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

Nivolumab in combination with ipilimumab is indicated for the first-line treatment of adult patients with unresectable malignant pleural mesothelioma.

Information on the Pharmacovigilance system

Provision of nivolumab and ipilimumab through EAMS is designed to provide early access to these medicines (prior to licensing the products in the UK) as combination therapy for the first-line treatment of adult patients with unresectable malignant pleural mesothelioma. The prescribing oncologist is reminded to adhere to the EAMS Treatment protocol – Information for Healthcare Professionals as provided in the Physician Pack.

Each prescribing oncologist interested in enrolling a patient in the programme should contact Bristol-Myers Squibb (BMS) via email to EAMS@bms.com including their up-to-date Curriculum Vitae (stating GMC number and current institution) and other documents as listed in the Registry Protocol.

To register a patient and request enrolment, the prescribing oncologist is required to complete online training to gain access to the Medidata RAVE system.

Once a prescribing oncologist has registered their intent to participate in the programme, they will receive a set of materials from the company or its designee which will include detailed information on the collection and reporting of Adverse Events/Safety Information and all the necessary forms and contact details. BMS will also arrange training of Healthcare Professionals (HCPs), pharmacists and other relevant team members (see below).

After receiving access, the prescribing oncologist must log into the Medidata RAVE electronic database system, confirm that patient informed consent has been obtained, and then enter the patient's details. The Medidata RAVE system will assign a unique patient identification number to be used in any future communications, including reporting of Adverse Events/Safety Information.

BMS will confirm the eligibility of the patient and once the required documents have been completed, which includes the Letter of Agreement that has been signed by the nominated oncologist and a legal representative from the Trust, an initial drug supply request can then be submitted by the prescriber in the Medidata RAVE system. BMS will supply 6 weeks of EAMS drug supply for each drug request.

The prescribing oncologist (or designee registered in Medidata RAVE) will also be required to request drug re-supply via the Medidata RAVE system. The order should be placed at least two weeks before the next planned cycle is due. When requesting drug re-supply, the prescribing HCP (or any HCP completing the request on their behalf) will also be asked for confirmation that they understand and agree with the obligations to report any Adverse Events/Safety Information to BMS and that they are complying with this requirement.

If concerns regarding the quality or appearance of any of the EAMS drugs supplied arise, the study treatment(s) should not be dispensed and sites should immediately contact BMS Medical Information on 0800 731 1736 or medical.information@bms.com. Batch details and expiry date for the EAMS drug(s) concerned should be included when contacting BMS Medical Information.

Adverse event/Adverse drug reaction reporting

All HCPs involved in EAMS will be instructed to report promptly to BMS (or designee) all Safety Information. This information must be provided no later than one business day or three calendar days, whichever is the earlier after becoming aware of the Safety Information. Safety Information refers to Adverse Events (AEs), Events associated with Special Situations and Pregnancy Related Information.

An **adverse event (AE)** is any untoward medical occurrence in a patient or clinical investigation subject

administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

Although not always adverse events by regulatory definition, the following **Special Situations** (SS) associated with a BMS product(s) must also be reported:

• Overdose
• Medication error and potential medication error

Pregnancy Related Information associated with a BMS product(s) must also be reported. Pregnancy Related Information includes any occurrence of a possible exposure of a pregnant woman to a product (this could involve a pregnant patient or the partner of a male patient or a pregnant female who came in contact with the medication while dispensing) or exposure (to infant) during lactation. All reports of elevated/ questionable or indeterminate beta human chorionic gonadotropins (β hCGs) or positive urine pregnancy tests after administration of a product must also be reported.

If only limited information is initially available, further follow-up will be requested by the company and all Adverse Events/SS will be followed to resolution or stabilisation. Follow-up regarding Pregnancy Related Information (including the course of the pregnancy, and where applicable offspring information) must also be reported to the company.

All Adverse Event/Safety Information reported will be entered into the BMS safety database in accordance with BMS procedures and will be linked to the patient by the unique patient number (assigned in the Medidata RAVE system) and EAMS Protocol Number.

The Scientific Opinion Holder is required to send all Adverse Events/Safety Information for the EAMS products to the MHRA within the agreed timelines.

Training for healthcare professionals

Once the prescribing oncologist has registered their intent to participate in the EAMS, the company or its designee will arrange the delivery of programme materials and training on recognising, managing and reporting of Adverse Events/Safety Information.

Additional risk minimisation materials

Patient Alert Card
Copies of the Patient Alert Card will be provided with the programme materials. This will be given to all patients before starting treatment. It is a wallet sized Patient Alert Card to be carried at all times by the patient during treatment and for at least 5 months after completing treatment 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 physicians that the patient is being treated with nivolumab and ipilimumab. It also contains important 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.

Additional information

Drug registry
The prescribing oncologist will be requested to provide the following information for each patient enrolled in the programme.

Mandatory data

- Condition for which the products are being used for, including primary tumour location
- Age/ Year of birth
- Gender

- Race
- Weight (kg)
- ECOG Performance Status
- History of smoking
- History of occupational asbestos exposure
- Tumour histology
- Number of organs with metastases
- Sites of metastasis
- Underlying co-morbidities
- Concomitant medications
- Dose and duration of nivolumab and ipilimumab treatment(s)
- Discontinuation data
- All Adverse Events/Safety Information

The prescribing oncologist is also requested to inform BMS if a patient discontinues treatment by completing a discontinuation form that is available in the Medidata RAVE system.

Additional data

No additional data will be collected as part of this EAMS.

Periodic reports

Periodic update reports describing the safety and usage of the product under the scheme will also be provided to the MHRA every three months within 30 days of the data lock point as per the EAMS periodic updates/renewal template up until the point of Marketing Authorisation as per the required EAMS process.

Contact details

Bristol-Myers Squibb Medical Information on 0800 731 1736 or medical.information@bms.com.