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 enrol 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 for a patient into 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.

All Healthcare Professionals (HCPs) involved in EAMS will be instructed to report to BMS (or designee) all AEs within one business day of awareness of the event. Although not always adverse events by regulatory definition, the following events associated with a BMS product must be reported:

- Exposure (to foetus) during pregnancy, exposure (to infant) during lactation, and paternal exposure
- Overdose (defined as the accidental or intentional administration of any dose of a product that is considered both excessive and medically important)
- 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.

The prescribing Oncologist will receive an email reminder on a monthly basis reminding them of the AE reporting requirements for their patients enrolled in this programme.

Training for Healthcare Professionals

Once a Letter of Agreement has been signed by all parties and returned to BMS, the company or its designee 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**
  Brief introduction to nivolumab (indication and the purpose of this tool). This helps to ensure understanding of the immunologic aetiology of important adverse reactions, the requirement of more frequent monitoring and/or unique interventions and also the list of important adverse reactions as referred to above, symptoms and guidelines for the management of adverse reactions. It also includes a reminder to distribute the Patient Alert Card and to educate patients/caregivers about symptoms of important adverse reactions and of the need to report them immediately to the physician.

- **Patient Alert Card**
  This will be given to all patients before they start treatment. It is a wallet-sized Patient Alert 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 physicians that the patient is being treated with nivolumab. It also contains all 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 a HCP first.

Additional information

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 advanced or recurrent gastric or gastroesophageal junction (GEJ) adenocarcinoma after two or more prior systemic therapies. The prescribing Oncologist is reminded to adhere to the EAMS Treatment protocol – Information for healthcare professionals as provided in the Physician Pack.

The prescribing Oncologist will be required to register on the BMS FastTrack online portal (https://fasttrack.bms.com/) in order to enrol patients. Following their registration on the FastTrack online portal, and prior to entering any patient relevant data, clinicians will be able to download the required materials from this BMS portal.

Once a patient has signed the informed consent form, and upon confirmation that consent has been obtained by the physician on the BMS FastTrack online portal, the patient can be registered for enrolment. BMS will check the eligibility and send a letter of agreement to the site for signature by the HCP and a responsible Trust Representative. Once signed by both parties, an initial drug supply request can then be submitted by the Physician in FastTrack.

The treating physician (or any HCP completing the request on their behalf) will also be required to request drug re-supply via the FastTrack online portal 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 2 weeks before the next planned cycle is due. When requesting drug re-supply via the FastTrack online portal, 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. The Prescribing Oncologist is also requested to inform BMS if a patient discontinues by completing a discontinuation form that is available on FastTrack.

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.

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 assigned FastTrack unique patient number (request #) and EAMS Protocol Number.

BMS will report all serious related events to the MHRA via EudraVigilance within 15 calendar days of receipt by the company and non-serious related events within 90 calendar days of receipt by the company. Any related adverse events elicited as part of the optional EQ-5D data collection will be reported in line with the above requirements and in aggregate in the final study report for the observational research.

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

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)

Additional contact details for the EAMS programme (excluding AE reporting):

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