



Early Access to Medicines Scheme – Treatment protocol – Information for patients

Introduction

The aim of the Early Access to Medicines Scheme (EAMS) is to provide earlier availability of promising new unlicensed medicines (medicines that do not have a marketing authorisation or are used outside their licence) to UK patients that have a high unmet clinical need. The medicines included in the scheme after they have received a positive scientific opinion are those that are intended to treat, diagnose or prevent seriously debilitating or life-threatening conditions where there are no adequate treatment options. More information about the scheme can be found here:

<https://www.gov.uk/guidance/apply-for-the-early-access-to-medicines-scheme-eams>

The information below is intended for you, the patient, and is provided by the pharmaceutical company (called scientific opinion holder) that manufactures the EAMS medicine. This medicine, which does not yet have a drug licence or is used outside its licence, may also be used in combination with other medicines. More information about medicines licensing can be found here:

<http://www.nhs.uk/conditions/medicines-information>

This medicine can be prescribed for individual patients to meet specific needs provided they are given sufficient information about the medicine to make an informed decision. Your physician will be responsible for giving you all the information you need to make this decision and for obtaining informed consent from you prior to treatment. You will be asked to sign a form to confirm that you are providing informed consent to receiving the EAMS treatment. Information on consent can be found here:

<https://www.nhs.uk/conditions/Consent-to-treatment>

The information below is provided to help you decide with your physician on whether to use the EAMS medicine and helps explain how to use it in accordance with the pharmaceutical company's instructions for safe and proper use. A positive scientific opinion is not a recommendation for use of the medicine and should not be interpreted as such. Under EAMS, the risk and legal responsibility for prescribing the medicine remains with the physician, and the opinion and EAMS documentation published by the MHRA are intended only to inform physicians' decision making and not to recommend use. An EAMS scientific opinion does not affect the civil liability of the manufacturer or any physician in relation to the product.

The information below may change during the time you are using the medicine if more data become available. Your physician will highlight to you any changes that you need to be aware of.

Whilst you are using this medicine, data will be collected on the use and safety profile of the medicine, to ensure that the benefits of taking the medicine continue to outweigh any potential risks. Your physician will answer all your questions during and after the treatment and will provide you with contact details that you should use in case of any events or problems.

Each patient enrolled in the scheme will continue to receive the EAMS product until the end of the treatment in line with prescribing and NHS guidance and as long as benefit is seen. In rare cases where the EAMS treatment may not be available anymore, your physician will discuss other options with you.

Information for the patient

Triheptanoin 0.96 g/mL oral liquid

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What triheptanoin is and what it is used for
2. What you need to know before you are given triheptanoin
3. How triheptanoin is given
4. Possible side effects
5. How to store triheptanoin
6. Contents of the pack and other information

1. What triheptanoin is and what it is used for

What triheptanoin is

Triheptanoin is a liquid taken by mouth or feeding tube.

What triheptanoin is used for

Triheptanoin is used to treat long-chain fatty acid oxidation disorders (LC-FAOD), a group of rare inherited disorders, in adults and children of all ages.

Patients with LC-FAOD may have difficulty producing enough energy because of their body's inability to use long-chain fatty acids as an energy source. This can put patients at risk for medical emergencies, especially during times of illness, fasting, or prolonged exercise.

How triheptanoin works

Triheptanoin enters the body's cells where it is broken down for energy. This helps prevent energy crises that can cause muscle breakdown (rhabdomyolysis), heart muscle damage (cardiomyopathy), and low blood sugar (hypoglycaemia).

Triheptanoin must be taken as part of a carefully controlled diet and is meant to be taken long-term.

2. What you need to know before you are given triheptanoin

You must not be given triheptanoin if:

- you are allergic to triheptanoin

Do not take triheptanoin if this applies to you.

Warnings and precautions

Talk to your doctor or nurse before taking triheptanoin.

- If you have **pancreas problems**, speak to your doctor or nurse as it may affect how well triheptanoin works.
- If you are **allergic to polyethylene or polypropylene** (types of plastic), do not use the measuring syringe and press-in bottle adaptor given in this pack. Ask your doctor or nurse about another way to measure your dose.

Tell your doctor or nurse if any of the above apply to you.

Feeding tubes

Feeding tubes may not work as well or may stop working over time when taking triheptanoin.

- **Do not use** triheptanoin in feeding tubes made of polyvinyl chloride (PVC).
- Check the feeding tube regularly to make sure it is working properly and not breaking down.

Children and adolescents

Triheptanoin may be used in adults and children of all ages.

Other medicines and triheptanoin

Tell your doctor or nurse about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

In particular, tell your doctor or nurse if you are taking a pancreatic lipase inhibitor - such as orlistat. This is because it may affect how well triheptanoin works.

The effects of combining medium-chain triglyceride (MCT) medicines and triheptanoin are not known. If you are currently taking another MCT, consult your health care provider before starting triheptanoin.

Contraception, pregnancy and breast-feeding

If you are pregnant, think you may be pregnant, or are planning to have a baby, ask your doctor or nurse for advice before taking this medicine. We do not know if triheptanoin will harm your unborn baby.

Tell your doctor or nurse if you are breastfeeding or plan to breastfeed. We do not know if triheptanoin passes into breast milk. Talk to your doctor or nurse about the best way to feed your baby if you take triheptanoin.

Driving, cycling and using machines

Triheptanoin is not likely to affect your ability to drive, cycle or use any machines.

3. How triheptanoin is given

Always take this medicine exactly as your doctor or nurse has told you. Check with your doctor or nurse if you are not sure.

Other MCT medicines

The effects of combining MCT medicines and triheptanoin are not known. If you are currently taking another MCT medicine, consult your health care provider before starting triheptanoin.

How much triheptanoin is given

Your doctor or nurse will tell you how much medicine you need to take each day. Your daily dose will depend on how much energy (how many calories) you need to get from food.

Take triheptanoin at least 4 times a day, as instructed by your doctor or nurse. You may start on a low dose of triheptanoin and slowly increase your dose to help avoid side effects. Ask your doctor or nurse to show you how to measure your dose.

Your doctor or nurse should advise you on how to maintain a proper diet when taking triheptanoin.

Taking triheptanoin with food

Take each dose with meals or snacks, and always mix well with soft food, a drink, medical food, or formula before taking.

If you take triheptanoin by mouth, mix well with soft food or drink such as:

- plain or artificially sweetened fat-free yogurt
- fat-free milk, formula, or cottage cheese
- whole grain hot porridge
- fat-free low-carbohydrate custard, smoothies, applesauce, or baby food

If you give triheptanoin by feeding tube, mix well with medical food or formula.

Important information about containers used to mix and give triheptanoin

Triheptanoin can gradually break down some types of plastics. Use the compatible measuring syringe provided with this medicine to measure your prescribed dose. Check the materials used to give triheptanoin regularly to make sure they are working properly and not breaking down.

When mixing triheptanoin with food, drink, or formula:

- Do not mix or give this medicine using containers or syringes made of polystyrene (a type of plastic that can be solid or foam) or polyvinyl chloride (PVC), a solid plastic material.

- Mix or give this medicine using containers or syringes made of materials such as stainless steel, glass, or high-density polyethylene (HDPE), polypropylene, low-density polyethylene, polyurethane, and silicone (types of plastic materials).
- After use, rinse materials and containers well with cold water and wipe dry. Clean the measuring syringe as described in the cleaning instructions below.

Preparing the dose

Preparing the bottle

Inserting the press-in bottle adaptor into the bottle

The box contains a press-in bottle adaptor that allows withdrawal of the correct dose without having to plunge a syringe into the medicine bottle or turn it upside down.

When opening the bottle for the first time, make sure the top of the bottle is clean with no traces of the seal remaining. Insert the press-in bottle adaptor in the bottle neck until the adaptor is flush with the top of the bottle, as shown in Figure 1.

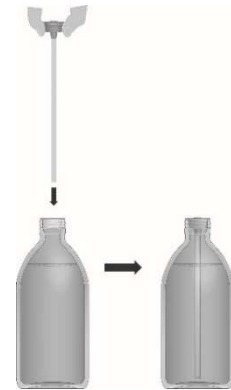


Figure 1

When you have finished, close the bottle without removing the bottle adaptor. Store the medicine upright where it is out of reach of children.

The press-in bottle adaptor does not stop leaks if the bottle is turned upside down.

Measuring the dose

Use the measuring syringe provided with this medicine to measure your dose.

Dosing with the use of the measuring syringe

1. Check the syringe is clean, dry, and that the measurement lines are readable before each use.
2. Remove the cap from the medicine bottle and check the press-in bottle adaptor is inside - put the adaptor into the bottle neck if it is not already in, as shown in Figure 1.
3. With the bottle placed upright on a flat surface, put the tip of the syringe into the press-in bottle adaptor, as shown in Figure 2.
4. Draw up the medicine and completely fill the syringe. Then push the liquid back out of the syringe, through the adaptor into the bottle. Repeat this step as many times as needed so that there are no air bubbles in the syringe.
5. To start measuring the dose, first make sure the plunger is pressed down all the way to the bottom of the barrel, as shown in Figure 3.
6. Slowly pull the plunger up, as shown in Figure 4, to measure the dose volume by lining up the black ring of the plunger with the right dose mark on the scale, see Figure 5. The plunger may rise back up the barrel on the first dosage, so make sure that the plunger is kept in position until the syringe is taken out of the bottle.
7. Remove the syringe from the press-in bottle adaptor.

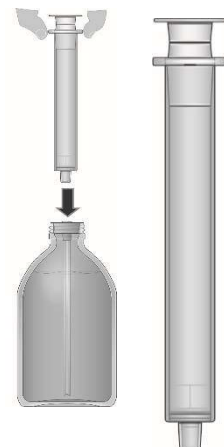


Figure 2

Figure 3

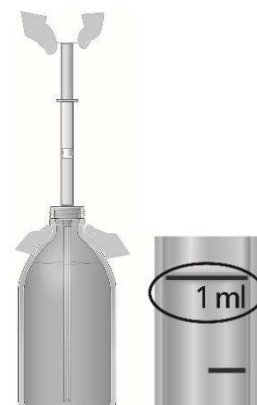


Figure 4

Figure 5

8. Add all of the dose to the food, drink, or formula by pressing the plunger down slowly. See 'Taking triheptanoin by mouth' or 'Giving triheptanoin by feeding tube' for mixing instructions.

If the amount of medicine the syringe can withdraw is smaller than the prescribed dose, repeat these steps using the same syringe to get the full dose.

9. Clean the syringe following the cleaning instructions below.
10. Place the syringe and the bottle in the original box and store the medicine upright and out of reach of children.

Check the syringe often to make sure it is working properly and is not breaking down. The syringe is intended to be used for a maximum of 60 doses. Throw away the syringe once it has been used for 60 doses.

Cleaning the measuring syringe

After each use:

1. Rinse the syringe with cold water - draw up water into the syringe and eject it again. Do this a few times, without separating the plunger from the barrel.
 2. Dry the syringe.
 3. Return the syringe to the box after cleaning.
- Do not wash by domestic hot sterilisation like a bottle steriliser (plastic parts may melt).
 - Do not wash in the dishwasher.
 - Do not heat the syringe in a microwave oven regardless of whether it contains any medicine.

Precautions

Do not allow children to use the syringe unsupervised.

When using the syringe:

- Use it at room temperature.
- It must be clean before use.
- It should only be in contact with the medicine for the time required to measure the dose needed.
- Do not twist the syringe when you are taking medicine from the bottle or giving it.

The syringe should only be used to give this medicine.

The measuring syringe and press-in bottle adaptor should only be used for taking the medicine provided in the same box. Please throw them away once the triheptanoin bottle is finished.

Taking triheptanoin by mouth

Check the items used to take triheptanoin often to make sure they are working properly and are not breaking down.

1. Use the measuring syringe provided with this medicine to measure the prescribed amount of triheptanoin from the bottle (see **Measuring the dose** above).
2. Add the prescribed amount of triheptanoin to a clean bowl, cup, or container, made of the materials listed above, with the amount of soft food or drink instructed by your doctor or nurse.
3. Mix triheptanoin well into the soft food or liquid and swallow the mixture.
 - **Do not** take triheptanoin on its own to avoid an upset stomach.

You can store any unused triheptanoin mixture for up to 24 hours in the refrigerator.

- **Do not** save the medicine for longer than 24 hours.

- If not used within 24 hours, throw away the medicine mixture in your household waste. **Do not** pour down the sink.

Giving triheptanoin by feeding tube

You can give triheptanoin by feeding tube. Check the feeding tube and other items used to give triheptanoin often to make sure they are working properly and are not breaking down. Mix triheptanoin well into medical food or formula before giving by a feeding tube, y-connector, or feeding tube extension set.

- **Only** give triheptanoin in a feeding tube made of silicone or polyurethane.
 - **Do not** give triheptanoin in a feeding tube made of polyvinyl chloride (PVC), a type of plastic.
 - **Do not** give triheptanoin on its own, to avoid an upset stomach and to avoid breakdown of the feeding tube.
 - **Do not** add triheptanoin to the feeding bag because the feeding equipment may break down over time.
1. Use the measuring syringe provided with this medicine to measure the prescribed amount of triheptanoin from the bottle (see **Measuring the dose** above).
 2. Add the prescribed amount of triheptanoin to a clean bowl, cup, or container with the amount of medical food or formula instructed by your doctor or nurse.
 3. Mix triheptanoin well into the medical food or formula and draw up the entire amount of the mixture into a separate slip tip syringe (used for the feeding tube - not provided in the triheptanoin pack).
 4. Remove the air from the syringe and connect the syringe directly into the feeding tube port.
 5. Push the contents of the syringe (triheptanoin mixture) into the feeding tube port using steady pressure until empty.
 6. Draw up between 5 mL to 30 mL of water with the slip tip syringe and flush the feeding tube port with the water.
 7. Throw away any unused triheptanoin mixture in your household waste. **Do not** pour down the sink. **Do not** save for later use.

If you take more triheptanoin than you should

Tell your doctor or nurse if you have taken more triheptanoin than what was prescribed to you.

If you miss a dose of triheptanoin

If you miss a dose, take the next dose as soon as possible.

- Do not take a double dose at one meal to make up for a missed dose.
- Take the next doses 3 to 4 hours apart.

If it is not possible to take all the doses for the day, skip the missed dose.

If you stop taking triheptanoin

Taking triheptanoin is important for the management of your disease. Talk to your doctor or nurse before stopping triheptanoin.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The following side effects have been reported with this medicine:

Serious side effects

If you experience any serious side effects, stop taking this medicine and tell your doctor immediately.

Tell your doctor straight away if you notice any of the following side effects – your doctor may need to adjust your dose:

Very common: (may affect more than 1 in 10 people):

- stomach pain
- diarrhoea (loose stools)
- vomiting

Common: (may affect up to 1 in 10 people):

- feeling sick (nausea)

If you notice any of the side effects listed above, tell your doctor straight away.

Reporting of side effects

If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. They will report side effects using the Triheptanoin EAMS Adverse Event Report Form, which they received when registering for the EAMS scheme. If you become pregnant while on the EAMS scheme (from the start of your first dose of triheptanoin), your doctor or nurse will also report this using the Triheptanoin EAMS Pregnancy Notification Form.

If your side effects might be related to any other medicines that you are taking whilst in the EAMS program, your doctor or nurse will also report them to the MHRA via the Yellow Card scheme. You can also report side effects directly via:

Yellow Card Scheme

Website: <https://yellowcard.mhra.gov.uk> or search for MHRA Yellow Card in the Google Play or Apple App Store.

By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store triheptanoin

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date that is stated on the bottle and carton after EXP. The expiry date refers to the last day of that month.

There are no special storage conditions. Do not freeze.

Triheptanoin can be used for up to 9 months after opening but not beyond the expiry date on the bottle.

Discard any unused triheptanoin mixture in the household waste. Do not pour down the sink.

6. Contents of the pack and other information

What triheptanoin contains

Triheptanoin is made of 100% triheptanoin and contains no other ingredients.

What triheptanoin looks like and contents of the pack

Triheptanoin is a clear, colourless to light yellow oral liquid. It is supplied in a 500 mL bottle containing 0.96 g/mL triheptanoin along with one low-density polyethylene (LDPE) press-in bottle adaptor and two 10 mL polypropylene measuring syringes.

Scientific Opinion Holder

Ultragenyx Netherlands B.V.
Evert Van De Beekstraat 1, Unit 104
1118 CL, Schiphol
Netherlands

Manufacturer

Almac Clinical Services Limited
Seagoe Industrial Estate
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United Kingdom

For any information about this medicine, please contact the local representative of the Scientific Opinion Holder:

Ultragenyx Netherlands B.V.
Tel: +31 800 2300663

This protocol was revised in <month YYYY>.

EAMS number: 41104/0001

Additional information

Informed Consent Form

The Early Access to Medicines Scheme (EAMS) will be explained to you by your doctor using the information contained in this leaflet and the EAMS consent form. You will be asked to sign this form and a copy will be given to you to keep.

Patient data to be collected

Patient data collected during the scheme are mostly used for safety surveillance and cannot replace a proper clinical trial to support a marketing authorisation. These data are required by the MHRA to help verify that the patient's condition complies with the EAMS indication and help interpret the side effects and other events occurring during and after the EAMS treatment. These data include your age and gender, details about your disease (LC-FAOD), medical history including hospitalizations in the past 18 months, triheptanoin dose, details of any other medicines you are taking for any medical reason, and side effects from the EAMS treatment.

Contact information

Contact details for medical information
Ultragenyx Netherlands B.V.
Tel: +31 800 2300663

Contact information for safety reporting
Adverse events must be reported to: ultragenyx@primevigilance.com
Adverse events must also be reported via Yellow Card to: <https://yellowcard.mhra.gov.uk>