Medicines & Healthcare products Regulatory Agency

MHRA

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: 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 (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

Berotralstat 150 mg Capsules
Read all of this leaflet carefully before you start taking 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 pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.
- It is important that you keep the EAMS Patient Card (which will fit in a wallet) with you at all times during treatment.
- Always tell any doctor or other healthcare professional that is treating you (including your GP, dentist, nurse, pharmacist) that you are taking berotralstat and show them the EAMS Patient Card.

What is in this leaflet

1. What berotralstat is and what it is used for

Berotralstat capsules contain the active substance berotralstat. This substance blocks the activity of plasma kallikrein in your bloodstream. This, in turn, reduces bradykinin activation which is what causes hereditary angioedema (HAE) consisting of swelling and pain which can limit your daily activity.

Berotralstat is a medicine used in adults and adolescents from 12 years and older to prevent recurrent angioedema attacks, in patients with HAE.

What hereditary angioedema (HAE) is

HAE is a condition that often runs in families. With this condition your blood does not have enough of a protein called ‘C1 inhibitor’, or your C1 inhibitor does not work properly. This leads to too much ‘plasma kallikrein’, which in turn produces higher levels of ‘bradykinin’ in your bloodstream. Too much bradykinin leads to symptoms of HAE like swelling and pain of the:

- hands and feet
- face, eyelids, lips or tongue
- voice-box (larynx), which may make breathing difficult
- stomach or intestine
- Genitals
- Stomach and intestines

2. What you need to know before you take berotralstat

Do not take berotralstat

- if you are allergic to berotralstat or any of the other ingredients of this medicine (listed in section 6)

Warnings and precautions

Talk to your doctor or pharmacist before taking berotralstat.
- If you have moderate or severely reduced liver function

The safety and efficacy of berotralstat as an acute treatment for hereditary angioedema attacks have not been shown. Patients should not take additional doses of berotralstat to treat an acute attack of hereditary angioedema.

If you have an **HAE attack**, you should **treat it with your regular rescue medicine**.

Children and adolescents

Berotralstat is not recommended in children under 12 years. This is because it has not been studied in this age group.

Adolescents from 12 years weighing less than 40 kg should inform the doctor before taking berotralstat.

Other medicines and berotralstat

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Particularly, inform your doctor before taking berotralstat if you are using:
- thioridazine, pimozide: medicines to treat mental disorders
- amlodipine: a medicine to treat high blood pressure or a certain type of chest pain called angina
- cyclosporine: a medicine to suppress the immune system, treat severe skin diseases and severe eye or joint inflammation
- dabigatran: a medicine to inhibit blood clotting
- desipramine and other medicines to treat depression called tricyclic antidepressants
- dextromethorphan: a cough-relieving medicine
- digoxin: a medicine to treat heart weakness and irregular heartbeat
- Monitoring digoxin blood levels is recommended during treatment with berotralstat
- fentanyl: a strong painkiller
- midazolam: a medicine to treat sleeping disorders and for anaesthesia
- oral contraceptives
- Berotralstat may reduce the effectiveness of hormonal contraceptives, such as desogestrel. Therefore, women using only desogestrel for contraception should switch to an alternative effective method of contraception, such as barrier method, injectable progesterone or combination oral hormonal contraception.

Pregnancy and breast-feeding

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

There is limited information on the safety of berotralstat use during pregnancy and breast-feeding. It is preferable to avoid the use of berotralstat during pregnancy and breast-feeding.

Your doctor will discuss with you the risks and benefits of taking this medicine.

Driving and using machines

Berotralstat has no or negligible influence on the ability to drive and use machines.

3. How to take berotralstat

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

The recommended dose is

The recommended dose for adults and adolescents from 12 years is one 150mg capsule of berotralstat once daily.

No dose adjustment is required for patients with mild, moderate or severely reduced kidney function or patients over 65 years. However, inform you doctor if you are on dialysis. No dosage recommendations can be given for patients on dialysis.

No dose adjustment is required for patients with reduced liver function. Inform your doctor before taking berotralstat if you have moderate or severely reduced liver function

Method of administration

Take one capsule with one glass of water at the same time each day. This can be at any time of the day, with or without food.

If you take more berotralstat than you should

Contact you doctor immediately if this occurs.

If you forget to take berotralstat

Do not take a double dose to make up for a forgotten capsule. Take a missed dose as soon as you remember; however, do not take more than one dose per day.

If you stop taking berotralstat

It is important to take berotralstat on a regular basis and for as long as your doctor prescribes it. Do not stop taking berotralstat without discussing this with your doctor.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. As this is a new medicine, there may be other side effects which are not yet known.

Side effects can occur with the following frequencies:

Very common, may affect more than 1 in 10 people
- Stomach pain, including abdominal discomfort, abdominal tenderness
- diarrhoea, including frequent bowel movement

Common, may affect up to 1 in 10 people
- vomiting
- Heartburn
- wind
- increased levels of liver enzymes called transaminase
- rash

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly to MHRA via the Yellow Card scheme via www.mhra.gov.uk/yellowcard. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store berotralstat

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

Do not use this medicine after the use by date which is stated on the container.

This medicinal product does not require any special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What berotralstat contains

- The active substance is berotralstat. Each capsule contains 150 mg berotralstat (as dihydrochloride).
- The other ingredients are pregelatinised starch, crospovidone, colloidal silicon dioxide and magnesium stearate., gelatine, titanium dioxide (E171), colourants (Indigo Carmine (E132), black iron oxide (E172), red iron oxide (E172)), edible printing ink (black iron oxide (E172), potassium hydroxide, shellac, propylene glycol)

What berotralstat looks like and contents of the pack

Berotralstat capsules have a white opaque body and light blue opaque cap with black bar (19.4 mm capsule length, 6.9 mm capsule diameter). They are packed in a white plastic bottle.

Pack size: a bottle contains 30 hard gelatine capsules

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Additional information

Informed Consent Form

You will have the Early Access to Medicines Scheme (EAMS) explained to you using 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 Alert Card

You will also be given a Patient Alert Card before you start treatment with berotralstat. You must keep this Patient Alert Card with you at all times during the treatment and for at least 5 months after completing your treatment with berotralstat. The card alerts any other healthcare professional who may treat you that you are currently receiving berotralstat through an early access scheme, provides information regarding the important known side effects for which you should seek assistance should they occur, contact details for the doctor managing your treatment and the company's contact details.

Patient data to be collected

Information collected during the scheme will mostly be 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 your 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 initials, year of birth, gender, information about HAE, comorbidities, and any medications you may be taking.

Contact information

Contact information

Adverse events reporting – Patient must contact their treating physician to report any adverse events. Adverse events may also be reported directly to the MHRA via the Yellow card scheme at **www.mhra.gov.uk/yellowcard**.