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.

EAMS Indication:

Lutetium (^{177}Lu) vipivotide tetraxetan is indicated for the treatment of adult patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor (AR) pathway inhibition and taxane-based chemotherapy or who are not medically suitable for taxanes.

Information on the Pharmacovigilance system:

A prescribing physician may request entry of their patients into the Early Access to Medicines Scheme (EAMS Protocol Number 35903/0001) by completing and submitting an Initial Application and Drug Supply Request Form. Upon review of the individual request and fulfilment of the eligibility criteria, AAA will provide EAMS materials which will include information on the collection and reporting of adverse events.

All Healthcare Professionals (HCPs) involved in the care of patients on EAMS will be instructed to report all adverse events (AEs) (including initial and follow up reports) within one business day of awareness on the provided electronic adverse event report form. Special situations (SS) with or without an associated AE are to be handled the same as AEs.

An ***AE*** is defined as any untoward medical occurrence in a patient or clinical-trial subject administered a medicinal product and which does not necessarily have to have a causal relationship with this treatment. An adverse event can therefore be any unfavourable and unintended sign (e.g. an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether considered related to the medicinal product.

Special situations (SSs) are cases of pregnancy of a partner up to 3 months after cessation of treatment, congenital abnormalities in children of parents treated with the product, occupational/accidental exposure, lack of efficacy/lack of therapeutic efficacy, unexpected benefit/potentially desirable side effects, patients hospitalised/hospitalisation prolonged (even if cause of hospitalisation is unknown) medical/surgical intervention, disease progression and aggravation, quality defects, medical device malfunctions including use error and abnormal use.

The AE reporting form and Drug Exposure in Pregnancy form is available electronically to physicians taking part in this EAMS. Any issues accessing the AE reporting form and Drug Exposure in Pregnancy form should be addressed by sending an email to uk.patientsafety@novartis.com. Additional follow-up may be requested on all reports received to obtain further information.

All AEs and SSs reported will be entered into the Novartis safety database and will be linked to the patient by the specific EAMS protocol number and unique patient number.

Training for Healthcare Professionals (HCPs)

A Physician Pack containing the Treatment Protocol for Healthcare Professionals, the Treatment Protocol for Patients, the Treatment Protocol on Pharmacovigilance Systems, the EAMS AE reporting form/Drug Exposure in Pregnancy form, the safety training slide set and Patient Alert Card will be provided to the HCPs. In addition to the Physician Pack, comprehensive AE and SS training will be provided to all relevant HCPs prior to commencement of patient treatment, focusing on recognising, managing and reporting AEs and SSs during the scheme. Equally, the HCP's obligation to keep their patients fully informed on their

treatment will be emphasised. Pertinent patient related supporting documents such as the Patient Alert Card will be provided to facilitate this activity.

Additional information:

The prescribing physician should carefully read the information provided in the rest of this document. Each prescribing physician interested in enrolling a patient in the programme should submit an initial request via the Novartis Grants, External Studies and Managed Access System (GEMS) via https://www.novartis.com/our-focus/healthcare-professionals/managed-access-programs. The prescribing physician will be required to register with Novartis Managed Access Programme Portal and patient details will need to be entered into the portal for each individual application. A unique initial request ID will be assigned to each eligible patient enrolled onto EAMS. This unique initial request ID will be used for future drug re-supply requests and adverse event reporting. As part of the requirement of the EAMS , AEs/SSs will be collected via uk.patientsafety@novartis.com and entered into the Argus safety database and the demographics and clinical characteristics of the patients enrolled in the EAMS will be collected using MACRO™.

Novartis will request the baseline demographics data at the time of initial application and additional information at the time of re-supply request. The purpose of this data collection (registry) is to ensure the safe and effective use of the product in line with the EAMS Treatment protocols and EAMS scientific opinion.

The prescribing physician will be requested to provide the following information by completing an Initial Application and Drug Supply Request for each patient to be enrolled on to the programme for eligibility assessment:

- Patient age and date of birth
- Patient sex
- Disease/condition to be treated (including date of diagnosis of prostate cancer and diagnosis of mCRPC)
- Previous therapy for prostate cancer (drug name and duration)
- Administration dose and number of cycles
- Co-morbid disease
- Concomitant medication
- PSA (only biomarker) stage of cancer (TNM stage and Gleason grade or score)
- PSMA PET scan date

Novartis will review the application for eligibility. If a patient is deemed eligible for EAMS, Novartis will assign a unique EAMS number and communicate it to the requesting physician.

An EAMS Agreement Letter with Novartis will be required to be signed by the prescribing Physician, the Trust and Novartis. The MAP Agreement Letter will be signed either on a per patient basis or on a Trust basis. Drug supply will only be shipped once a fully executed MAP Agreement Letter and attestation has been completed.

For patients approved under this scheme and requiring ongoing drug supply, the HCPs will be required to complete the Re-supply Form on GEMS to request further cycles of treatment. The HCPs will be asked for

confirmation that they understand and agree to comply with their obligations to report all AEs and SSs to Novartis and that they are complying with this requirement. They will be also asked to confirm that all AEs and SSs experienced since the last re-supply request have been reported or there are no new AEs to report. HCPs will also be requested to confirm at the time of first re-supply request if the patient alert card has been given to the patient and the patient understands the purpose of the Patient Alert Card. HCPs will also be requested to confirm that patient agrees to carry the Patient Alert Card with them at all times.

HCPs should also report all known and suspected adverse drug reactions (ADRs) (i.e. those AEs which are related to the use of $^{(177)}$Lu-PSMA-617) to the MHRA via the Yellow Card scheme, www.mhra.gov.uk/yellowcard. In addition to this, the EAMS patient ID number should be provided in the report narrative to help the MHRA identify that the AE is related to EAMS product and to help Novartis link the AE report to the correct EAMS patient.

A 3-monthly periodic safety report will be submitted to the MHRA to summarise data on safety and usage of (177)Lu-PSMA-617 under the scheme.

For NHS England only - additional requirement for registering a patient:

Following notification from Novartis of eligibility approval, the physician must complete a Blueteq form online and register their patient with NHS England, which is located at https://www.blueteq-secure.co.uk/Trust/default.aspx. Once the Blueteq form has been completed, an approval email will be received by the user and pharmacy stating the request has been approved, also stating an EAMS number. This EAMS number must be communicated back to Novartis.

Contact details: obu.medical@novartis.com

AE reporting: uk.patientsafety@novartis.com (Contact number: 0845 601 1387)

Contact Details for Medical Information
Tel: +44 (0)20 7258 5200
Email: infomed@adacap.com