Medicines & Healthcare products Regulatory Agency

Early Access to Medicines Scientific Opinion - Public Assessment Report	
Product	**Glofitamab**
EAMS indication	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.
Company	**Roche Products Limited**
EAMS number	**00031/0018**
EAMS Scientific Opinion date	**30/06/2023**

Introduction

The aim of the Early Access to Medicines Scheme (EAMS) is to provide earlier availability of promising new unlicensed medicines and medicines used outside their licence, to UK patients that have a high unmet clinical need. The MHRA scientific opinion provides benefit and risk information to physicians who may wish to prescribe the EAMS medicine under their own responsibility. More information about the scheme can be found here:
http://www.mhra.gov.uk/Howweregulate/Innovation/EarlyaccesstomedicinesschemeEAMS/index.htm

The scientific opinion is based on assessment of the information supplied to the MHRA on the benefits and risks of the medicine. As such this is a scientific opinion and should not be regarded as a medicine licensed by the MHRA or a future commitment by the MHRA to license such a medicine, nor should it be regarded as an authorisation to sell or supply such a medicine. 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 a ‘special’ 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 General Medical Council’s guidance on prescribing unlicensed medicines can be found here:
https://www.gmc-uk.org/guidance/ethical_guidance/14327.asp

What is Glofitamab?

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.

Glofitamab is given as a drip into a vein (an intravenous infusion).

What is Glofitamab used to treat?
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 is Glofitamab used?
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.

How does Glofitamab work?
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.

How has Glofitamab been studied?
An open-label multicenter, multi-cohort trial (NP30179) was conducted to evaluate glofitamab. In the single-arm monotherapy DLBCL cohort (n=108), patients with relapsed or refractory DLBCL were required to have received at least two prior lines of systemic therapy, including an anti-CD20 monoclonal antibody and an anthracycline agent.

The main outcome measure was complete response (CR) rate.

What are the benefits and risks of Glofitamab?

Benefits
38 out of 108 patients with relapsed or refractory DLBCL had a complete response to Glofitamab.

Risks
Serious side effects

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

Other side effects
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.

Why has Glofitamab been given a positive Early Access to Medicine Scientific opinion?

Glofitamab appears to have similar effectiveness compared to CAR-T cell therapy.
Glofitamab does not require special preparation, unlike CAR-T cell therapy so it is more convenient.

What are the uncertainties?

It is not certain whether selection of patients based on CD20 status before the use of Glofitamab would lead to better response.
The company that makes Glofitamab will provide additional information when it becomes available.

Are there on-going clinical studies?

There is no on-going study of Glofitamab in the EAMS indication.

What measures are in place to monitor and manage risks?

A risk management plan has been developed to ensure that glofitamab is used as safely as possible. Based on this plan, the company that makes glofitamab must ensure that all healthcare professionals

expected to use the medicine, as well as patients, are provided with information on the medicine including the side effects and recommendations for minimising these side effects.

Information will be collected about patients before they enter the scheme. Healthcare professionals will be asked by the company to report side effects experienced by patients receiving glofitamab through the scheme. Safety data will be reviewed and reported to the MHRA on a regular basis by the company.

Healthcare professionals involved in the management of the scheme will receive specific training from the company prior to commencement of patient treatment. This will include product information, information on storage and reconstitution of the medicine, infusion protocol and the adverse event reporting process.

Patients will receive an alert card summarising the important risks with the medicine and the details of their treating doctor. Patients should carry the card with them at all times to inform any other healthcare professional that they are receiving glofitamab through an EAMS.

Other information about Glofitamab – see EAMS Treatment Protocol