Medicines & Healthcare products Regulatory Agency

MHRA

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

Atezolizumab, in combination with bevacizumab, is indicated for the treatment of adult patients with unresectable hepatocellular carcinoma who have received no prior systemic therapy.

Information on the Pharmacovigilance system

A prescribing oncologist may request entry of their patients into the Early Access to Medicines Scheme (EAMS) **AL42617 (00031/0012)** by completing and submitting an Initial Application and Drug Supply Request Form. Upon review of the individual request and fulfilment of the eligibility criteria, Roche will provide EAMS materials which will include information on the collection and reporting of adverse events.

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), and special situations (SS) whether or not there is an associated AE within one business day of awareness as specified in the Safety Reporting Cover Letter in the physicians pack.

The SS may include the following:

- Use of a medicinal product during pregnancy and breastfeeding
- Overdose
- Medication error

The E-reporting form is also included in the physician pack. HCPs can request additional copies of this AE reporting form by sending email to welwyn.hcceams@roche.com Additional follow-up may be requested on all reports received to obtain further information.

All AEs and SSs reported will be entered into the Roche safety database and will be linked to the patient by the specific EAMS protocol number and unique patient number. Once Roche enrolls the patient in the scheme, a number (a unique EAMS identification number) will be allocated to each patient.

Roche is required to send ADRs suspected to be related to the EAMS products to the MHRA within the agreed timelines.

Training for healthcare professionals

In addition to the Physician Pack, comprehensive AE and SS training will be provided to all relevant HCPs prior to commencement of patient treatment, focusing on recognising, managing and reporting AEs and SSs during the scheme. Equally, the HCPs obligation to keep their patients fully informed on their treatment will be emphasised. Pertinent patient-related supporting documents such as the Patient Alert Card will be provided to facilitate this activity.

Additional risk minimisation materials

Patient Alert 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 other than the prescribers (e.g., emergency HCPs). It has contact details of the treating physician and it alerts other HCPs physicians that the patient is treated with atezolizumab. It also contains information on the main symptoms of the important adverse reactions 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 with an HCP first.

HCP brochure – This will be provided to all treating physicians with patients enrolled in the scheme after conducting safety training.

Additional information

Drug registry

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

Mandatory data

- Patient's initials
- Year of birth
- Gender
- Diagnosis (including staging information)
- Date of Diagnosis (DD/MM/YYYY)
- Unresectable HCC (Y/N)
- Prior systemic therapy (Y/N)
- ECOG Performance Status
- Child-Pugh class status
- Prior locoregional therapy received
- Duration of prior locoregional therapy
- Comorbidities
- Concomitant medications

Roche will also provide a physician agreement and the safety data exchange agreement for signature. This document outlines the requirements for reporting AEs in line with the instructions below. Once signed documents are returned by the oncologist, Roche will arrange safety training and delivery of the AE management guide and the patient alert card to the HCPs. The safety training will contain the instructions on recognising, managing and reporting AEs and SSs.

For patients approved under this scheme and requiring ongoing drug supply, the HCPs will be required to complete the Re-supply Form provided in the physician pack to request further treatment.

The 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. They will be also asked to confirm that all AEs and SSs experienced since the last re-supply 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.

Periodic reports

A 3-monthly periodic safety report will be submitted to the MHRA to summarise data on safety and usage of atezolizumab 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

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