a kidney transplant. All patients were also treated with ciclosporin and corticosteroids and were at low to moderate risk of rejection. The main measure of effectiveness was the number of treatment failures (rejection or loss of the new kidney, or death) after 6 months. In the first study, treatment failed in 19% (53 out of 284) of the patients adding Rapamune after 6 months, compared with 32% (52 out of 161) of those adding azathioprine. In the second study, treatment failed in 30% (68 out of 277) of the patients adding Rapamune, compared with 48% (62 out of 130) of those adding placebo.

Two additional studies looked at Rapamune as continuing treatment for up to 5 years in 765 patients who were able to stop ciclosporin after 2 to 3 months. Rapamune was effective in helping the new kidney to survive, with an improvement in how well it worked and an improvement in blood pressure when ciclosporin treatment was stopped.

Treatment of S-LAM

Rapamune was more effective than placebo in improving lung function in a study involving 81 patients with S-LAM. The main measure of effectiveness was a change of FEV_1 (the maximum volume of air a person can breathe out in 1 second). FEV_1 improved by an average of 1 ml per month in patients treated with Rapamune compared with a worsening by 12 ml per month in patients receiving placebo.

What are the risks associated with Rapamune?

The most common side effects with Rapamune (which may affect more than 1 in 10 people) are infections, fever, slow wound healing, low counts of various blood cells, blood tests showing altered levels of various substances (including low potassium and phosphate; raised fats, cholesterol, glucose and markers for tissue breakdown and for liver and kidney function), diabetes, lymphocele (collection of lymph fluid usually in the lower belly), pain in various parts of the body, rapid heartbeat, raised blood pressure, problems affecting the gut, proteinuria (protein in the urine), menstrual disorders, oedema (swelling because of fluid build-up), rash and acne.

Patients allergic to peanut or soya must not take Rapamune oral solution because the solution contains soya oil.

For the full list of side effects and restrictions of Rapamune, see the package leaflet.

Why is Rapamune authorised in the EU?

The European Medicines Agency considered that Rapamune is effective for the prevention of rejection of a transplanted kidney in patients at low to moderate risk of rejection. The Agency noted that no medicinal product has been approved for the treatment of S-LAM and Rapamune's effect on lung function is considered important. The Agency decided that Rapamune'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 Rapamune?

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

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

Other information about Rapamune

Rapamune received a marketing authorisation valid throughout the EU on 14 March 2001.

Further information on Rapamune can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports.

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