PATIENT INFORMATION LEAFLET: RAPAMUNE

Read all of this leaflet carefully before you start using Rapamune

- Keep this leaflet. You may need to read it again.
- If you have any questions, consult your doctor, pharmacist or other health care professional for advice.
- Rapamune has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

SCHEDULING STATUS:

S 4

PROPRIETARY NAME AND DOSAGE FORM:

Rapamune® 1 mg tablets

Rapamune® 1 mg/ml oral solution

WHAT RAPAMUNE CONTAINS:

Tablets:

Each Rapamune tablet contains 1 mg of the active ingredient sirolimus.

The other inactive ingredients are:

Lactose monohydrate; polyethylene glycol 8000; magnesium stearate; purified talc; polyethylene glycol 20 000; denatured alcohol 23 A; glyceryl monooleate; pharmaceutical glaze(Shellac); anhydrous calcium sulphate; microcrystalline cellulose; sucrose; titanium dioxide, red opacode S-1-15095; povidone (k29/32); carnauba wax; opacode red ink S-I-15095

Rapamune does not contain gluten, tartrazine or any other azo dyes.

Oral solution:

Each ml of Rapamune solution contains 1 mg of the active ingredient sirolimus.

The other inactive ingredients are: Polysorbate 80 and phosal 50 PG.

phosal 50 PG contains:

phosphatidylcholine; propylene glycol; monodiglycerides; ethanol; soya fatty acids; ascorbyl palmitate.

Rapamune solution does not contain lactose, sucrose, gluten, tartrazine or any other azo dyes.

WHAT RAPAMUNE IS USED FOR:

Rapamune belongs to a group of medicines called immunosuppressants. It helps to control your body's immune system after you have received an organ transplant. It is used to prevent your body from rejecting transplanted kidneys and is normally used with medicines called corticosteroids and initially with cyclosporin.

INSTRUCTION BEFORE TAKING RAPAMUNE:

Do not take Rapamune:

- if you are hypersensitive (allergic) to sirolimus or any other ingredients in the tablet or solution.

  Symptoms of an allergic reaction may include wheezing, shortness of breath, difficulty breathing or a tight feeling in your chest, swelling of the face, lips, tongue or other parts of the body, rash, itching, hives or flushed red skin, dizziness or light-headedness.

  If you are not sure whether this applies to you, check with your doctor.

Do not take Rapamune if the packaging is torn or shows signs of tampering.
Do not take Rapamune after the expiry date printed on the pack.
If you take Rapamune after the expiry date has passed, it may not work as well as it should.

Take special care with Rapamune:

- if you have any medical conditions, especially the following:
  a) liver problems or have had a disease which may have affected your liver, please tell your doctor as this may affect the dose of Rapamune that you receive.
  b) high fat levels in the blood.
- Rapamune should not be used during pregnancy unless clearly necessary. You must use effective contraception methods during treatment with Rapamune and for 12 weeks after treatment has stopped. If you are unsure, talk to your doctor or pharmacist.

If you are breastfeeding or plan to breastfeed. Ask your doctor or pharmacist for advice before breastfeeding your baby. It is not known whether Rapamune passes into breastmilk. Patients taking Rapamune should discontinue breastfeeding.
Your doctor will perform tests to monitor the levels of Rapamune in your blood. Your doctor will also perform tests to monitor your kidney function and, possibly, your liver function, during therapy with Rapamune.

Limit your exposure to sunlight and UV light by wearing protective clothing and using a sunscreen with a high protection factor.

Immunosuppressive medicines like Rapamune may increase the risk of developing cancer of the lymph glands and skin. It may also increase the risk of getting an infection.

Taking Rapamune with food and drink:

Rapamune should be taken consistently, either with or without food. Rapamune should not be taken with grapefruit juice.

Use in children:

There is limited experience of the use of Rapamune in children and adolescents.

Pregnancy and breastfeeding

Rapamune should not be used during pregnancy and breastfeeding.

If you are pregnant or breast feeding your baby while taking Rapamune please consult your doctor, pharmacist or other health care professional for advice.

If you are taking other medicines on a regular basis, including complementary or traditional medicines, the use of Rapamune with these medicines may cause undesirable interactions. Please consult your doctor, pharmacist or other healthcare professional, for advice.

Driving and operating machinery:

No specific studies on the effects of Rapamune on the ability to drive and operate machines have been conducted. Although Rapamune treatment is not expected to affect your ability to drive, if you have any concerns please consult your doctor.

Important Information about some of the ingredients of Rapamune

If you have been told by your doctor that you have an intolerance to some sugars such as lactose, contact your doctor before taking Rapamune.

Taking other medicines with Rapamune:

Please inform your doctor or pharmacist if you are taking, or have recently taken any other medicines, including those that you buy without a prescription from your

pharmacy.

Some medicines can interfere with the action of Rapamune. In particular, you should inform your doctor or pharmacist if you are taking any of the following:

- any other immunosuppressive agents excluding cyclosporine or corticosteroids.
- Antibiotics or antifungal medicines used to treat infection e.g. rifampicin, clarithromycin, erythromycin, troleandomycin, rifabutin, clotrimazole, fluconazole, itraconazole, ketoconazole.
- High blood pressure medicines or medicines for heart problems including nicardipine, verapamil and diltiazem.
- Anti-epileptic medicines including carbamazepine, phenobarbital, phenytoin.
- Medicines used to treat ulcers or other gastrointestinal disorders such as cisapride, cimetidine, metoclopramide. Bromocriptine (used in the treatment of Parkinsons' disease and various hormonal disorders), danazol (used in the treatment of gynaecological disorders), or protease inhibitors (used in the treatment of HIV).
- St. John's Wort (*Hypericum perforatum)*

The use of live vaccines should be avoided with the use of Rapamune. Before vaccinations, please inform your doctor or pharmacist that you are receiving Rapamune.

These medicines may be affected by Rapamune, or may affect how well it works. You may need different amounts of your medicine, or you may need to take different medicines.

The use of Rapamune may lead to increased blood levels of cholesterol and triglycerides that may require treatment. Medicines known as "statins" and fibrates used to treat elevated cholesterol and triglycerides have been associated with an increased risk of muscle breakdown (rhabdomyolysis). Please inform your doctor if you are taking medicines to lower your blood fats.

INSTRUCTIONS ON HOW TO TAKE RAPAMUNE:

Rapamune is for oral use only. Always take Rapamune exactly as you doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

How much to take: You doctor will decide exactly what dose of Rapamune you must take and how often to take it. Follow your doctor's instructions exactly and never

change the dose yourself. Do not stop taking your medicine unless your doctor tells you to.

The usual starting dose is 6 mg after transplantation and then 2 mg once daily. You will also need to take medicines such as cyclosporin and corticosteroids.

Your dose may be adjusted depending on the level of Rapamune in your blood. Your doctor will need to perform a blood test to measure Rapamune levels.

After 2 to 4 months your doctor may need to start reducing the dose of cyclosporine you take and increasing your dose of Rapamune. Your doctor will determine how much you need to take.

How to take it: Take Rapamune consistently with or without food. Do not take Rapamune with grapefruit juice.

Swallow Rapamune tablets with a glass of water or orange juice.

For the Rapamune solution, do not use any liquids other than water or orange juice for dilution. Do not use containers made from plastic, paper or polystyrene for dilution. Use the dosing syringe and syringe cap once only and then discard.

When to take it: Take Rapamune once a day at about the same time each day. It will have the best effect and it will also help you to remember when to take it.

If you are also taking cyclosporine, then you must take Rapamune 4 hours after the cyclosporin dose.

Additional information:

If you forget to take it: If you forget to take Rapamune, take it as soon as you remember, but not within 4 hours of the next dose of cyclosporin. After that, continue to take your medicines as usual. Do not take a double dose to make up for a missed dose, and always take Rapamune and cyclosporin approximately 4 hours apart.

If you are not sure what to do, ask your doctor or pharmacist.

If you take too much (overdose):

If you have taken more Rapamune than you were told to take, see a doctor or go to the nearest hospital emergency department as soon as possible.

Do this even if there are no signs of discomfort or poisoning. Take the labelled medicine container with you, even if it is empty.

While you are using Rapamune:

Things you must do:

Tell any other doctors, dentists, and pharmacists who are treating you that you are taking Rapamune.

Attend all doctor's appointments to monitor your condition.

Do not stop taking Rapamune, or change the dosage, without checking with your doctor.

Do not share medicines prescribed for you with others.

In the event of over-dosage, consult your doctor or pharmacist. If neither is available, rush the patient to the nearest hospital or poison control centre.

POSSIBLE SIDE EFFECTS:

If you get any side effects, do not stop taking Rapamune without first talking to your doctor.

Rapamune helps most people undergoing kidney transplants but it may have unwanted side effects.

Possible side effects are listed according to the following categories:

Very common: greater than 10 %

Common: between 1 % and 10 %

- Body as a whole:

Very common: A cyst containing lymph; fluid collection around the kidney, swelling of the extremities, fever, headache, pain

Common: abnormal wound healing (this may include separation of the layers of a surgical wound or suture line), swelling, infections (including blood poisoning)

- Cardiac disorders:

Very common: increased blood pressure

Common: Rapid heart rate, blood clots in the lungs or legs

- Gastrointestinal reactions:

Very common: stomach pain; diarrhoea, constipation, nausea

Common: Mouth sores, fluid collection in the abdomen

- Blood and lymph disorders:

Very common: low red blood cells; low blood platelets;

Common: kidney damage with low blood platelets and low red cell counts, with or without rash (thrombocytopenic purpura/haemolytic uraemia syndrome)

- Metabolism and nutrition disorders:

Very common: low blood potassium; elevated lactate dehydrogenase protein in the blood, elevated cholesterol, elevated fat in the blood, elevated blood sugar, elevated blood phosphate

Common: Abnormal liver function tests; elevated ALT and/or AST liver enzymes, fluid accumulation

- Bone and joint disorders:

Very common: Joint pain

Common: Deterioration of bone

- Respiratory tract disorders:

Common: Nose bleeds; pneumonia and other inflammations of the lung, fluid around the lungs

- Skin disorders:

Very common: Acne

Common: Rash, skin cancer

- Kidney disorders:

Very common: Urinary tract infection

Common: Kidney infection, protein in the urine

The above side effects may require medical intervention and some may be life-threatening or fatal. Not all side effects reported for Rapamune are included in this leaflet. Should your general health worsen while taking Rapamune, please consult your doctor, pharmacist or other health care professional for advice.

STORAGE AND DISPOSAL INFORMATION:

Tablets:

Keep Rapamune tablets in their blister pack until it is time to take them. If you take them out of their blister pack, they may not last as well.

Store below 25 °C. Protect from light.

Store all medicines out of reach of children.

Oral Solution:

Keep Rapamune in its original container. Store protected from light, in a refrigerator (2 to 8 °C). Once the bottle has been opened, keep the contents in the fridge and use within one month. Discard the syringe after one use only. Store all medicines out of reach of children.

Disposal: If your doctor tells you to stop taking Rapamune or the tablets have passed their expiry date, ask your pharmacist what to do with the left over tablets.

PRESENTATION:

Tablets:

The tablets are supplied in white HDPE bottles of 100's and blister packs of 30's and 100's. Not all pack sizes may be marketed.

Oral solution:

Rapamune oral solution is supplied in 60 ml amber glass bottles, with syringe adapter and 30 amber, plastic dosing syringes.

IDENTIFICATION:

Tablets:

Rapamune 1 mg tablets are white, triangular-shaped, sugar-coated tablets branded "RAPAMUNE 1 mg" in red ink on one side.

Oral solution:

Rapamune oral solution is a pale yellow to yellow viscous solution free from foreign particles.

REGISTRATION NUMBERS:

Rapamune 1 mg tablets: 35/34/0009

Rapamune oral solution: 34/34/0428

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Pfizer Laboratories (Pty) Ltd

85 Bute Lane

Sandton, 2196

SOUTH AFRICA

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