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:

Berotralstat is indicated for routine prevention of recurrent attacks of hereditary angioedema (HAE) in adult and adolescent patients aged 12 years and older.

Information on the Pharmacovigilance system:

A prescribing physician may request entry of their patients into the Early Access to Medicines Scheme (EAMS 32080/0001) (Protocol Number BCX7353-309) by completing and submitting an Initial Application and Drug Supply Request Form. Upon review of the individual request and fulfilment of the eligibility criteria, BioCryst will provide EAMS materials which will include information on the collection and reporting of adverse events and safety training. Eligible patients will be provided with a unique EAMS ID number. These EAMS materials include:

• Drug Supply Form and Drug re-supply request form
• EAMS Treatment Protocol – Information on the pharmacovigilance system and requirements for reporting safety data (this document)
• EAMS adverse event reporting form
• EAMS Treatment Protocol – Information for Healthcare Professionals
• EAMS Treatment Protocol – Information for Patients
• Patient Informed Consent form
• Patient Alert Card

Adverse event reporting requirements

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 electronic report form.

The SS may include the following:

- Use of a medicinal product during pregnancy and breastfeeding
- Overdose
- Misuse
- Abuse
- Off-label use
- Medication error
- Occupational exposure
- Lack of therapeutic efficacy
- Disease progression
- Suspected Transmission of Infectious Agent (STIAMP)
- Drug Interactions
- Class action lawsuits
- 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. Any issues accessing the AE reporting form should be addressed by sending an email to access@inceptua.com. Additional follow-up may be requested on all reports received to obtain further information.

All AEs and SSs including reported will be entered into the BioCryst 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.

Patients should be advised by their HCP to report any AEs they experience to their physician or directly to the MHRA via the Yellow Card Scheme www.mhra.gov.uk/yellowcard or call toll free at 0800 731 6789 (10am to 2pm Monday-Friday only).

Training for Healthcare Professionals (HCPs)

In addition to the Physician Pack, comprehensive training on reporting of AE, SS's and pregnancies will be provided to all relevant HCPs prior to commencement of patient enrollment and treatment, focusing on recognising, managing and reporting AEs and pregnancies during the scheme. Equally, the HCP's obligation to keep their patients fully informed on the benefits and risks of their treatment will be emphasised. Pertinent patient related supporting documents such as the Patient Alert Card will be provided to facilitate this activity. The physician will be informed to provide this Patient Alert Card to each patient prior to starting treatment, and to counsel their patient on why they have recieved the Patient Alert Card and what they should do with it i.e the patient should be advised to provide the card to all HCPs responsible for prescribing other than the specialist, for example a GP or emergency/ hospital physican.

Discontinuations for adverse events

Decisions on discontinuations for AEs should be made on an individual basis, taking into account each patient's benefit risk assessment. Those patients who are receiving benefit may continue berotralstat if they consider the medical risk is acceptable. AEs with berotralstat occurred early in treatment and improved with time, in many patients while continuing berotralstat. If a patient discontinues berotralstat because of an AE, this should be clearly reported on the AE reporting form. This information will be provided to MHRA in the periodic reports.

Additional information:

Drug Registry

BioCryst will request the baseline demographics data at the time of initial application and additional information at the time of re-supply request. This information will be recorded in a secure, password protected database. 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

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:

- Condition for which the product is being used
- Patient's initials
- Year of birth
- Gender
- Average frequency of HAE attacks per month over last 3 months Location of last HAE attack
- Average severity of symptoms of attack/s over last 3 months (negligible, mild, moderate, severe)
- Severity of symptoms of worst attack over last 3 months (negligible, mild, moderate, severe)
- On demand and prior prophylactic treatment(s) for HAE (if applicable)
- Comorbidities, including baseline data on history of diseases that may be relevant to know, for example cardiac or liver disease.
- Concomitant medications
- Dose and duration of treatment
- Weight (Kg)

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

HCP in England will be required to register their patient with NHS England using the BlueTeq form. Assigned EAMS numbers should be used for all future communications including re-supply requests and reporting of any adverse events.

Patient Alert Card – This will be given to all patients before they start treatment. It is a wallet-sized 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 HCPs that the patient is receiving berotralstat. It includes information on important potential risks which may be associated with berotralstat treatment, i.e.:

- QT prolongation in patients with moderate or severe hepatic impairment (Child-Pugh Class B or C), body weight <40 kg, or in patients with concomitant intrinsic or extrinsic factors that may be associated with QT prolongation;
- Important drug-drug interactions. Certain medicines should be used cautiously as they may increase the risk of serious side-effects which means that it is important for HCPs to be aware of the advice on how to reduce these risks.

Re-supply Form – For patients approved under this scheme and requiring ongoing drug supply, the HCPs will be required to complete the Re-supply Form provided in the physician pack to request further cycles of treatment. The HCPs will also be asked for confirmation that they understand and agree to comply with their obligations to report all AEs and SSs to BioCryst 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.

Adverse event reporting – All HCPs involved in the care of the patient on the EAMS should report all adverse events (serious and non-serious, related and unrelated) and special situations including overdose, pregnancy and related events, and known side effects (Adverse Drug Reactions or ADRs) listed in the Treatment Protocol for HCPs for berotralstat to the MHRA via the Yellow Card scheme, www.mhra.gov.uk/yellowcard or to BioCryst. The treating physician should use the provided AE reporting form. While reporting these AE and ADRs, reporters are requested to state the manufacturer and that the product is unlicensed on the AE report. 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 BioCryst link the AE report to the correct EAMS patient.

If a patient experiences an AE which could represent a cardiac arrythmia or experiences a pregnancy, BioCryst will follow-up with a specialised form to obtain structured information on these occurrences to enable comprehensive assessment and evaluation.

Periodic reports – A 3-monthly periodic safety report will be submitted to the MHRA to summarise data on safety and usage of berotralstat under the scheme.

Contact details

Contact details: medinfo@BIOCRYST.com

AE reporting: clinicalsafety@propharmagroup.com