Sirolimus 1mg/1ml oral solution to treat congenital hyperinsulinism (CHI): information for families

This information sheet from Great Ormond Street Hospital (GOSH) explains about sirolimus (also known as rapamycin) oral solution, 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.

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.

Sirolimus (also known as rapamycin) is an immunosuppressant medicine, which damps down the immune system. It is most commonly used following kidney transplant to prevent the new kidney being rejected by the body. However it is now being used for other medical conditions.

It is also used to treat congenital hyperinsulinism (CHI), which is characterized by inappropriate and unregulated insulin secretion from the beta-cells of the pancreas. In CHI the beta-cells release insulin inappropriately all the time and insulin secretion is not regulated by the blood glucose level (as occurs normally). Sirolimus appears to act against the beta-cells, reducing the release of insulin and stopping the beta-cells multiplying.

Sirolimus is used in children with diffuse CHI and who are unresponsive to both high doses of diazoxide and octreotide and would otherwise need a major operation to remove the whole pancreas.

Sirolimus oral solution comes in a strength of 1mg/1ml - that is 1ml of liquid contains 1mg of the active ingredient.

Sirolimus is ‘unlicensed’ for use in children and the use of sirolimus for CHI is also outside of its product licence. 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. Sirolimus also contains a small amount of alcohol but the benefits of using sirolimus outweigh any risk.

How is sirolimus given?

Sirolimus 1mg/1ml oral solution comes in a bottle and is a yellow colour. The oral solution sometimes develops a hazy appearance. 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 use 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.

Diluting the dose

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

What to do

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 of 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 to your child to drink
10. Put the top back on the bottle

Dispose of the used syringe as you have been taught and wash the cup in warm, soapy water. If you need to give the dose later in the day, you can store the filled syringe for up to 24 hours at room temperature. When it is mixed with water or orange juice, you should give it to your child immediately.

Who should not use sirolimus?

People with the following conditions should discuss using sirolimus with their doctor:

- Babies born at full term but aged 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

Children have baseline blood tests (including urea and electrolytes, liver function, thyroid function, full blood counts, fasting cholesterol and triglycerides) before starting treatment with sirolimus and then at regular intervals during treatment.

Sirolimus blood level will be regularly monitored usually every four weeks. If the dose or formulation changes, this should be repeated seven days after the change has been introduced.

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 (if your child has a high blood sugar level), 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 be caught more often than usual, such as infections of the skin, mouth, stomach and intestines, lungs and urinary tract.

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 (including Sunny Delight®) or grapefruit should not be eaten during treatment with sirolimus.

Important

- 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 syringe, this can be stored at room 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, chicken pox or BCG while taking sirolimus. Inactivated or killed vaccines such as influenza/flu, 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 polio vaccine. If you have any questions about vaccines and immunisations, please ask your doctor.
- Exposure to sunlight and UV light should be limited by covering the skin with clothing and using sunscreen with a high protection factor due to an increased risk of skin cancer.

- If your doctor decides to stop treatment with sirolimus, return any unused oral solution to the pharmacist. Do not flush it down the toilet or throw it away.

Useful numbers

- GOSH switchboard: 020 7405 9200
- Pharmacy Medicines Information: 020 7829 8608 – Monday to Friday from 9am to 5pm
- Congenital Nurse Specialists for Hyperinsulinism: ext 0360 or bleep 1016
- Out of hours: 020 7405 9200 and ask for the on call doctor for endocrinology

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.