

PART III: CONSUMER INFORMATION

Pr **Rapamune**[®] (Sirolimus Oral Solution and Tablets)

This leaflet is part III of a three-part "Product Monograph" published when Rapamune was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about Rapamune. Contact your doctor or pharmacist if have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

Rapamune belongs to a group of medicines called immunosuppressants. It is used to prevent your body from rejecting transplanted kidneys and is often used in combination with medicines called cyclosporine and corticosteroids.

What it does:

Rapamune is a drug that is used to help your body accept your transplanted kidney. In order to prevent rejection, Rapamune suppresses the body's natural immune system. When a patient receives an organ transplant, the body's white blood cells will try to get rid of (reject) the transplanted organ. Sirolimus works by preventing the white blood cells from getting rid of the transplanted organ.

When it should not be used:

- If you are allergic to sirolimus and any ingredient in Rapamune.

What the medicinal ingredient is:

Sirolimus (pronounced sih-ROW-lih-mus).

What the nonmedicinal ingredients are:

- Oral solution: Phosal 50 PG[®] (ascorbyl palmitate, ethanol, phosphatidyl-choline, propylene glycol, soybean oil fatty acids and sunflower mono and diglycerides) and Polysorbate 80.
- Tablets: Calcium sulfate anhydrous, carnauba wax, glyceryl monooleate, lactose monohydrate, magnesium stearate, microcrystalline cellulose, pharmaceutical glaze, polaxamer 188, polyethylene glycol 8000 powdered, polyethylene glycol type 20,000, povidone, vitamin E (*d,l*-alpha tocopherol), sucrose, talc, titanium dioxide and ink. In addition, the 2 mg tablet contains brown #70 iron oxide and yellow #10 iron oxide; the 5 mg tablet contains brown #75 iron oxide, and yellow #10 iron oxide.

What dosage form it comes in:

- Oral solution: 1 mg/mL.
- Tablet: 1 mg, 2 mg and 5 mg.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

- Rapamune may reduce the body's ability to fight infections.
- The development of cancer of the lymphoid tissues (called lymphoma) and skin may result from using immunosuppressants such as Rapamune.
- Cases of severe allergic reaction including skin reaction have been associated with Rapamune.

BEFORE you use Rapamune talk to your doctor or pharmacist if any of the following situations apply to you:

- Allergies: Tell your doctor if you have any allergies to medicines or any other substances such as foods, preservatives, or dyes.
- Pregnancy: Women must avoid pregnancy while taking Rapamune as it may cause damage to the unborn baby. Women must use effective contraception methods before taking Rapamune, during treatment with Rapamune and for 12 weeks after treatment has stopped. If you are unsure, or think you may become pregnant, talk to your doctor or pharmacist.
- Breast-feeding: It is not known whether Rapamune passes into breast milk. Ask your doctor or pharmacist for advice before breast-feeding your baby.
- Liver problems: You should inform your doctor if you have any liver problems or have had a disease which may have affected your liver, as this may affect the dose of Rapamune that you receive.
- If you have high cholesterol or triglycerides (fat in blood). Your doctor may order blood tests for you.
- If you are going to have an operation, or if you still have a wound that hasn't healed completely after a surgery, you should tell your doctor before receiving this medicine, as Rapamune may prevent these wounds from healing properly.
- Talk to your doctor before switching from the oral solution to the tablet, since your doctor may need to adjust the dose of Rapamune you receive.
- Limit your exposure to sunlight and UV light by wearing protective clothing and using a sunscreen with a high protection factor.
- Driving and operating machinery: No specific studies on the effects of Rapamune on the ability to drive and operate machines have been conducted. If you have any concerns please consult your doctor.
- Alcohol: Rapamune oral solution contains 1.5-2.5% ethanol. Each 2 mg dose contains up to 50 mg of alcohol, approximately the same amount of alcohol as half a teaspoon of a light beer. If you have any concerns please consult your doctor.
- Tell any other doctors, dentists, and pharmacists who are treating you that you are taking Rapamune.

INTERACTIONS WITH THIS MEDICATION

With drugs:

Some medicines and Rapamune may interfere with each other. Your doctor or pharmacist should know if you are taking, or have recently taken, other medicines, even those not prescribed for you, including non-prescription (over-the-counter) drugs and herbal preparations. Drugs that may interact with Rapamune include:

- Any other immunosuppressive agents.
- Antibiotics or antifungal medicines used to treat infection e.g. rifampicin, clarithromycin, erythromycin, telithromycin, troleandomycin, rifabutin, rifapentine, clotrimazole, fluconazole, itraconazole, ketoconazole, voriconazole.
- High blood pressure medicines or medicines for heart problems including nicardipine, verapamil and diltiazem.
- Anti-convulsant medicines including carbamazepine, phenobarbital, phenytoin.
- Cisapride (not marketed in Canada), metoclopramide, bromocriptine, cimetidine, danazol, protease inhibitors (eg, for HIV that include drugs such as ritonavir, indinavir, and hepatitis C drugs such as boceprevir, and telaprevir).
- Immunosuppressive drugs like Rapamune may alter the effectiveness of vaccinations. If you plan on being vaccinated, inform your doctor that you are taking Rapamune.
- Herbal preparations, such as St. John's Wort.

With food:

- Grapefruit juice

These medicines/foods may be affected by Rapamune or may affect how well Rapamune works.

PROPER USE OF THIS MEDICATION

- Rapamune is for oral use only.
- Your doctor will decide exactly what dose of Rapamune you must take and how often to take it.
- Your doctor may need to monitor the quantity of the drug in your blood.
- Always take the medicine exactly as your doctor tells you. Follow your doctor's instructions exactly and never change the dose yourself.
- Do not stop taking your medicine unless your doctor tells you to.

Usual dose:

- Usually, for an adult, your doctor will give you an initial Rapamune dose of 6 mg at the time of your kidney transplant operation and then 2 mg each day.
- Your doctor may adjust your dose depending on your age, certain other medications which you may be taking, and/or the presence of other medical conditions. A lower dose may be required by elderly patients (older than 65 years).
- If you are also taking cyclosporine, Rapamune should be taken 4 hours after cyclosporine.
- Take Rapamune once a day at about the same time each day.
- Rapamune should be taken consistently, either with or without food.

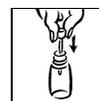
- Do NOT take Rapamune with grapefruit or grapefruit juice.
- Do NOT take Rapamune after the expiry date printed on the container.
- If you are taking Rapamune tablets, do not crush, chew, or split the tablets. Inform your doctor if you have difficulty taking the tablet.
- After 2-4 months, your doctor may stop your dose of cyclosporine and increase your dose of Rapamune.
- If taking Rapamune oral solution, avoid contact with the skin, mucous membranes or eyes. In case of accidental contact with the skin, wash with soap and water. In case of eye contact, rinse with plain water.

How to dilute Rapamune oral solution supplied in a bottle:

1. Open the solution bottle. Remove the safety cap by squeezing the tabs on the cap and twisting counterclockwise.



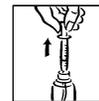
2. On first use, insert the adapter assembly (plastic tube with stopper) tightly into the bottle until it is even with the top of the bottle. Do not remove the adaptor assembly from the bottle once inserted.



3. For each use, tightly insert one of the amber syringes with the plunger fully depressed into the opening in the adapter.



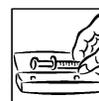
4. Withdraw the prescribed amount of Rapamune oral solution by gently pulling out the plunger of the syringe until the bottom of the black line of the plunger is even with the appropriate mark on the syringe. Always keep the bottle in an upright position. If bubbles form in the syringe, empty the syringe into the bottle and repeat the procedure.



5. You may have been instructed to carry your medication with you. If it is necessary to carry the filled syringe, place a cap securely on the syringe - the cap should snap into place.



6. Then place the capped syringe in the enclosed carrying case. Once in the syringe, the medication may be kept at room temperature or refrigerated and should be used within 24 hours. Extreme temperatures below 2°C and above 30°C should be avoided.



7. Empty the syringe into a glass or plastic cup containing at least 2 ounces (¼ cup; 60 mL) of water or orange juice, stir vigorously for one (1) minute and drink immediately. Refill the container with at least 4 ounces (½ cup; 120 mL) of water or orange juice, stir vigorously again and drink the rinse solution. Apple juice, grapefruit juice, or other liquids are NOT to be used. Only glass or plastic cups should be used to dilute Rapamune oral solution. The syringe and cap should be used once and then discarded.



8. Always store the bottles of medication in the refrigerator. When refrigerated, a slight haze may develop in the solution. The presence of a haze does not affect the quality of the product. If this happens, bring the Rapamune oral solution to room temperature and shake until the haze disappears. If it is necessary to wipe clean the mouth of the bottle before returning the medication to the refrigerator, wipe with a dry cloth to avoid introducing water, or any other liquid into the bottle.



Overdose:

In case of drug overdosage, contact a healthcare professional (e.g. doctor), hospital emergency department, or regional poison control centre, even if there are no symptoms.

- Always take the labelled medicine bottle with you, even if it is empty.

Missed Dose:

If you forget to take Rapamune:

- If it is almost time for your next dose (within 4 hours), skip the dose you missed and take your next dose when you are meant to.
- Otherwise, take it as soon as you remember.
- After that, continue to take your medicine as usual.
- Do not take a double dose to make up for a forgotten dose, and always take Rapamune approximately 4 hours after cyclosporine.
- If you are not sure what to do, call your doctor or pharmacist.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, Rapamune can have side effects. However, since Rapamune is taken in combination with other medicines, Rapamune may not have been the cause of the side effects experienced.

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

Tell your doctor if you have any of these symptoms and they concern you:

Very common side effects (occur in 10% or more of patients) include:

- Abnormal healing
- Abnormal vision
- Acne
- Constipation
- Diarrhea
- Headache
- Insomnia
- Joint, bone or back pain
- Nausea or upset stomach
- Stomach pain
- Swelling of the hands, feet, ankles, or lower legs
- Shaking (tremor)
- Urinary tract infection
- Weakness

Common side effects (occur in 1% to 9% of patients) include:

- Abnormal bleeding or bruising
- Cold or flu-like symptoms (lung infection)
- Dizziness upon standing
- Feeling anxious
- Fever or chills
- Fluid accumulation/retention

- Increased heart rate or heart palpitations
- Kidney infection
- Leg pain or muscle pain
- Menstrual disorders (Absence of menstrual period or abnormal heavy and prolonged menstrual period)
- Mouth ulcers or cold sores
- Nose bleed
- Ovarian Cysts
- Rash
- Shortness of breath
- Skin cancer
- Surgical wounds slow to heal
- Swollen abdomen

Uncommon or rare side effects (occur in less than 1% of patients) include:

- Melanoma (a type of skin cancer)
- Pancreatitis (inflammation of the pancreas)
- Severe allergic reaction including skin reaction

Unwanted side effects that you may not be aware of while taking your medicine include changes in levels of blood cells or substances in your blood (e.g. cholesterol, creatinine, or sugar). Your doctor may do blood tests to look for any changes.

Immunosuppressive drugs may increase the risk of infections.

Immunosuppressive drugs like Rapamune may increase your risk of developing lymphoma (a type of cancer) or cancer of the skin. Contact your doctor immediately if you notice a lump in your neck, armpits, collarbone region, or groin, or unintended weight loss (may be signs of lymphoma). Talk to your doctor if you notice any new moles or any changes in the size, shape, or colour of moles you already have (may be a sign of skin cancer).

Other side effects not listed above may also occur in some patients. Tell your doctor if you notice anything that concerns you, even if you do not think the problem is connected with Rapamune or the problem is not listed in this leaflet.

Do NOT stop taking Rapamune without talking to your doctor.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Symptom / effect		Contact your doctor or pharmacist immediately		Stop taking the drug and call your doctor or pharmacist immediately
		Only if severe	In all cases	
Very Common or Common	Bladder infection		√	
	Headache	√		
	Cough or shortness of breath		√	
	Increased heart rate		√	
	Isolated fever		√	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect	Contact your doctor or pharmacist immediately		Stop taking the drug and call your doctor or pharmacist immediately
	Only if severe	In all cases	
Sore throat, fever, chills, or swelling of glands Swelling of hands, feet, ankles or lower legs	Increased heart rate	√	√
		√	
Unusual bleeding or bruising		√	
Uncommon Possible signs of lymphoma: • Lump in your neck, armpits, collarbone region, or groin • Unintended weight loss		√	
	Coughing up blood	√	
Rare Signs of severe allergic reaction. Signs may include: • Chest tightness • Dizziness • Faintness • Rapid heartbeat • Shortness of breath • Skin reaction • Swollen face, lips, or tongue • Wheezing			√

This is not a complete list of side effects. For any unexpected effects while taking Rapamune contact your doctor or pharmacist.

HOW TO STORE IT

- Keep Rapamune oral solution in its original container.
- Protect from light.
- Store oral solution at 2°C to 8°C, in a refrigerator for up to the expiration date indicated on the container label.
- Do NOT freeze.

- Once the bottle has been opened, the contents should be kept refrigerated and used within 30 days.
- If it is necessary to wipe clean the mouth of the bottle before returning the medication to the refrigerator, wipe with a dry cloth to avoid introducing water, or any other liquid into the bottle.
- When refrigerated the solution in the bottle may develop a slight haze. If this occurs, simply bring your Rapamune oral solution to room temperature and shake gently until the haze disappears. The presence of this haze does not affect the quality of Rapamune.
- If necessary, you may store bottles at 15°C to 30°C for a short time, but no longer than 5 days.
- Storage of Rapamune oral solution in capped syringe: Rapamune can only be stored refrigerated (2°C to 8°C) or at room temperatures (15°C to 30°C) for a maximum of 24 hours. The syringe should be discarded after one use. After dilution, preparation should be used immediately.
- Rapamune tablets should be stored at 15°C to 30°C for up to the expiration date indicated on the container label. Use cartons to protect blister cards from light.

Keep Rapamune oral solution and tablets out of reach of children.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
 - Fax toll-free to 1-866-678-6789, or
 - Mail to: Canada Vigilance Program
Health Canada
Postal Locator 0701D
Ottawa, Ontario
K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full Product Monograph, prepared for health professionals, can be found at: www.pfizer.ca or can be requested by contacting the sponsor, Pfizer Canada Inc., at 1-800-463-6001.

This leaflet was prepared by Pfizer Canada Inc.

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