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.

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

Cipaglucosidase alfa in conjunction with miglustat is indicated in the long-term treatment of adult symptomatic patients with confirmed diagnosis of late-onset Pompe disease (acid α-glucosidase [GAA] deficiency) who have received enzyme replacement therapy with alglucosidase alfa for ≥ 2 years.

The posology is as follows:

- Cipaglucosidase alfa (105 mg powder for concentrate for solution for infusion/vial): the dosing regimen is 20 mg/kg administered intravenously every other week (QOW).

- Miglustat (65 mg capsule, hard): the dosing regimen is 260 mg (4 capsules) for adults weighting ≥ 50 kg or 195 mg (3 capsules) for adults weighting ≥ 30 kg to < 50 kg. Miglustat capsules are administered QOW, orally, one hour prior to cipaglucosidase alfa IV infusion.

Information on the Pharmacovigilance system

A prescribing physician may request entry of their patient(s) into the Early Access to Medicines Scheme (EAMS 50636/0001) by completing and submitting an Initial Application at: https://www.amicusrx.com/advocacy/expanded-access/

Upon review of the individual request and fulfilment of the eligibility criteria, Amicus will provide the prescribing physician with access to a secure portal that contains EAMS materials which will include information on the collection and reporting of adverse events. Eligible patients will be provided with a unique EAMS ID number.

The EAMS materials include:

Scheme application and pharmacy set-up:
- Initial Application and Drug Supply Request Form
- Drug Re-Supply Request Form (includes AE reporting reminder)

Information for the physician:
- EAMS Treatment Protocol – Guidance for treatment administration, including managing any known risks
- Adverse Event Management Guide – Information on the pharmacovigilance system and requirements for reporting safety data (this document)
- EAMS Case Report Form to collect information on patients progress during scheduled visits
- EAMS adverse event reporting form

Information for the patient:
- Patient informed consent form
- Treatment protocol for patients
- Patient Guide
- Patient Alert Card

Adverse event/Adverse drug reaction reporting

All Healthcare Professionals (HCPs) involved in the care of patients participating in the EAMS program are requested 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 adverse event reporting form.

Special situation reports 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
- Drug Interactions
- Death cases
- Product Complaints with associated AEs/SSs
- Product Complaints without associated AEs/SSs

The AE reporting form will be made available to all physicians taking part in this EAMS. Any issues in completing the form should be addressed by sending an email to drugsafety@amicusrx.com.

Additional follow-up may be requested by Amicus on all reports received to obtain further information.

All AEs and SSs reported will be entered into the Amicus 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.

Periodic reports, summarising the emerging safety data for cipaglucosidase alfa/ miglustat, will be reported to the MHRA. Any change to the benefit-risk profile of the product will be notified to physicians participating in the EAMS by the Amicus medical team immediately.

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).

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

Once patient eligibility is confirmed, Amicus will provide requesting HCPs with the EAMS materials described above and provide training on this AE Management Guide and associated AE reporting form. HCPs will be required to confirm their understanding of obligations regarding adverse event reporting at this time. Additionally, there are no mandatory visits, tests, or assessments required for this registry. All visits will be scheduled and conducted according to the clinical site's standard of care. HCPs must provide adequate oversight and monitoring to ensure the safe and effective use of cipaglucosidase alfa/miglustat that is in line with the treatment protocol for healthcare professionals. The collection of real world data in the electronic data capture (EDC) system is voluntary.

Additional risk minimisation materials

Patient Alert Card: Patients will be provided with a patient alert card, which they must always carry with them. This card summarizes the symptoms of potential adverse effects of the treatment and gives advice on what to do if these symptoms develop. The patient alert card also informs other HCPs that the patient is receiving the treatment and provides the company's contact details.

Additional information

Drug registry

Amicus will request baseline patient demographic data at the time of initial application. 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. Additional follow-up data for patient visits will be reported in accordance with the clinical site's standard of care or clinical judgment.

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 program for eligibility assessment:

Mandatory data

The following information will need to be collected at the time of initial application:

- Patient Age;
- Patient Gender;
- Pompe disease diagnosis including molecular confirmation of *GAA* pathogenic variants and enzyme assay;
- Medical history and underlying co-morbidities;
- Dose and duration of treatment and other relevant dosing information;
- Concomitant and prior medications

Additional data

Additional follow-up data for patient visits will be reported in accordance with the clinical site's standard of care or clinical judgment:

- Pompe disease history;
- Physical examination (including height, weight, blood pressure, heart rate examination of general appearance as well as standard systems);
- Laboratory test results (pregnancy test, haematology; biochemistry (including AST and ALT); urinalysis (including biomarker evaluation of muscle damage such as creatine kinase); urine Hex4);
- ECG: 12-lead ECG;
- Pulmonary function tests;
- Muscle strength test;
- Physical functioning (Six-Minute Walk Test)

The following PRO data will be collected on a voluntary basis, and subject to patient consent:

- PRO outcomes: Quality of life questionnaire (EQ-5D-5L), Fatigue Severity Scale)
- Healthcare encounters & need in assistance: Ambulation, Respiratory assistance

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

Periodic reports

A 3-monthly periodic report will be submitted to the MHRA to summarise data on safety and usage of cipaglucosidase alfa in conjunction with miglustat.

Contact details

Amicus general enquiries and EAMS support:

Phone: +44 (0)1753 888567

Email: EAMS@amicusrx.com

Contact details for reporting Adverse Events/Special Situations:

Email: drugsafety@amicusrx.com