



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 as monotherapy for the treatment of adult patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma after prior fluoropyrimidine- and platinum-based chemotherapy.

Information on the Pharmacovigilance system

Provision of nivolumab through EAMS is designed to provide early access to this medicine (prior to licensing the product in the UK) as monotherapy for the treatment of adult patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma after prior fluoropyrimidine- and platinum-based chemotherapy. 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 current institution).

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 (AEs) 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 informed consent has been obtained, and then enter the patient's details on the eligibility page of the system. The Medidata RAVE system will assign a unique patient identification number to be used in any future communications, including reporting adverse events.

BMS will check 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 4 weeks (2 cycles) 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 to BMS and that they are complying with this requirement.

If concerns regarding the quality or appearance of the EAMS drug supply arise, the study treatment should not be dispensed and sites should immediately contact BMS Medical Information on 0800 731 1736 or medical.information@bms.com including the batch details for nivolumab.

Adverse event/Adverse drug reaction reporting

All HCPs involved in EAMS will be instructed to report to BMS (or designee) all AEs within one business day of awareness of the event.

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 events associated with a BMS product must be reported:

- Exposure (to fetus) during pregnancy, exposure (to infant) during lactation, and paternal exposure
- Overdose
- Lack of efficacy
- Abuse
- Misuse
- Occupational exposure
- Medication error and potential medication error
- Suspected transmission of an infectious agent e.g., any organism, virus or infectious particle pathogenic or non-pathogenic, via the medicinal product

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.

All adverse event data 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 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.

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 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. 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

- Unique Patient EAMS Number (England Only)
- Age/ Year of birth
- Gender
- Race
- Weight
- ECOG Performance Status
- Condition for which the product is being used for, including primary tumour location
- Tumour histology
- Sites of metastasis
- Number and type of prior systemic treatments received for advanced oesophageal cancer
- Any prior surgery for condition
- Underlying co-morbidities
- Concomitant medications

- Dose and duration of nivolumab treatment
- All adverse events

Additional data

In addition to pharmacovigilance data, additional data will be collected on clinical efficacy and quality of life on a voluntary basis and subject to additional patient consent.

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

Periodic reports

In addition, data on the safety and usage of the product under the scheme will be discussed in periodic update reports submitted to the MHRA.

Contact details

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