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

Avelumab as monotherapy for the first-line maintenance treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC) whose disease has not progressed with first-line platinum-based induction chemotherapy.

Information on the Pharmacovigilance system

A prescribing oncologist registers and requests entry of their patients into the Early Access to Medicines Scheme (EAMS) ***MSB0010718C*** **(11648/0003)** via Clinigen Cliniport portal by completing a patient access form (https://cliniport.co.uk).

Upon successful registration on the EAMS, each prescribing oncologist will be provided with an electronic version of the physician's pack containing the following documents:

• Healthcare professionals training slide deck on adverse event reporting
• Patient Access Form to make first drug order and subsequent re-supply requests
• EAMS Treatment Protocol – Information on the pharmacovigilance system and requirements for reporting safety data (this document)
• EAMS adverse event reporting form
• EAMS Treatment Protocol – Information for Healthcare Professionals
• EAMS Treatment Protocol – Information for Patients
• Patient Informed Consent form
• Information for Patients Brochure
• Patient Alert Card
• EAMS Protocol number: 11648/0003

Adverse event/Adverse drug reaction reporting

All Healthcare Professionals (HCPs) involved in the care of patients on the EAMS will be instructed to report all adverse events (serious and non-serious), any exposure during pregnancy (including exposure from male participants of the EAMS) and lactation, medication errors, and overdose, within 24 hours to Merck UK Pharmacovigilance, as specified in the relevant documentation within the physician's pack which shall contain a relevant EAMS AE reporting form. HCPs will be required to confirm to Merck that they understand their obligation to report adverse events before EAMS registration.

Patients/caregivers will be trained by the EAMS Physicians to recognise and document adverse events. Training will be provided by the EAMS Physicians at the time the patient enters the EAMS program.

Each patient will be allocated a unique identifier upon enrolment into the EAMS program for UC. This will allow tracking of patients from baseline and throughout the treatment period.
Patients/caregivers will be instructed to contact their EAMS physician immediately if they experience any adverse events (AEs) which shall be reported electronically via the EAMS AE reporting form directly to Merck or via the MHRA Yellow Card scheme. The EAMS AE reporting form will be available to HCPs via the Clinigen Cliniport portal for relevant entry and onward reporting. The EAMS AE reporting form can also be obtained from Merck UK via the contact details as provided below under contact details.

Merck UK shall collate, store and process ADR/AE data as per internal processes and procedures which shall ensure quality assurance of these data. In the instances where AE/ADR information is either incomplete or missing, the Merck UK Pharmacovigilance team will execute relevant follow-up activities to enable comprehensive ADR/AE assessment and evaluation. Collated data shall be stored in the local inbound module of the global PV database and ADR/AE reports will be linked to the patient via a unique patient identifier. The EAMS AE form (which includes the EAMS number) is populated with a full description of the ADR/AE and submitted preferably by email to the Merck UK Pharmacovigilance department at ICSR_UKI@merckgroup.com

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

Training for healthcare professionals

All healthcare professionals involved with the management of the EAMS will receive a physician's pack upon set up which includes training material for AE reporting. The material includes provisions for recognising, managing and reporting AE/ADRs. HCPs must confirm they have read and understood their AE reporting obligations prior to EAMS registration. To reaffirm the importance of reporting obligations, reminders shall also be provided throughout the duration of the EAMS program at the time of each order.

HCPs will also be provided with pertinent patient-related supporting documents such as the Patients Brochure and a Patient Alert Card to be provided to each patient at initiation of their treatment. HCPs will inform patients/caregivers to report adverse events so they can receive appropriate medical attention

Additional risk minimisation materials

Patient Brochure and Patient Alert Card

A patient brochure and alert card will be given to all patients before they start treatment. The brochure covers immune related adverse events in order to educate patients on the characteristic signs and symptoms of such adverse events.

The patient alert card is a wallet-sized card to be carried that can be shown at all medical visits to HCPs other than the treating physician (e.g. emergency HCPs). The card has contact details of the treating physician and alerts other physicians that the patient is treated with Avelumab. 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 whilst reaffirming the importance of not attempting to self-treat any symptoms without consulting with an HCP first.

Additional information

Drug registry

The prescribing oncologist will be requested to provide the following information by completing a patient access form for each patient to be enrolled on to the EAMS program for eligibility assessment:

Mandatory data

- Demography (age and gender)
- ECOG performance status 0–2
- Confirmation that the patient has locally advanced or metastatic urothelial carcinoma
- Confirmation that the patient has received prior first-line induction treatment with platinum-based chemotherapy regimen and the patient's disease has not progressed following induction treatment
- Description of prior first-line platinum-based chemotherapy regimen administered to the patient prior to enrolling the patient in the EAMS
- Duration of time (in weeks) since last dose of first-line platinum-based chemotherapy prior to first dose of avelumab treatment
- Confirmation that the patient has no prior treatment with an immune checkpoint inhibitor
- Confirmation that the patient has given consent and meets all inclusion criteria
- Confirmation that the patient is fit for treatment and has adequate bone marrow, liver and renal function
- Contraception/pregnancy check (female subjects of childbearing potential and male patients able to father children)
- Confirmation that the healthcare professional understands the risks and treatment guidance for immune-related adverse events associated with avelumab

- Confirmation that all adverse events will be submitted

As part of the EAMS registration the HCP will confirm their understanding and agree to comply with their obligation to report all AEs/ADRs.

All HCP registration, patient registration and stock ordering will be done through Clinigen Cliniport portal: https://cliniport.co.uk

Periodic reports

A 3-monthly periodic report will be submitted to the MHRA.

Contact details

Contact details for reporting AEs: 0208 818 7373

Email Address: ICSR_UKI@merckgroup.com
Telephone Contact: Merck Medical Information number (including out of hours): 0208 818 7373

Contact email for Merck Medical Information: medinfo.uk@merckgroup.com

Contact details for Clinigen Cliniport portal:
Telephone: 01932 824 100
Email: ukcustomerservice@clinigengroup.com