Medicines & Healthcare products Regulatory Agency

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

Glofitamab 10 mg 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.
  - Your doctor will give you a Patient Card. Read it carefully and follow the instructions on it. Keep this Patient Card with you at all times.
  - Always show the Patient Card to the doctor, pharmacist or nurse when you see them or if you go to hospital.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What glofitamab is and what it is used for

Glofitamab is used to treat adults with a cancer called “diffuse large B-cell lymphoma” (DLBCL). It is used when:

- the cancer has come back (relapsed) or
- the cancer did not respond to previous treatments.

Diffuse large B-cell lymphoma is a cancer of a part of your immune system (the body’s defences).

- It affects a type of white blood cell called ‘B-cells’.
- In DLBCL, B-cells multiply in an uncontrolled manner and build up in your tissues.

How glofitamab works

Glofitamab is a bispecific monoclonal antibody, a type of protein that attaches to two specific targets in the body. It attaches to a specific protein on the surface of B cells, including cancerous B cells, and also to another protein on the surface of T cells (another type of white blood cell). This activates T cells and causes them to multiply. This, in turn, results in the destruction of the B cells, including the cancerous cells.

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

You must not be given glofitamab

- if you are allergic to glofitamab or any of the other ingredients of this medicine (listed in section 6)
- if you are allergic to obinutuzumab, which is another medicine given before starting glofitamab treatment (see also section 3 ‘How glofitamab is given’), or any of the other ingredients of this medicine

If you are not sure, talk to your doctor or nurse before you are given glofitamab

Warnings and precautions

Talk to your doctor before you are given glofitamab if:

- you have an infection
- you have had a long-lasting infection (chronic), or an infection which keeps coming back
- (recurring)
- you have or had any kidney, liver or heart problems
- you are due to have a vaccine, or you know you may need to have a vaccine in the near future

If any of the above apply to you (or you are not sure), talk to your doctor or nurse before being given glofitamab.

Children and adolescents

This medicine should not be given to children and adolescents below 18 years of age. This is because glofitamab has not been studied in this age group.

Other medicines and glofitamab

Tell your doctor or nurse if you are taking, have recently taken or might start
taking any other medicines. This includes medicines obtained without a prescription and herbal medicines.

Pregnancy and contraception

- If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.
- You should not be given glofitamab if you are pregnant. This is because it is possible that glofitamab could harm your unborn baby.
- If you could become pregnant, you must use effective contraception while you are being treated with glofitamab and for 2 months after the last dose.
- If you become pregnant while you are being treated with glofitamab tell your doctor immediately.

Breast-feeding

Do not breast-feed while receiving glofitamab and for at least 2 months after the last dose. This is because it is not known if this medicine can pass into breast milk and harm your baby.

Driving, cycling and using machines

Glofitamab may affect your ability to drive, cycle or use any tools or machines. If you feel any symptoms that may affect your ability to drive, including symptoms of cytokine release syndrome (such as fever, fast heartbeat, feeling dizzy or lightheaded, chills or shortness of breath) or have any symptom that makes you feel unwell – do not drive, cycle or use any tools or machines until you feel better. See section 4 for more information about side effects.

3. How glofitamab is given

You will be given glofitamab under the supervision of a doctor experienced in cancer treatment, in a hospital or clinic. Follow the treatment schedule explained to you by your doctor. Check with your doctor if you are not sure.

Medicines given before glofitamab treatment

- **Seven days before starting glofitamab treatment**, you will be given another medicine, obinutuzumab, to reduce the number of B cells in your blood.
  - **30 to 60 minutes before you are given glofitamab,** you may be given other medicines (pre-medication) to help reduce reactions associated with cytokine release syndrome.

  These medicines may include:
  - A corticosteroid such as dexamethasone
  - A fever-reducing medicine such as paracetamol
  - An antihistamine such as diphenhydramine

How much and how often you will receive glofitamab

You may be given up to 12 treatment cycles of glofitamab. Each cycle lasts 21 days. During the first two cycles, your doctor will begin glofitamab treatment with a low dose and will gradually increase it to the full dose.

A typical schedule is shown below.

Cycle 1: This will include a pre-treatment and 2 low doses of glofitamab during the 21 days:
- Day 1 – Pre-treatment with obinutuzumab
- Day 8 – 2.5 mg starting dose of glofitamab
- Day 15 – 10 mg intermediate dose of glofitamab

Cycle 2 to Cycle 12: One 30 mg dose of glofitamab will be given every 21 days:

How glofitamab is given and monitoring

Glofitamab is given as a drip into a vein (an intravenous infusion). Your doctor will adjust the time required for infusion depending on how you respond to treatment.

- Your first infusion will be given over 4 hours. Your doctor will monitor you carefully during the first infusion and for 24 hours after completion of infusion. This is to watch for any signs or symptoms of cytokine release syndrome.
- For following infusions, your doctor may require to monitor you after completion of infusion. This will be necessary if you have had moderate or severe CRS with your previous dose.
- If you do not have any cytokine release syndrome after 3 doses, your doctor may give the following infusions over 2 hours.

If you miss a dose of glofitamab

If you miss a dose of glofitamab, contact your doctor, pharmacist or nurse immediately

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

Tell your doctor straight away if you get any symptom of the serious side effects listed below – you may need urgent medical treatment.

- **Cytokine release syndrome (very common);**
  symptoms include:

- fever (38°C or higher),
- fast or uneven heartbeat,
- feeling dizzy or lightheaded,
- chills,
- shortness of breath,
- difficulty breathing,
- cold or pale clammy skin,
- feeling very tired or weak,
- fainting,
- blurred vision,
- headache,
- confusion

- **Infection (very common);**
  symptoms include:
  - fever,
  - chills,
  - difficulty breathing,
  - burning pain when passing urine,
  - cough,
  - chest pain,
  - painful rash,
  - sore throat,
  - feeling weak and
  - generally unwell
- **Tumour flare (very common);**
  symptoms include:
  - tender swollen lymph nodes,
  - chest pain,
  - cough or difficulty breathing easily,
  - pain at the site of the tumour
- **Tumour lysis syndrome (common)**;
  symptoms include:
  - fever,
  - chills,
  - feeling or being sick (nausea and vomiting),
  - fits (seizures),
  - irregular heartbeat,
  - weakness,
  - shortness of breath,
  - feeling confused,
  - muscle cramps

Your doctor may:
- give you other medicines to reduce possible side effects and prevent complications
- stop glofitamab for a short time or
- stop glofitamab completely.

Other side effects:
If you notice any of the side effects above or if they get worse, tell your doctor:

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

- lowered levels, as measured in blood tests, of:
  - neutrophils (a type of white blood cell; neutropenia), which may cause fever or any symptoms of an infection
  - red blood cells (anaemia), which may cause tiredness, feeling unwell and pale skin
  - platelets (a type of blood cell; thrombocytopenia), which may cause bruising or bleeding
- fever
- low levels, as measured in blood tests, of phosphate, magnesium, calcium or potassium
- rash
- constipation
- diarrhoea
- feeling sick (nausea)
- viral infections, such as lung infection, shingles
- headache

Common (may affect up to 1 in 10 people)

- low sodium levels, as measured in blood tests, which may cause tiredness, muscle twitching or cramps
- increased levels, as measured in blood tests, of liver enzymes and bilirubin (yellow substance in blood), which may cause yellowing of skin or eyes, and dark urine
- bacterial infections, such as urinary tract infection, infection in or around the stomach
- fungal infection
- nose and throat infections (upper respiratory tract infections)
- infections of the lungs such as bronchitis or pneumonia (lower respiratory tract infections), which may cause fever, cough, and difficulty breathing
- blood poisoning (sepsis), which may cause fever, chills and confusion
- low levels, as measured in blood tests, of lymphocytes (a type of white blood cell; lymphopenia)
- fever with low levels of neutrophils (febrile neutropenia)
- vomiting
- bleeding in the stomach or gut (gastrointestinal haemorrhage), which may cause black stools or blood in vomit
- confusion
- trembling
- sleepiness

Uncommon (may affect less than 1 in 100 people)

- swelling of the spinal cord (myelitis), which may cause muscle weakness or numbness.

If you notice any of the side effects above or if they get worse, tell your doctor straight away.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in the package leaflet. You can also report side effects directly via the Yellow Card Scheme https://yellowcard.mhra.gov.uk/ .

You should also report side effects to Roche Products Ltd by emailing the Roche Drug Safety Centre at

welwyn.uk_dsc@roche.com or calling +44 (0) 1707 367554. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store glofitamab

Your doctor, pharmacist or nurse is responsible for storing this medicine and disposing of any unused product correctly. The following information is intended for healthcare professionals.

- 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 and the vial label 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.
- Keep the vial in the outer carton in order to protect from light.
- Do not use this medicine if it appears cloudy, discoloured or contains particles.

Any unused medicine or waste material should be disposed of in accordance with local requirements

6. Contents of the pack and other information

What glofitamab contains

- The active substance is glofitamab.
- glofitamab 10 mg/10 mL: Each vial contains 10 milligrams of glofitamab (in 10 mL)
- The other ingredients are: L-histidine, L-histidine hydrochloride monohydrate, L-methionine, sucrose, polysorbate 20 (E432) and water for injections.

What glofitamab looks like and contents of the pack

Glofitamab concentrate for solution for infusion is a colourless, clear solution provided in a glass vial. Each pack of glofitamab contains one vial.

Scientific Opinion Holder and manufacturer

Roche Products Limited
6 Falcon Way
Shire Park
Welwyn Garden City
AL7 1TW
United Kingdom

This protocol was revised in June 2023

Additional information

Informed Consent Form

All patients will have the Early Access to Medicines Scheme explained to them using the informed consent form. The patient will be asked to sign this form and a copy will be given to them to keep.

Patient Alert Card

Patients must be given a Patient Alert Card before they start treatment with glofitamab. They must keep this alert card with them at all times during the treatment and for at 1 month after completing their treatment with glofitamab. The card summarises that they are currently receiving glofitamab, the important side effects for which patients need to seek assistance should they occur, details of the patients treating haematologist managing their treatment, out of hours contact details and the company contact details.

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 :

- Patient ethnicity
- Confirmation the patient meets the EAMS indication
- Patient Age (please do not include full Date of Birth):
- Patient Initials:
- Patient Gender
- Comorbidities
- Concomitant medication

Additional data will be collected on a voluntary basis and subject to additional patient consent. These data include:

- Date of DLBCL diagnosis
- ECOG Performance Status
- Size of the sites of the lymphoma
- Whether or not responded to last lymphoma treatment
- Number of previous treatments for lymphoma
- Which previous types of treatment received for lymphoma
- GP Postcode- This information will be used to assess the geographical spread of patients enrolled onto the scheme EAMS programme.
- Treatment centre type
    - a centre approved to treat with CAR-T cell therapy
    - a centre not approved to treat with CAR-T cell therapy
    - a centre approved to deliver Stem Cell Transplants (SCT)
    - a centre not approved to deliver Stem Cell Transplants (SCT) non accredited

The reasons for collecting these additional data are to understand how glofitamab may be used in clinical practice. This information is optional to provide, and patients will not be denied access to treatment with glofitamab if they do not consent.

Contact information

Contact details for reporting Adverse Events/Special

Situations/Pregnancies: SAE Email Address: welwyn.uk_dsc@roche.com

SAE Facsimile Transmission: +44 1707 367582

SAE TELEPHONE CONTACT: +44 1707 367554

Name: UK Drug Safety Centre

Contact email for the EAMS programme (excluding AE reporting):

welwyn.glofitamabEAMS@roche.com

Contact Details for Medical Information

Roche Medical Information on 0800 328 1629 or email medinfo.uk@roche.com