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) to UK patients that have a high unmet clinical need. The medicines included in the scheme 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: http://www.mhra.gov.uk/Howweregulate/Innovation/EarlyaccesstomedicinesschemeEAMS/index.htm

The information below is intended for you, the patient, and is provided by the pharmaceutical company that manufactures the medicine. This medicine does not yet have a drug licence (also called a marketing authorisation). More information about medicines licensing can be found here: http://www.mhra.gov.uk/Safetyinformation/Generalsafetyinformationandadvice/Adviceandinformationforconsumers/MymedicineFromlaboratorytopharmacyshelf/Licensingmarketingauthorisation/index.htm

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. Informed consent should be obtained from you prior to treatment.

This information is provided to help you decide with your doctor on whether to use the medicine and helps explain how to use the medicine in accordance with the pharmaceutical company's instructions for safe and proper use. 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 outweigh any potential risks.

Information for the patient:

Patisiran-LNP 2 mg/mL concentrate for solution for infusion

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.
- Always tell any doctor or other health care professional that is treating you that you are taking patisiran-LNP.

What is in this leaflet:

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

1. What patisiran-LNP is and what it is used for

The active substance in patisiran-LNP is patisiran.

Patisiran-LNP is a medicine that treats an illness which runs in families called hereditary ATTR (hATTR) amyloidosis.

hATTR amyloidosis is caused by problems with a protein in the body called 'transthyretin' (TTR).

- This protein is made mostly in the liver and carries vitamin A and other substances around the body.
- In people with this illness, abnormally shaped TTR proteins clump together to make deposits called 'amyloid'.
- Amyloid can build up around the nerves, heart, and other places in the body, preventing them from working normally. This causes the symptoms of this illness.

Patisiran-LNP works by lowering the amount of TTR protein that the liver makes.

- This means there is less TTR protein in the blood that can form amyloid.
- This can help to reduce the effects of this illness.

Patisiran-LNP is used in adults only.

2. What you need to know before you are given patisiran-LNP

You must not be given patisiran-LNP

- if you have ever had a severe allergic reaction to patisiran, or any of the other ingredients of this medicine (listed in section 6). If you are not sure, talk to your doctor or nurse before you are given patisiran-LNP.

Warnings and precautions

- **Infusion-related reactions**
  Patisiran-LNP is given as a drip into a vein (called an 'intravenous infusion'). Infusion-related reactions may happen during treatment with patisiran-LNP. Before each infusion you will be given medicines that help to lower the chance of infusion-related reactions (see "Medicines given during treatment with patisiran-LNP" in section 3).

  Tell your doctor or nurse straight away if you get any signs of an infusion-related reaction. These signs are listed at the beginning of section 4.

  If you have an infusion-related reaction, your doctor or nurse may slow down or stop your infusion, and you may need to take other medicines to control the symptoms. When these reactions stop, or get better, your doctor or nurse may decide to start the infusion again.

- **Vitamin A deficiency**
  Treatment with patisiran-LNP lowers the amount of vitamin A in your blood. Your doctor will measure your vitamin A levels, and if they are too low they should have returned to normal and any symptoms due to vitamin A deficiency should have resolved before you start treatment with patisiran-LNP. Symptoms of vitamin A deficiency may include:
  - Decrease in night vision, dry eyes, poor vision, hazy or cloudy vision

  If you have problems with your vision or any other eye problems whilst using patisiran-LNP, you should talk to your doctor. Your doctor may refer you to an eye specialist for a check-up if it is necessary.

  Your doctor will ask you to take a daily vitamin A supplement during treatment with patisiran-LNP.

  Both too high and too low levels of vitamin A can harm the development of your unborn child. Therefore, women of child-bearing age should not be pregnant when starting treatment with patisiran-LNP and should practice effective contraception (see section "Pregnancy, breast-feeding and contraception" below).

  Tell your doctor if you are planning to become pregnant. Your doctor may tell you to stop taking patisiran-LNP. Your doctor will ensure that your vitamin A levels have returned to normal before you try to become pregnant.

  Tell your doctor if you have an unplanned pregnancy. Your doctor may tell you to stop taking patisiran-LNP and your vitamin A supplement. You should resume vitamin A supplementation during the last 6 months of your pregnancy if the vitamin A levels in your blood have not yet returned to normal, because of an increased risk of vitamin A deficiency during the last 3 months of your pregnancy.

Children and adolescents
Patisiran-LNP is not recommended in children and adolescents under 18 years of age.

Other medicines and patisiran-LNP
Tell your doctor or nurse if you are taking, have recently taken or might take any other medicines. It is important to tell your doctor or nurse if you are taking any of the following medicines as your doctor may need to change the dose:

- Bupropion, a medicine used to treat depression or to help you to stop smoking
- Efavirenz, a medicine used to treat HIV infection and AIDS

Pregnancy, breast-feeding and contraception
If you are pregnant or breast-feeding, think you may be pregnant, or are planning to have a baby, ask your doctor for advice before starting this medicine.

Women of child-bearing age
Patisiran-LNP will reduce the level of vitamin A in your blood, which is important for normal development of your unborn child. If you are a woman of child-bearing age, you should practice effective contraception during treatment with patisiran-LNP. Talk to your doctor or nurse about suitable methods of contraception. Pregnancy should be excluded before starting treatment with patisiran-LNP.

Pregnancy
You should not use patisiran-LNP if you are pregnant, unless advised by your doctor. If you are of child-bearing age and intend to use patisiran-LNP, you should practise effective contraception.

Breast-feeding
Ingredients of patisiran-LNP may pass into breast milk. Talk to your doctor about stopping breast-feeding or treatment with patisiran-LNP.

Driving and using machines
Patisiran-LNP is believed to have no or negligible influence on the ability to drive or use machines. Your doctor will tell you whether your condition allows you to drive vehicles and use machines safely.

Patisiran-LNP contains sodium
This medicine contains 3.99 milligrams (mg) of sodium (main component of cooking/table salt) per millilitre (mL). This is 0.2% of the recommended maximum daily dietary intake of sodium for an adult.

3. How patisiran-LNP is given

How much patisiran-LNP is given

- Your doctor will work out how much patisiran-LNP to give you – this will depend on your body weight.
- The usual dose of patisiran-LNP is 300 micrograms per kilogram (kg) of body weight given once every 3 weeks.

How patisiran-LNP is given

- Patisiran-LNP will be given to you by a doctor or nurse.
- It is given as a drip into a vein ('intravenous infusion') usually over about 80 minutes.

If you do not have problems with your infusions well in the clinic, your doctor may talk with you about a healthcare provider giving you your infusions at home.

Medicines given during treatment with patisiran-LNP

Before each infusion of patisiran-LNP, you will be given approved medicines that help to lower the risk of infusion-related reactions. These include anti-histamines (an anti-allergy medicine), a corticosteroid (an anti-inflammatory medicine), and a pain reliever (to reduce fever).

How long to use patisiran-LNP

Your doctor will tell you how long you need to receive patisiran-LNP. Do not stop treatment with patisiran-LNP unless your doctor tells you to.

If you are given more patisiran-LNP than you should receive

This medicine will be given to you by your doctor or nurse. In the unlikely event that you are given too much (an overdose) your doctor or nurse will check you for side effects.

If you miss your dose of patisiran-LNP

If you miss an appointment to have patisiran-LNP, ask your doctor or nurse when to book your next treatment.

If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Infusion-related reactions

Infusion-related reactions are very common (may affect more than 1 in 10 people).

Tell your doctor or nurse straight away if you get any of the following signs of an infusion-related reaction during treatment. The infusion may need to be slowed down or stopped, and you may need to take other medicines to manage the reaction.

- Stomach pain
- Feeling sick (nausea)
- Body aches or pain, including pain in the back, neck, or joints
- Headache
- Feeling tired (fatigue)
- Chills
- Dizziness
- Cough, feeling short of breath, or other breathing problems
- Reddening of the face or body (flushing), warm skin, or rash
- Chest discomfort or chest pain

- Rapid heart rate
- Low or high blood pressure
- Pain, redness, burning sensation, or swelling at or near the infusion site
- Swelling of the face

Other side effects
Tell your doctor or nurse if you notice any of the following side effects:

Very common: may affect more than 1 in 10 people
- Swelling of the arms or legs (peripheral oedema)

Common: may affect up to 1 in 10 people
- Pain in the joints (arthralgia)
- Muscle spasms
- Indigestion (dyspepsia)
- Shortness of breath (dyspnoea)
- Redness of the skin (erythema)
- Feeling dizzy or faint (vertigo)
- Stuffy or runny nose (rhinitis)
- Irritation or infection of the airways (sinusitis, bronchitis)

Uncommon: may occur in up to 1 in 100 infusions
- Leakage of the drug into the surrounding tissue at the site of infusion, which may cause swelling or redness

Tell your doctor or nurse if you notice any of the side effects listed above.

Reporting of side effects
If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet.

You should also report any side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or call freephone 0800 731 6789 (10am to 2pm Monday-Friday only).

Your doctor or pharmacist will complete an EAMS Safety Information Reporting Form, and a Discontinuation Form if you stop treatment.

5. How to store patisiran-LNP

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

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

Store in a refrigerator (2°C to 8°C). Do not freeze.

If refrigeration is not available, patisiran-LNP can be stored at room temperature (up to 25°C) for up to 14 days.

Medicines should not be disposed of via wastewater or household waste. Your healthcare professional will throw away any medicines that are no longer being used. These measures will help protect the environment.

6. Contents of the pack and other information

What patisiran-LNP contains

- The active substance is patisiran.
- Each 5mL vial contains patisiran sodium equivalent to 10 mg of patisiran.
- Each mL contains 2 mg patisiran.
- The other ingredients are DLin-MC3-DMA ((6Z,9Z,28Z,31Z)-heptatriaconta-6,9,28,31-tetraen-19-yl-4-(dimethylamino) butanoate), PEG_{2000}-C-DMG (α-(3'-{[1,2-di(myristyloxy)propanoxy]carbonylamino}propyl)-ω-methoxy, polyoxyethylene), DSPC (1,2-distearoyl-*sn*-glycero-3-phosphocholine), cholesterol, disodium hydrogen phosphate heptahydrate, potassium dihydrogen phosphate,anhydrous, and water for injections (see "patisiran-LNP contains sodium" in section 2).

What patisiran-LNP looks like and contents of the pack

- Patisiran-LNP is a white to off-white, opalescent, homogeneous concentrate for solution for infusion.
- Patisiran-LNP is supplied in cartons containing one vial each.

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Additional information:

Prior to requesting access to patisiran-LNP, you will have the scheme explained to you using this leaflet. You will be requested to sign an Informed Consent Form and will be given a copy to keep.

In addition to pharmacovigilance reporting, data may be collected on clinical efficacy and quality of life on a voluntary basis. These tests can include: results of blood tests, quality of life tests, blood pressure, physical assessments, echocardiography, cardiac Magnetic Resonance Imaging, and other imaging to measure your disease, questionnaires and nerve conduction studies. These data may be shared with the EAMS Scientific Opinion Holder, and regulatory authorities.

Contact information:

If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet.

Your doctor or pharmacist will complete an EAMS Safety Information Reporting Form, and a Discontinuation Form if you stop treatment.

You should report any side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or call freephone 0800 731 6789 (10am to 2pm Monday-Friday only).