Medicines & Healthcare products Regulatory Agency

Early Access to Medicines Scheme – Treatment protocol – Information on the pharmacovigilance system and requirements for reporting safety data

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 medicinal products 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.

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 licensed indication or a future commitment by the MHRA to licence 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 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.

As the safety profile of the EAMS medicine may not yet be fully established it is particularly important that any harmful or unintended responses to EAMS medicines are reported. More information about the scheme can be found here: http://www.mhra.gov.uk/Howweregulate/Innovation/EarlyaccesstomedicinesschemeEAMS/index.htm

Physicians should enroll any patients receiving EAMS medicines in the drug registry put in place by the pharmaceutical company to enable systematic collection of information on adverse events. Suspected adverse drug reactions (ADRs) for any patients can also be reported directly to the MHRA via the Yellow card scheme at www.mhra.gov.uk/yellowcard. When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, outcome and results of any test results or investigations.

The information below is intended for healthcare professionals and is provided by the pharmaceutical company that manufactures the EAMS medicine. It summarises the requirements for clinical monitoring and reporting of adverse events with medicines used under the scheme.

Healthcare professionals should also consult the relevant detailed information provided by the company.

EAMS Indication
Glofitamab as monotherapy is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), after two or more lines of systemic therapy.

Information on the Pharmacovigilance system

Healthcare professionals who express an interest in this EAMS (AL44449) through contacting the dedicated mailbox (welwyn.glofitamabEAMS@roche.com) will be provided with the EAMS documentation (e.g. the Application and Initial Drug Supply Form [including the Treating Physician Responsibilities, Safety Obligations and Roche contacts], Institution Agreement, Treatment Protocols and Informed Consent Form, etc) by Roche. Additionally, treating physicians involved in the care of patients on EAMS will receive safety training.

Upon receipt of the Application and Initial Drug Supply Form, signed Treating Physician/Institution agreements and completion of safety training, eligible patients will be assigned a unique EAMS identification number and Roche will arrange initial drug shipment for the patient (covering two cycles' worth of treatment).

Adverse event/Adverse drug reaction reporting

All Healthcare Professionals (HCPs) involved in the care of patients on EAMS will be instructed to report all adverse events (AE) (including serious, non-serious, and special situations (SS) whether or not there is an associated AE) within one business day of awareness as specified in the EAMS documents and HCP training.

The SS may include the following:

- Use of a medicinal product during pregnancy and breastfeeding
- Overdose
- Misuse
- Abuse
- Off-label use
- Medication error
- Occupational exposure
- Accidental exposure
- Missed dose
- Lack of therapeutic efficacy
- Disease progression
- Suspected Transmission of Infectious Agent (STIAMP)
- Drug Interactions
- Unexpected Beneficial Effect
- Drug dependence
- Withdrawal syndrome
- Product Complaints with associated AEs/SSs
- Product Complaints without associated AEs/SSs
- Counterfeit products

The AE reporting forms are provided with the first email Roche send to the physician with all of the documentation. HCPs can download the document. Additionally, they can request copies of this AE reporting form by sending an email to welwyn.glofitamabEAMS@roche.com

All AEs reported will be entered into the Roche safety database which will form part of the EAMS Drug Registry and will be linked to the patient by the specific EAMS protocol number and unique EAMS patient number. The dose and duration of treatment of the program drug should be captured in the EAMS Adverse Event Reporting form, along with details of any treatment for AEs/SAEs.

The Scientific Opinion Holder is required to send ADRs suspected to be related to the EAMS

products to the MHRA within the agreed timelines.

HCPs should also report AEs to the MHRA via the Yellow Card scheme at https://yellowcard.mhra.gov.uk/ and reporters are requested to state the manufacturer and that the product is unlicensed on the AE report.
In addition to this, the EAMS patient ID number should be provided in the report narrative to help the MHRA identify that the AE is related to EAMS product and to help Roche link the AE report to the correct EAMS patient.

Training for healthcare professionals

Training for adverse events will be provided to treating physicians prior to commencement of patient treatment, focusing on recognising and reporting AEs during the scheme. Equally, the HCP's obligation to keep their patients fully informed on their treatment will be emphasised. AE reporting forms and the below additional risk minimisation material will be provided to facilitate this activity.

Additional risk minimisation materials

The following risk minimisation material will be utilised as part of the EAMS Drug Registry:

- **Patient Card** – This will be given to all patients before they start treatment. It is a wallet-sized card to be carried at all times to show at all medical visits to HCPs (e.g. emergency HCPs). It has the contact details of the treating physician and alerts other HCPs that the patient is receiving glofitamab. It also contains information on the main symptoms of the important adverse reactions (cytokine release syndrome) and highlights the importance of notifying the treating physician immediately if symptoms occur, persist or worsen and also the importance of not attempting to self-treat any symptoms without consulting a HCP first.
- **Healthcare Professional (HCP) Guide** - The HCP Guide will aim to educate and raise HCPs' awareness and comprehension of the key signs and symptoms of the risks of the important adverse reactions such that HCPs can detect and manage tumour flare (TF) in a timely and appropriate manner. Optimizing the time to intervention and appropriate management of TF will prevent it from worsening and maximize recovery potential. The HCP brochure will provide a description of TF, and information on early recognition, appropriate diagnosis, and monitoring of TF.
- The HCP brochure will alert HCPs to educate patients when giving them a Patient Card about the signs and symptoms of cytokine release syndrome and the need to seek medical attention immediately if these signs and symptoms appear.

Additional information

Drug registry

Mandatory data

The prescribing oncologist will be requested to provide the following information for all patients by completing an Application and Initial Drug Supply Request for each patient to be enrolled on to the programme for eligibility assessment:

- Confirmation the patient meets the EAMS indication
- Patient Age (please do not include full Date of Birth)
- Patient Initials
- Patient Gender
- Patient Ethnicity

- Comorbidities
- Concomitant medication

Healthcare professionals will be required to capture the treatment start date of glofitamab in the Drug Resupply Form. Healthcare professionals are advised to inform Roche when a patient discontinues treatment. When completing the Drug Resupply Form, healthcare professionals will be required to confirm whether patients are receiving the full 30 mg dose or have reverted to step-up dosing as a result of a treatment interruption. This will allow Roche to determine dose and treatment duration for each patient.

Additional data

There will also be additional data elements included within the EAMS Application and Initial Drug Supply Form. This data is being collected by Roche to understand how glofitamab will be used in clinical practice in this setting. The additional data collected will be limited to:

- Date of DLBCL diagnosis
- ECOG Performance Status
- Bulky disease (>6cm) - Yes / No
- Refractory to last treatment? - No response or relapse within 6 months of last treatment
- No of Previous treatment lines?
- Previous treatments
- Patient GP postcode: This information will be used to assess the geographical spread of patients enrolled onto the EAMS
- Treatment center type: CART accredited
  CART non accredited
  Stem Cell Transplant (SCT) accredited

Upon receipt of the completed Application and Initial Drug Supply Form, Roche will confirm eligibility and assign a unique EAMS Patient number to the patient. This unique EAMS patient number will be communicated back to the physician to be used in all future communications including re-ordering drug supplies and reporting adverse events. All data collected will be recorded under this number, making it anonymous for the purpose of this programme.

Drug Resupply

For patients approved under this scheme and requiring ongoing drug supply, HCPs will be required to complete the Resupply Form provided in the initial email sent by Roche to request further treatment. HCPs will also be asked for confirmation that they understand and agree to comply with their obligations to report all AEs and SSs to Roche and that they are complying with this requirement. In addition, HCPs will be asked to confirm that all AEs and SSs experienced since the last resupply request have been reported and there are no new AEs to report. Roche will produce a quarterly line-listing for all single case reports received in the preceding time period and send this to the Physician. Once received, the Physician will confirm receipt and completeness of the line-listing within five (5) business days. This process is referred to as ‘Case Transmission Verification (CTV)’ in the physician agreement.

Patient withdrawal

For patients withdrawing from the EAMS, the HCP needs to send an email to Roche welwyn.glofitamabEAMS@roche.com within 1 business day of awareness with the reason for

discontinuation and last date of treatment. If the reason for discontinuation is due to an AE, this should also be reported to Roche Drug Safety (welwyn.uk_dsc@roche.com) within 1 business day of awareness.

Periodic reports

A 3-monthly periodic safety report will be submitted to the MHRA to summarise data on safety, efficacy/effectiveness and usage of glofitamab under the scheme.

Contact details

Contact details for reporting Adverse Events and Special Situations:

Name: UK Drug Safety Centre
SAE Email Address: welwyn.uk_dsc@roche.com
SAE Facsimile Transmission: +44 1707 367582
SAE TELEPHONE CONTACT: +44 1707 367554 (A voicemail message can be left. The messages are routinely monitored by the UK Drug Safety Centre).

Contact email for the EAMS programme (excluding AE reporting):
welwyn.glofitamabEAMS@roche.com