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 and 'off label' medicines 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. In some cases the safety profile of the EAMS medicine may not yet be fully established and it is therefore 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

Healthcare professionals should enroll any patients receiving EAMS medicines in the registry which the pharmaceutical company will have in place to enable systematic collection of information on adverse events.

Suspected adverse drug reactions (ADRs) for any patients, particularly those not enrolled in a study (or registry), can 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. Alternatively, healthcare professionals can report ADRs which occur in patients not enrolled in any study (or registry) directly to the pharmaceutical company who manufactures the EAMS medicine.

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

Prescribing doctors should also consult the relevant detailed information provided by the company.

Information on the Pharmacovigilance system

When a prescribing oncologist requests access into EAMS and a patient is accepted following positive programmed death ligand-1 (PD-L1) testing, they will receive a set of programme materials from the company which will include detailed information on the collection and reporting of adverse events (AEs) and all the necessary forms and contact details.

All Healthcare Professionals involved in EAMS will be instructed to report to the company all serious adverse events (SAEs) within 24 hours and all non-serious adverse events within 7 days of first knowledge of such events. Although pregnancy, overdose, cancer and drug-induced liver injury (DILI) are not always serious by regulatory definition, these events must be handled as SAEs.

If only limited information is initially available, further follow-up will be requested by the company and all events will be followed to resolution or stabilisation.

Training for Healthcare Professionals (HCPs)

Once the prescribing oncologist signs a Letter of Agreement and the patient has been confirmed as expressing PD-L1 on their tumours, the company will arrange the delivery of programme materials and training on recognising, managing and reporting of adverse events. The programme materials provided will include the following:

- **Adverse Reaction Management Guide**
  This guide will ensure understanding of the immunologic aetiology of important adverse reactions, the requirement for more frequent monitoring and/or unique interventions and the guidelines for the management of adverse reactions.

- **Patient Alert Card**
  This is a wallet-sized card to be carried at all times to show at all medical visits to HCPs other than the prescriber (e.g., emergency HCPs). It has contact details of the treating physician and it alerts other physicians that the patient is treated with nivolumab. During the training, the HCP will be instructed to provide a Patient Alert Card to each patient prior to starting treatment.

Additional information

Provision of nivolumab through EAMS is designed to provide early access to this medicine for the treatment of locally advanced or metastatic non-squamous non-small cell lung cancer (NSCLC) after prior chemotherapy in adult patients whose tumours express PD-L1, prior to licensing the product in the UK for this indication.
The treatment physicians will be requested to provide anonymised patient data for each patient to be enrolled in EAMS. This includes:

- Age
- Year of Birth
- Initials
- Gender
- Diagnosis
- Biopsy material availability for PD-L1 status
- Weight
- ECOG PS
- Previous treatment history for Non Squamous NSCLC
- Comorbidities
- Concomitant medications

BMS will also assign a unique patient EAMS number. This number will be communicated back to the prescribing Oncologist to be used in all future communications including re-ordering drug supplies and reporting adverse events.

Once the patient is registered with BMS, the Oncologist will receive a sample requisition form for each patient from BMS. Oncologists will complete the form and send the biopsy materials to the Central laboratory for a PD-L1 test. The Central laboratory will provide test results to the Oncologist and BMS simultaneously, and BMS will provide nivolumab for patients whose tumours express PD-L1.

For patients approved under this scheme and requiring ongoing drug supply, the prescribing Oncologist will be required to complete the Drug Re-supply and Case Report Form every four weeks (except for the first re-supply which will be after two weeks) to order the next two treatment cycles of nivolumab for their patient. The order should be placed two weeks before the patient's next planned cycle is due. They will be requested to provide some additional information including the start date of treatment (first cycle), most recent patient weight, the dates of treatment cycles since last supply, dose received and any new concomitant medications. The prescribing Oncologists will also be asked for confirmation that they understand and agree with the obligations to report any adverse events to BMS and that they are complying with this requirement.

All adverse event data reported will be entered into the BMS safety database and will be linked to the patient by the assigned EAMS Protocol Number and unique patient number. BMS will report all Serious related events to the MHRA within 15 calendar days of receipt by the company. In addition data on the safety and usage of the product under the scheme will be discussed in periodic reports submitted to the MHRA.

Patient Alert Card

Before treatment starts, all patients will have the scheme explained to them by the prescribing oncologist or specialist nurse and will be given a Patient Alert Card.

Contact details

Contact details for reporting AEs:

Email Address: worldwide.safety@bms.com

Facsimile Transmission: 001 609 818 3804

Telephone Contact: 01895 523735 (or 0800 731 1736 for out of hours contact)

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

EAMS@bms.com