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 late-onset Pompe disease (LOPD) in symptomatic patients who have received Pompe disease ERT with alglucosidase alfa for ≥ 2 years.

Treatment of infantile-onset Pompe disease (IOPD) in symptomatic patients ≥ 1 year old who have received Pompe disease ERT with alglucosidase alfa for ≥ 6 months.

Infusion of avalglucosidase alfa at home may be considered for patients who are tolerating their infusions well and have no history of moderate or severe infusion-associated reactions (IARs) for a few months. The decision to have a patient move to home infusion should be made after evaluation and upon recommendation by the treating physician.

Information on the Pharmacovigilance system

When a prescribing physician requests entry into the EAMS scheme they will receive a physician pack which includes information on reporting of adverse events (AEs) and all the necessary forms and contact details (see below).

In addition, by contacting GB-EAMS-Pompe@sanofi.com, each prescribing physician who is approved for entry into the EAMS will be able to obtain electronic copies of the documents contained in the physician's pack:

The physician's pack will contain a copy of all documents being used in EAMS:
- Instructions on entering patients into EAMS
- Physician form for registering the patient for EAMS
- Treatment Protocol for Health Care Professional (HCP)
- Treatment Protocol for Patients (Information for patients and parents/guardians)
- Patient Alert Card
- Avalglucosidase alfa EAMS Adverse Event Report Form (for HCP)
- HCP Training slides
- Pregnancy Information Form
- Drug Hypersensitivity Questionnaire
- Homecare Training Slides

Adverse event/Adverse drug reaction reporting

All HCPs, (physicians, pharmacists and nurses (including those involved in the provision of homecare)) involved with the EAMS will be directed to report any adverse events (AEs), any pregnancies/drug exposure via parent, lack of efficacy, occupational exposure, transmission of infectious agents, off-label use, unintended beneficial effect, medication errors, overdose, misuse, abuse, or drug interactions, within 1 working day using the Avalglucosidase alfa EAMS Adverse Event Report Form (for HCPs) included in the physicians pack.

Upon enrolment into the Avalglucosidase alfa EAMS, Sanofi will allocate a unique identifier to each patient. This will allow tracking of patients from baseline and throughout the treatment period. This will also be used for monitoring safety information.

This unique identification number will be composed of the code for the institution and 3-digit patient's identifier. For example, the first patient enrolled in Salford Royal NHS Foundation Trust would have the code SA-001. This number will remain in a database of patients entered into EAMS. This identifier is required from the site and homecare company when returning AE data.

The patient or patients parents/guardian's (as appropriate) will be trained to contact the emergency services or their EAMS physician immediately if the patient experiences any of the following signs/symptoms: (Infusion associated reactions including hypersensitivity and anaphylactic reactions, with or without development of IgG and IgE antibodies).

Observed signs and symptoms of hypersensitivity/anaphylactic/Infusion associated reactions:

Anaphylaxis: Respiratory distress, chest pressure, generalized flushing, cough, dizziness, nausea, redness on palms, swollen lower lip, decreased breath sounds, redness on feet, swollen tongue, itchy palms and feet, and oxygen desaturation.
Severe hypersensitivity: Respiratory failure, respiratory distress and rash.
Infusion associated reactions (IARs): Mild to moderate symptoms including: chills, cough, diarrhoea, erythema, fatigue, headache, influenza like illness, nausea, ocular hyperaemia, pain in extremity, pruritus, rash, rash erythematous, tachycardia, urticaria, and vomiting.
Severe IARs including symptoms of chest discomfort, nausea and increased blood pressure.

All safety information identified or recorded will be reported by the EAMS Physician to the Sanofi Pharmacovigilance team using the Avalglucosidase alfa EAMS Adverse Event Report Form. If Safety information is identified by the Homecare staff, the information will be reported to the EAMS physician with the Sanofi PV team on copy (so as to avoid delays). The EAMs Physician is ultimately responsible for ensuring that Sanofi is aware of all safety data related to their EAMS patients and hence at 2 weekly intervals in line with the patients treatment schedule Sanofi will require the EAMS physician to return an Adverse event reporting form for each patient, indicating the patients status post infusion. This process will continue throughout the scheme including every two weeks after initiation of treatment, until the end of EAMS for a particular patient. For patients who withdraw from the EAMS every effort will be made to obtain follow-up information for up to 3 months after withdrawal.

The Sanofi Pharmacovigilance team will collect additional information from the centres, including adverse events of special interest [AESIs], pregnancies, treatment discontinuation and/or product complaints. These will be recorded on the appropriate Sanofi data collection form. All AEs will be notified to Sanofi Pharmacovigilance either directly by the EAMS physician for any infusions taking place in a hospital setting, or indirectly via the homecare staff for patients who are receiving treatment in a home setting. The homecare company will notify the EAMS physician with Sanofi pharmacovigilance copied in to the email within 1 working day of their awareness. Reconciliation will be completed by the physician.

In accordance with Sanofi pharmacovigilance procedures and in alignment with the EMA GVP module VI guidance and the MHRA Exceptions and modifications to the EU guidance on good pharmacovigilance practices that apply to UK marketing authorisation holders and the licensing authority, all AEs received by the Sanofi pharmacovigilance team will be validated, assessed for causality and reported to MHRA within 15 calendar days of day zero for serious cases and 90 calendar days of day zero for non-serious cases if appropriate.

All AE reports will be followed-up with the EAMS physician as necessary to obtain supplementary detailed information significant for the scientific evaluation of the cases. The data management of all AE/safety information will be in accordance with Sanofi pharmacovigilance procedures and the guidance listed in section VI. B4 of EMA GVP module VI and the MHRA Exceptions and modifications to the EU guidance on good pharmacovigilance practices that apply to UK marketing authorisation holders and the licensing authority.

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 they receive in the physician's pack upon set up, all HCPs involved with the management of the EAMS will receive training from Sanofi.

Before requesting to register the patients into EAMS, each participating HCP administering avalglucosidase alfa will be trained by the Sanofi medical team. This will include a presentation of key clinical data, product information, the infusion protocol, the pharmacy manual on reconstitution and storage, the logistics of EAMS, the AE reporting process, including details on the completion of the Avalglucosidase alfa EAMS Adverse event Report Form, and a presentation to make the participating HCPs aware of the additional risk minimisation measures. The training will be documented and participation sheet(s) kept on record by Sanofi.

The training will pay particular attention to recognising, managing and reporting adverse events and ensuring that participating HCPs are aware of the additional risk minimisation measures that have been put in place and the necessary actions required by them as a result.

As part of this training, the HCP will receive and will be asked to provide a Patient Alert Card to each patient/their parent(s)/Guardian(s) as appropriate at initiation of their treatment (see below- Additional risk Minimisation materials).

Additional risk minimisation materials

Patient Alert Card:

Before treatment starts, all patients/their parents/guardians (as appropriate) will have the scheme explained to them by the treating physician and will be given a Patient Alert Card. This is a wallet- sized card and the patient/their parent/ guardian must be instructed to always carry it with them. It summarises what to do should they experience any side effects and ensures they are aware of the signs and symptoms to look out for. In addition, it serves to inform any other healthcare professional that may treat the patient that they are receiving Avalglucosidase alfa through an early access scheme. Further it provides information about their physician's out of hours contact details and the Company's contact information.

HCP Training Slides:

All HCPs involved with the management of the EAMS will receive training from Sanofi that includes the additional risk minimisation measures for Avaglucosidase alfa.

The training will pay particular attention to recognising, managing and reporting adverse events and ensuring that physicians are aware of the additional risk minimisation measures that have been put in place and the necessary actions required by them as a result.

As part of this training, the HCP will receive and will be asked to provide a Patient Alert Card to each patient/their parent(s)/Guardian(s) as appropriate at initiation of their treatment (see above).

Homecare Training Slides:

All HCPs involved with the management of the EAMS in Homecare setting will receive training from Sanofi that includes the additional risk minimisation measures for Avaglucosidase alfa.

The training is aimed at HCPs who will perform infusion at home to increase awareness of the following risks "Medication error in the home infusion setting" and "Infusion associated reactions including hypersensitivity and anaphylactic reactions, with or without development of IgG and IgE antibodies" and ensure awareness of the risks associated with home infusion and guidance on how to minimise them. The training will also pay particular attention to recognising, managing and reporting adverse events and ensuring that are aware of the additional risk minimisation measures that have been put in place and the necessary actions required by them as a result. This training deck has been created specifically for the home infusion team should the physician decide to transition the patient to homecare.

Additional information

Mandatory data

The following information will need to be collected for all EAMS products:

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

Additional data
The data being collected, and their use are described in detail in The 'Information and consent form for HCP's'. Entry criteria must be met, and baseline demographic will be provided to Sanofi. No further data will be collected.

Periodic reports
Sanofi will produce a 6 monthly periodic report of all AE reports received via the EAMS following agreement with the MHRA as no patients enrolled at 3 months and then revert back to 3 monthly periodic reports. The first data lock point (DLP) will be 6 months from the date of the MHRA's scientific opinion. Submission of the report will be 1 month post DLP. Sanofi will continue to submit the 3 monthly reports until 1 year from the date of the MHRA's scientific opinion where Sanofi will then produce 6 monthly periodic reports. At the end of the EAMS a final report to be submitted 1 month after the expiry of the EAMS scientific opinion.

Contact details

Contact details for reporting AEs
Tel: 0800 0902314
Email Address: uk-drugsafety@sanofi.com
Facsimile Transmission: 08004716122

Medical Information (including out of hours):
Tel: 0800 035 2525
Email address: uk-medicalinformation@sanofi.com

EAMS programme Contact details
Email: GB-EAMS-Pompe@sanofi.com