

MEDICATION GUIDE

Sirolimus (sir-OH-li-mus) Oral Solution

What is the most important information I should know about sirolimus?

Sirolimus can cause serious side effects, including:

1 Increased risk of getting infections. Serious infections can happen including infections caused by viruses, bacteria, and fungi (yeast). Your doctor may put you on medicine to help prevent some of these infections.

Call your doctor right away if you have symptoms of infection including fever or chills while taking sirolimus.

2 Increased risk of getting certain cancers. People who take sirolimus have a higher risk of getting lymphoma, and other cancers, especially skin cancer. Talk with your doctor about your risk for cancer.

Sirolimus has not been shown to be safe and effective in people who have had liver or lung transplants. Serious complications and death may happen in people who take sirolimus after a liver or lung transplant. You should not take sirolimus if you have had a liver or lung transplant without talking with your doctor.

See the section “What are the possible side effects of sirolimus?” for information about other side effects of sirolimus.

What is sirolimus?

Sirolimus is a prescription medicine used to prevent rejection (anti-rejection medicine) in people 13 years of age and older who have received a kidney transplant. Rejection is when your body’s immune system recognizes the new organ as a “foreign” threat and attacks it.

Sirolimus is used with other medicines called cyclosporine (Gengraf, Neoral, Sandimmune), and corticosteroids. Your doctor will decide:

- if sirolimus is right for you, and
- how to best use it with cyclosporine and corticosteroids after your transplant.

It is not known if sirolimus is safe and effective in children under 13 years of age.

Who should not take sirolimus?

Do not take Sirolimus Oral Solution if you are allergic to sirolimus or any of the other ingredients in Sirolimus Oral Solution. See the end of this leaflet for a complete list of ingredients in Sirolimus Oral Solution.

What should I tell my doctor before taking sirolimus?

- have liver problems
- have skin cancer or it runs in your family
- have high cholesterol or triglycerides (fat in your blood)
- are pregnant or are a female who can become pregnant. Sirolimus may harm your unborn baby. You should not become pregnant during treatment with sirolimus and for 12 weeks after ending treatment with sirolimus. In order to avoid pregnancy, a female who can get pregnant should use effective birth control during treatment and for 12 weeks after your final dose of sirolimus. Talk with your doctor about what birth control method is right for you during this time. Tell your doctor right away if you become pregnant or think you are pregnant during treatment with sirolimus or within 12 weeks after your final dose of sirolimus.
- It is not known whether sirolimus passes into breast milk. You and your doctor should decide if you will take sirolimus or breastfeed. You should not do both.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements. Using sirolimus with certain medicines may affect each other causing serious side effects.

Sirolimus may affect the way other medicines work, and other medicines may affect how sirolimus works.

Especially tell your doctor if you take:

- a medicine to lower your cholesterol or triglycerides
- cyclosporine (including Gengraf, Neoral, Sandimmune) or tacrolimus (Prograf) or other medicines that suppress the immune system
- an antibiotic
- an antifungal medicine
- a medicine for high blood pressure or heart problems

- an anti-seizure medicine
- medicines used to treat stomach acid, ulcers, or other gastrointestinal problems
- bromocriptine mesylate (Parlodel, Cycloset)
- danazol
- medicines to treat HIV or hepatitis C
- St. John’s Wort

How should I take sirolimus?

- Read the Instructions for Use that comes with your Sirolimus Oral Solution for information about the right way to take Sirolimus Oral Solution.
- Take sirolimus exactly as your doctor tells you to take it.
- Your doctor will tell you how much sirolimus to take and when to take it. Do not change your dose of sirolimus unless your doctor tells you to.
- If you also take cyclosporine (Gengraf, Neoral, Sandimmune), you should take your sirolimus and cyclosporine about 4 hours apart.
- Do not stop taking sirolimus or your other anti-rejection medicines unless your doctor tells you to.
- Your doctor will check the levels of sirolimus in your blood. Your doctor may change your dose of sirolimus depending on your blood test results.
- Sirolimus is taken by mouth 1 time each day.
- Take each dose of sirolimus the same way, either with or without food. Food can affect the amount of medicine that gets into your bloodstream. Taking each dose of sirolimus the same way helps keep your blood levels of sirolimus more stable. Do not take sirolimus with grapefruit juice.
- Sirolimus Oral Solution can develop a slight haze when it is refrigerated. If this happens, bring the Sirolimus Oral Solution to room temperature and then gently shake the bottle until the haze goes away.
- If you get Sirolimus Oral Solution on your skin, wash the area with soap and water.
- If you get Sirolimus Oral Solution in your eyes, rinse your eyes with water.
- If you have taken more medicine than you were told, contact a doctor or go to the nearest hospital emergency department right away.

What should I avoid while taking Sirolimus Oral Solution?

- Avoid receiving live vaccines while taking sirolimus. Some vaccines may not work as well while you are taking sirolimus.
- Limit your time in sunlight and UV light. Cover your skin with clothing and use a sunscreen with a high protection factor because of the increased risk for skin cancer with sirolimus.

What are the possible side effects of sirolimus?

Sirolimus may cause serious side effects, including:

- See “**What is the most important information I should know about sirolimus?**”
- **Serious allergic reactions.** Tell your doctor or get medical help right away if you get any of following symptoms of an allergic reaction:
 - swelling of your face, eyes, or mouth
 - trouble breathing or wheezing
 - throat tightness
 - chest pain or tightness
 - feeling dizzy or faint
 - rash or peeling of your skin
- **Swelling (edema).** Fluid may collect in your hands and feet and in various tissues of your body, including in the sac around your heart or lungs. Call your doctor if you have trouble breathing.
- **Poor wound healing.** Sirolimus may cause your wounds to heal slowly or not heal well. Tell your doctor if you have any redness or drainage, your wound does not heal, or the wound opens up.
- **Increased levels of cholesterol and triglycerides (lipids or fat) in your blood.** Your doctor should do blood tests to check your lipids during treatment with sirolimus. Your doctor may prescribe treatment with diet, exercise, or medicine if your lipid levels are too high. During treatment with sirolimus, your blood levels of cholesterol and triglycerides may remain high even if you follow your prescribed treatment plan.
- **Effects on kidney function.** When sirolimus is taken with cyclosporine (Gengraf, Neoral, Sandimmune), the function of your transplanted kidney may be affected. Your doctor should regularly do tests to check your kidney function while you are taking sirolimus with cyclosporine (Gengraf, Neoral, Sandimmune).
- **Increased protein in your urine.** Your doctor may regularly test your urine protein.

- **Increased risk for viral infections.**
- Certain viruses can live in your body and cause active infections when your immune system is weak. BK virus can affect how your kidney works and cause your transplanted kidney to fail.
- A certain virus can cause a rare serious brain infection called Progressive Multifocal Leukoencephalopathy (PML). PML usually causes death or severe disability. Call your doctor right away if you notice any new or worsening medical problems such as:

- confusion
 - sudden change in thinking, walking, strength on one side of your body
 - other problems that have lasted over several days.
- **Lung or breathing problems.** This can sometimes lead to death. Tell your doctor if you have a new or worsening cough, shortness of breath, difficulty breathing or any new breathing problems. Your doctor may need to stop sirolimus or lower your dose.
 - **Blood clotting problems.** When sirolimus is taken with cyclosporine or tacrolimus, you may develop a blood clotting problem. Tell your doctor if you get any unexplained bleeding or bruising.

The most common side effects of sirolimus in people with renal transplant include:

- high blood pressure
- pain (including stomach and joint pain)
- diarrhea
- headache
- fever
- urinary tract infection
- low red blood cell count (anemia)
- nausea
- low platelet count (cells that help blood to clot)
- high blood sugar (diabetes)

Tell your doctor if you have any side effect that bothers you or that does not go away.

These are not all of the possible side effects of sirolimus. For more information ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1- 800-FDA-1088.

How should I store Sirolimus Oral Solution?

- Store bottles of Sirolimus Oral Solution in the refrigerator between 36°F to 46°F (2°C to 8°C).
- Protect from light.
- If necessary, bottles of Sirolimus Oral Solution can be stored at room temperature up to 77°F (25°C) for up to 15 days.
- When a bottle of Sirolimus Oral Solution is opened, it should be used within 1 month.
- Use any diluted Sirolimus Oral Solution right away.

Do not use Sirolimus Oral Solution after the expiration date, which is located on the carton. The expiration date refers to the last day of that month.

Safely throw away medicine that is out of date or no longer needed.

Keep Sirolimus Oral Solution and all medicines out of the reach of children.

General Information about the safe and effective use of Sirolimus Oral Solution.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use Sirolimus Oral Solution for a condition for which it was not prescribed. Do not give Sirolimus Oral Solution to other people even if they have the same symptoms that you have. It may harm them.

This Medication Guide summarizes the most important information about Sirolimus Oral Solution. If you would like more information talk to your doctor. You can ask your pharmacist or doctor for information about Sirolimus Oral Solution that is written for health professionals.

What are the ingredients in Sirolimus Oral Solution?

Active ingredients: Sirolimus

Inactive ingredients: Phosal® 50 PG (alcohol, ascorbyl palmitate, phosphatidylcholine, propylene glycol, soy acid, soy lecithin sunflower seed oil glyceride, and tocopherol) and polysorbate 80. Sirolimus Oral Solution contains 1.5% - 2.5% ethanol.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

INSTRUCTIONS FOR USE

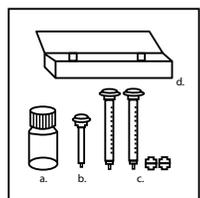
Sirolimus (sir-OH-li-mus) Oral Solution

Be sure that you read and understand the following instructions for the correct way to dilute and take Sirolimus Oral Solution. Ask your pharmacist or doctor if you are not sure.

Important:

- Always keep the bottle in an upright position.
- You may store Sirolimus Oral Solution that is in a syringe at room temperature up to 77°F (25°C) or in the refrigerator at 36°F to 46°F (2°C to 8°C) for up to 24 hours. See “How should I store Sirolimus Oral Solution?” at the end of these Instructions for Use.
- Sirolimus Oral Solution can develop a slight haze when it is refrigerated. If this happens, bring the Sirolimus Oral Solution to room temperature and then gently shake the bottle until the haze goes away.
- Only use a glass or plastic cup to dilute Sirolimus Oral Solution.
- If you are a caregiver, do not let Sirolimus Oral Solution come in contact with your skin or eyes. If you get the oral solution on your skin, wash the area well with soap and water. If you get the oral solution in your eyes, rinse with plain water.
- If you spill Sirolimus Oral Solution, dry the area with a dry paper towel and then wipe the area with a wet paper towel. Throw away the paper towels in the trash and wash your hands well with soap and water.

Each Sirolimus Oral Solution carton contains:



- a) a 2 oz. (60 mL fill) amber glass bottle of sirolimus (concentration of 1 mg/mL)
- b) 1 oral syringe adapter for fitting into the neck of the bottle
- c) enough disposable amber oral syringes and caps for daily dosing
- d) 1 carrying case

You will also need:

- glass or plastic cup
- 6 oz. of water or orange juice only.

Figure 1: Opening the bottle

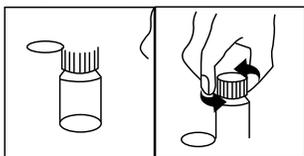


Figure 2: Inserting adapter

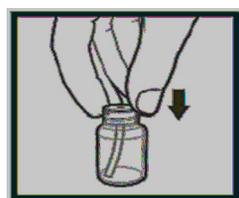


Figure 3: Inserting syringe

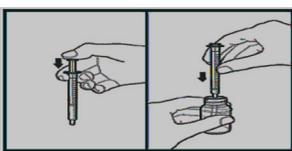


Figure 4: Withdrawing solution

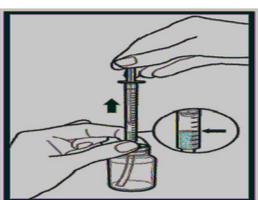


Figure 5: Capping syringe

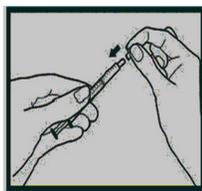


Figure 6: Placing syringe in carrying case

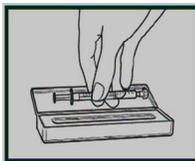
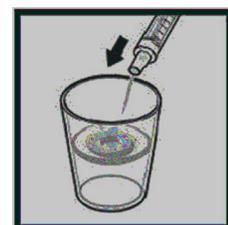


Figure 7: Emptying syringe into glass



5. If your doctor tells you to carry your medicine with you:

- If you need to carry your Sirolimus Oral Solution in a filled syringe, place a cap securely on each syringe. The cap should snap into place (Figure 5).

- Place the capped syringe in the enclosed carrying case (Figure 6). If you need more than 1 carrying case, talk with your doctor or pharmacist.

6. Taking a dose of Sirolimus Oral Solution:

- Choose a clean flat work surface. Place a clean paper towel on the work surface. Wash and dry your hands.
 - Empty the syringe into a glass or plastic cup containing at least 2 ounces (1/4 cup, 60 mL) of water or orange juice, stir vigorously for 1 minute and drink right away (Figure 7).
 - If more than 1 syringe is needed for your prescribed dose, empty the oral solution from each syringe into the same glass or plastic cup of water or orange juice.
 - Refill the container with at least 4 ounces (1/2 cup, 120 mL) of water or orange juice, stir vigorously again and drink the rinse solution. Do not mix Sirolimus Oral Solution with apple juice, grapefruit juice, or other liquids. Only glass or plastic cups should be used to mix Sirolimus Oral Solution.
 - The syringe and cap should be used only one time and then thrown away.
 - Throw away the paper towel and clean the work surface. Wash your hands.
7. Always store the bottles of medication in the refrigerator.

How should I store Sirolimus Oral Solution?

- Store bottles of Sirolimus Oral Solution in the refrigerator at 36°F to 46°F (2°C to 8°C).
- Protect from light.
- Store Sirolimus Oral Solution that is in a syringe at room temperature up to 77°F (25°C) or in the refrigerator at 36°F to 46°F (2°C to 8°C) for up to 24 hours.
- If necessary, bottles of Sirolimus Oral Solution can be stored at room temperature up to 77°F (25°C) for up to 15 days.
- When a bottle of Sirolimus Oral Solution is opened, it should be used within 1 month.
- Use any diluted Sirolimus Oral Solution right away.

Keep Sirolimus Oral Solution and all medicines out of the reach of children.

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

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