



Great Ormond Street Hospital for Children NHS Foundation Trust

Oral sirolimus to treat vascular problems: information for families

This information sheet from Great Ormond Street Hospital (GOSH) provides information about sirolimus (also known as rapamycin) oral solution and tablets, how it is given and some of the possible side effects. Each person reacts differently to medicines, so your child will not necessarily suffer every side effect mentioned.

This information sheet describes how sirolimus is used to treat vascular problems – for use in other specialties, please see our other information sheets. If you have any questions or concerns, please ask your doctor, nurse or pharmacist or telephone one of the contact numbers on the information sheet.

What is sirolimus?

Sirolimus (also known as rapamycin) is an immunosuppressant medicine, which dampens down the immune system. It is most commonly used following kidney transplant to prevent the new kidney being rejected by the body.

Sirolimus is also used for certain vascular conditions such as vascular tumours and malformations which may be associated with overgrowth of body tissues. It acts by interfering with a specific pathway in the body involved in the growth of cells and blood vessels.

Sirolimus is not a curative treatment but can help with some of the issues associated with the condition such as pain, reduced mobility, pain or stiffness, recurrent infections, abnormal clotting and organ dysfunction.

Oral sirolimus comes as an oral solution and in tablets. The oral solution contains 1mg of sirolimus in 1mL (1mg/mL). The sirolimus oral solution contains a small amount of alcohol but

the benefits of using sirolimus have been deemed by your doctor to outweigh any risk. The tablets come in 0.5mg, 1mg or 2mg tablets and also contain sucrose and lactose.

Sirolimus is 'unlicensed' for use in children with these conditions. You can be assured that your doctor has only prescribed an 'unlicensed' medicine because they think that the medicine will benefit your child and no licensed alternative is available.

How is sirolimus given?

Oral solution

Sirolimus oral solution comes in a bottle and is a yellow colour. It needs to be stored in the fridge and will last for 30 days once opened. The oral solution sometimes develops a hazy appearance but this is not harmful and will disappear when the bottle is brought up to room temperature.

The dose of sirolimus should be given consistently, either with food or without food, to ensure that the same amount of active ingredient is absorbed by the body with every dose.

The manufacturer recommends that each dose be diluted – instructions are given below. Please discuss the volume of water or orange juice to be used with your doctor. However if your child cannot tolerate this volume, it can be given undiluted but the thickness and taste of the medicine can make it difficult to give. If given undiluted, we recommend giving your child a drink of water afterwards to reduce the risk of mouth ulcers.

If you are diluting the medicine, you will need:

- The bottle of sirolimus 1mg/1ml oral solution
 - Syringe adapter
 - Oral syringe with dose marked on it
 - Glass or plastic cup
 - Water or orange juice – do not use any other liquid to mix the dose
1. Wash your hands with soap and water
 2. Shake the bottle and remove the top and put to one side
 3. Insert the syringe adapter into the top of the bottle – leave this in the bottle when you have given the dose
 4. Draw up the dose of sirolimus in the syringe provided
 5. Pour half the volume of water or orange juice into a glass or plastic cup
 6. Empty the syringe into the water or orange juice and mix thoroughly
 7. Give to your child to drink
 8. Add the rest of the volume of water or orange juice to the cup and mix thoroughly to pick up any remaining sirolimus oral solution
 9. Give it to your child to drink
 10. Put the top back on the bottle

Tablets

A combination of different strengths of tablets may be needed to achieve the correct dose. Therefore your doctor will discuss this with you when you start treatment and each time the dose is adjusted. It is important to note that taking multiples of 0.5 mg tablets should not be used as a substitute for 1 mg or other strength tablets as the absorption rate is different.

Who should not use sirolimus?

- Babies less than four weeks old
- Hypersensitivity to sirolimus or any of its ingredients – it is not suitable for people allergic to soya or peanuts
- Pregnant, could be pregnant, planning to become pregnant or breastfeeding
- Existing liver problems
- Low immune system

How is sirolimus monitored?

Several tests need to be carried out both before starting and while on treatment. These help your doctor work out if it is both safe to start and continue treatment. Some tests also provide your doctor with baseline information so that they can later assess if the treatment is working.

Blood tests

Children have the following tests before starting sirolimus:

- Urea and electrolytes
- Liver function
- Full blood count
- Clotting profile
- Fasting cholesterol and triglycerides
- Immunoglobulins
- Immune response to certain vaccines such as tetanus, pneumococcus, measles
- Immunity to chicken pox
- Tests for certain viruses such as HIV, hepatitis B and C, CMV and EBV

If any of these results are abnormal, your doctor will discuss what needs to be done.

Once treatment has been started, the following blood tests will be needed:

- Sirolimus level
- Urea and electrolytes
- Liver function
- Full blood counts
- Clotting profile
- Fasting cholesterol and triglycerides

The sirolimus level needs to be taken just before the dose is due to be given. Therefore levels are usually checked in the morning and your doctor will ask you NOT to give the dose of sirolimus that morning until after the bloods have been taken. As fasting cholesterol and triglyceride levels need to be checked, your child should not have anything to eat or drink from midnight before the blood test.

Blood tests will be need to be repeated every seven days until the dose of sirolimus has been adjusted for your child. After this, tests will be required monthly and then three monthly. If the dose or formulation changes, these blood tests will need to be repeated seven days after the change has been introduced. Your doctor will explain this to you in more detail.

Scans

Before starting sirolimus, your child may need an MRI of the area affected by their condition (usually with injected contrast) and a whole body MRI. This provides your doctor with more information and acts as a baseline before starting treatment. A repeat MRI scan may be needed approximately one year after starting treatment but this will again be discussed by your doctor.

What are the side effects?

Possible fever, headache, fatigue, stomach pain, diarrhoea, constipation, nausea, low red blood cells, low blood platelets, increased fat in the blood (cholesterol and/or triglycerides), low blood potassium, low blood phosphorus, slow healing, rapid heart rate, mouth sores, fluid collection in the abdomen, kidney problems, protein in the urine, reduced number of infection-fighting cells in the blood (white blood cells), abnormal tests of liver function, rash.

Sirolimus can reduce the body's own defence mechanisms and consequently the body will not be as good at fighting infections. So, infections can occur more often than usual, including infections of the skin, mouth, stomach and intestines, lungs and urinary tract. If your child develops an infection while taking sirolimus, please let your doctor know and they will give you advice on whether treatment needs to be paused or can be continued.

Uncommon: Fluid collection in the sac around the heart, inflammation of the pancreas, blood clots, cancer of the lymph tissue (lymphoma), bleeding from the lung.

Rare: Protein build-up in the air sacs of the lungs that may interfere with breathing, too much fluid collecting in the tissues due to irregular lymph function, serious allergic reactions

As with all medications, there can be allergic reactions. Signs of a mild allergic reaction include skin rashes and itching, high temperature, shivering, redness of the face, a feeling of dizziness or a headache. If you see any of these signs, please report them to a doctor or nurse.

Signs of a severe allergic reaction include any of the above, as well as shortness of breath or chest pain. If you are in hospital and your child shows signs of a severe allergic reaction, call a doctor or nurse immediately. If you are at home and your child shows signs of a severe allergic reaction, call

an ambulance immediately. If your child has a severe reaction to sirolimus the subsequent treatment will probably be changed.

Sirolimus and interactions with other medicines

Some medicines can react with sirolimus, altering how well it works. Always check with your doctor or pharmacist before giving your child any other medicine, including medicines on prescription from your family doctor (GP), medicines bought from a pharmacy (chemist) or any herbal or complementary medicines.

The following medicines are known to react with sirolimus:

- Other immunosuppressant medicines
- Certain antibiotics or antifungal medicines
- Anti-hypertension medicines
- Anti-epilepsy medicines
- Certain anti-ulcer medicines

Sirolimus reacts with grapefruit so should never be mixed with grapefruit juice drinks and grapefruit should not be eaten during treatment with sirolimus.

Important information

- Keep medicines in a safe place where children cannot reach them.
- Sirolimus oral solution should be kept in its original packaging in the refrigerator. When you have drawn a dose up into the oral syringe, this can be stored at room

Useful numbers

- GOSH switchboard: 020 7405 9200
- Pharmacy Medicines Information: 020 7829 8608 – Monday to Friday from 9am to 5pm
- Vascular Clinical Nurse Specialist: ext 1113 or email vascularanomalynurses@gosh.nhs.uk
- Out of hours: 020 7405 9200 and ask for the on call doctor for Dermatology

- temperature for up to 24 hours. When it is mixed with water or orange juice, you should give it to your child immediately.
- If your child vomits immediately after a dose of sirolimus, repeat the dose. Otherwise do not give a second dose. Please ring your doctor or nurse to inform them and for further advice.
- Your child should NOT have any live vaccinations such as MMR, oral polio, oral typhoid, rotavirus, chicken pox, nasal flu vaccine or BCG while taking sirolimus. Inactivated or killed vaccines such as the influenza/flu (injection ONLY), meningitis C, pneumococcal, hepatitis, Hib, tetanus, diphtheria, whooping cough/pertussis and the killed version of the polio immunisation are permitted. If you have other children who need vaccines while your child is taking sirolimus, they should have these as normal, but they should also receive the 'killed' or inactivated vaccine. If you have any questions about vaccines and immunisations, please ask your doctor.
- Due to an increased risk of skin cancer, exposure to sunlight and UV light should be limited by covering the skin with clothing and using sunscreen with a high protection factor.
- If your doctor decides to stop treatment with sirolimus, please return any unused oral solution to the pharmacist. Do not flush it down the toilet or throw it away.

Disclaimer

Please read this information sheet from GOSH alongside the patient information leaflet (PIL) provided by the manufacturer. If you do not have a copy of the manufacturer's patient information leaflet please talk to your pharmacist. A few products do not have a marketing authorisation (licence) as a medicine and therefore there is no PIL.

For children in particular, there may be conflicts of information between the manufacturer's patient information leaflet (PIL) and guidance provided by GOSH and other healthcare providers. For example, some manufacturers may recommend, in the patient information leaflet, that a medicine is not given to children aged under 12 years. In most cases, this is because the manufacturer will recruit adults to clinical trials in the first instance and therefore the initial marketing authorisation (licence) only covers adults and older children.

For new medicines, the manufacturer then has to recruit children and newborns into trials (unless the medicine is not going to be used in children and newborns) and subsequently amend the PIL with the approved information. Older medicines may have been used effectively for many years in children without problems but the manufacturer has not been required to collect data and amend the licence. This does not mean that it is unsafe for children and young people to be prescribed such a medicine 'off-licence/off-label'. However, if you are concerned about any conflicts of information, please discuss with your doctor, nurse or pharmacist.