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

The treatment of hereditary angioedema (HAE) attacks in adult and adolescents aged 12 years and older.

Information on the Pharmacovigilance System

Healthcare Professionals (HCPs) participating in the EAMS program will be granted access to the designated vendor, Inceptua Managed Access Portal (IMAP) to submit their medical license and institutions details for validation and registration.

Enrolment of patients into the EAMS program by a HCP will be initiated through the IMAP portal. Registered HCP will be granted access to an electronic Patient Access Form (ePAF) via the IMAP portal to provide anonymised patient information and complete the inclusion/exclusion criteria for Kalvista to check patient eligibility against the EAMS criteria. A unique anonymized identifier is assigned automatically to each patient once the ePAF is completed. The identifier is used for all treatment orders/re-supply requests and when entering real-world data and AE/adverse drug reactions reporting by the HCP. Any patient data entered via IMAP will be pseudonymized with only the HCP being able to link patient identity and the unique anonymized identifier.

HCP will be notified if their patient request is approved, allowing them to submit an initial order for sebetralstat via the IMAP portal, but only once the following required documents/details have been provided:

- Regulatory and/or Import Approval
- Confirmation of patient informed consent
- Necessary HCP declarations within the ePAF
- Pharmacy details for shipment of drug

If the eligibility criteria are not met for a particular patient, the request will be rejected, and the requesting HCP will be notified.

Upon successful registration, each HCP will be granted access to the following EAMS materials via the IMAP portal.

- EAMS Study Protocol
- EAMS Treatment Protocol – Information on the pharmacovigilance system and requirements for reporting safety data (this document)
- EAMS Adverse Event Reporting Form
- EAMS Pregnancy Reporting Form
- EAMS Treatment Protocol – Information for Healthcare Professionals
- EAMS Treatment Protocol – Information Patient Information and Assent Forms

Adverse Event/Adverse Drug Reaction Reporting

Prior to enrolment of a patient into the program, HCPs will be required to understand their obligations regarding reporting of all adverse events/ADR and special situations reports (SSRs) as per the EAMS Study protocol.

All HCPs involved in the EAMS program will be instructed to report all adverse events/ADRs/SSRs within one business day of awareness using the EAMS adverse event reporting form. SSRs with or without an associated AE are to be handled the same way as AEs/ADRs. All pregnancy cases to be reported using the EAMS pregnancy reporting form.

If only limited information is available initially, further follow-up will be requested by the company and all events will be followed to resolution or stabilisation.

During the EAMS program, the designated vendor Inceptua will send a monthly blanket email reminder to participating HCPs to remind them to report adverse events/ADRs per the program instructions.

Upon request of sebetralstat drug supply, HCPs will be asked if there have been any AEs/ADRs/SSRs report following the last dose?", and "If "Yes", whether they have been reported according to the program instructions." Drug supply will only be initiated if they answer Yes.

All reported AEs/ADRs (serious and non-serious) including SSRs reported by HCPs will be entered onto the KalVista Global Safety Database. All serious suspected adverse drug reactions (ADRs) will be reported to the MHRA within 15 calendar days of receipt. All suspected ADRs with a fatal outcome will be reported to the MHRA within 7 calendar days of receipt, further information will be provided within 8 days.

All non-serious suspected ADRs will be reported to the MHRA within 90 calendar days of receipt.

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

HCPs involved in the EAMS program will be required to read and understand their obligations regarding adverse event reporting before enrolling a patient into the program.

Additional Risk Minimisation Materials

Not applicable.

Additional Information

Drug Registry

To ensure sebetralstat is being used per the EAMS study protocol, HCPs will document and capture patient baseline data via the IMAP portal.

The following mandatory baseline data in relation to sebetralstat safety will be collected.

- Condition which the product is being used for
- Patient Age
- Patient Gender
- Dose and uration of treatment
- Underlying co-morbidities
- Concomitant medications
- All medically confirmed adverse events

Additional Data

The following additional data will be collected

Patient demographics will comprise:

- Height
- Weight
- Race/ethnicity (where permitted)
- Clinical background

Patient's clinical information will comprise:

- Age at diagnosis/first attack
- HAE type and how confirmed
- Family history details
- Number of attacks experienced/treated in the last 12 months

- Details of any preventive treatments prescribed
- Details of most recent attack, including date, duration, symptoms/severity, location(s) affected
- Details of on-demand treatment(s) employed for most recent attack (drug name, dosing, when initiated, time to resolution)
- Diagnosed comorbidities
- Details of concomitant medications
- AECT-4 (Angioedema-control test, 4-week recall) instrument
- EQ-VAS (Visual Analogue Scale)

Periodic Reports

In addition, data on safety and usage of the sebetralstat under the scheme will be discussed in 3 monthly periodic reports prepared by KalVista. These reports will be submitted to the MHRA every 3 months for the first year after positive scientific opinion.

A final periodic report will be provided following scientific opinion expiry and will be submitted within 1 month after EAMS expiry.

Contact details

Contact details for reporting adverse events/ADRs
Email transmission: kalvista.safety@arriello.com
Fax transmission fax to +420 296 181 216

Contact details for the EAMS programme (excluding AE reporting)
Inceptua Ltd, Email: access@inceptua.com