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
Treatment of paediatric and adult patients with thymidine kinase 2 deficiency (TK2d) with an age of symptom onset on or before 12 years.

Information on the Pharmacovigilance system

A prescribing physician may request entry of their patients into the Early Access to Medicines Scheme (EAMS Protocol Number- 00039/0004) by completing and submitting an Initial Application and Drug Supply Request Form on the Bionical Emas portal. Access will be provided to applicable EAMS materials which will include information on the collection and reporting of adverse events.

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 contact Bionical Emas at Patient.Access@BionicalEmas.com. The prescribing physician will be required to register on the Bionical Emas Portal and patient details will need to be entered into this system for each individual application. A unique patient ID will be assigned to each eligible patient enrolled onto EAMS. This unique patient ID will be used for future drug re-supply requests and adverse event reporting. Requests for resupplies and management of existing patients including notification of discontinuation are also through the Bionical Emas portal.

Adverse event/Adverse drug reaction reporting

All Healthcare Professionals (HCPs) involved in the care of patients on EAMS will be instructed to report all adverse events (AE), and special situations (SS) whether or not there is an associated AE within one business day of awareness on the provided report form to GLOBALICSR@ucb.com.

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

The SS may include the following:

- Use of a medicinal product during pregnancy and breastfeeding
- Overdose
- Off-label use
- Medication error
- Lack of therapeutic efficacy
- Disease progression
- Drug Interactions
- Death cases
- Product Complaints with associated AEs/SSs
- Product Complaints without associated AEs/SSs

The AE reporting form is available electronically to physicians taking part in this EAMS through the Bionical Emas Portal. Additional follow-up may be requested by UCB on all reports received to obtain further information.

All AEs and SSs reported will be entered into the UCB safety database and will be linked to the patient by the specific EAMS protocol number and unique patient number. The patient's identity will remain anonymous.

The Scientific Opinion Holder is required to send ADRs suspected to be related to the EAMS products to the MHRA within the agreed timelines.

Training for healthcare professionals

In addition to the information provided on the Bionical Emas portal related to AE reporting, at the time that a patient request is approved, a representative from the UCB Medical Affairs team will provide, either face-

to-face or virtually, a training session for the healthcare professionals identified on the portal as responsible for the care of the patient. It is expected that this will be the treating physician, and associated pharmacist. The training session will cover the safety profile of doxecitine and doxribtimine, the management of AEs/ADRs and reporting of these events. In addition, information in relation to dosing and administration, including the preparation of doxecitine and doxribtimine will be provided.

Additional risk minimisation materials

There are no specific risk minimisation materials associated with doxecitine and doxribtimine.

Additional information regarding the use of doxecitine and doxribtimine can be found in the Treatment Guideline for Doxecitine and Doxribtimine for Patients with Thymidine Kinase 2 Deficiency (TK2d) [TK0115], Pharmacy Manual which are located on and can be downloaded from the 'Your Patient Access' portal as well as in the HCP and Patient treatment protocols.

Mandatory data

UCB will request the certain 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's initials
- Date of birth
- Gender
- Diagnosis, date of diagnosis,
- Eligibility Criteria
- Laboratory Test Results
- Medical history
- Concomitant medications
- Prescribed dose, frequency, route; dates and duration of treatment (after treatment initiation)
- Other supporting information

UCB will review the application for eligibility to receive treatment under the EAMS programme. If a patient is deemed eligible for EAMS, a unique patient number will be assigned, and this will be communicated to the requesting physician.

As mentioned above all AEs and SSs reported will be entered into the UCB safety database and will be linked to the patient by the specific EAMS protocol number and unique patient number. The patient's identity will remain anonymous.

Additional data

The primary goal of this programme is to provide access to doxecitine and doxribtimine through the EAMS programme.

However, capturing Real World Data (RWD), with its potential to provide important information for the benefit of future participants, is increasingly being collected throughsuch programs, especially when it comes to rare diseases. For this reason, there will be the optional collection and use of additional data. This will contribute towards better understanding of early real world clinical experience of treatment with doxecitine and doxribtimine. **Entry status into the RWD collection component will have no impact on**

access to doxecitine and doxribtimine and is not mandated via the EAMS programme and is subject to patient consent.

The additional data to be collected includes:

- Clinician and Caregiver Global Impression Scales of TK2d severity and change.
- Developmental motor milestone checklist.
- Feeding and respiratory and ventilatory status.

Periodic reports

A 3-monthly periodic safety report will be submitted to the MHRA to summarise data on safety and usage of doxecitine and doxribtimine under the scheme. A final periodic report will be provided following scientific opinion expiry and will be submitted within 1 month after EAMS expiry.

Contact details

AE reporting: GLOBALICSR@ucb.com

Access to the EAMS program: Patient.Access@BionicalEmas.com