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 and 'off label' medicines 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. In some cases the safety profile of the EAMS medicine may not yet be fully established and it is therefore 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

Healthcare professionals should enroll any patients receiving EAMS medicines in the registry which the pharmaceutical company will have in place to enable systematic collection of information on adverse events.

Suspected adverse drug reactions (ADRs) for any patients, particularly those not enrolled in a study (or registry), can 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. Alternatively, healthcare professionals can report ADRs which occur in patients not enrolled in any study (or registry) directly to the pharmaceutical company who manufactures the EAMS medicine.

The information below is intended for healthcare professionals and is provided by the pharmaceutical company that manufactures the medicine. The description below summarises the requirements for clinical monitoring and reporting of adverse events with medicines used under the scheme.

Prescribing doctors should also consult the relevant detailed information provided by the company.

Information on the Pharmacovigilance system:

Provision of patisiran-LNP through the Early Access to Medicines Scheme (EAMS) is designed to provide early access to this medicine for the treatment of adults with hereditary transthyretin-mediated amyloidosis (hATTR amyloidosis).

All patients should be made aware of the benefits and risks associated with the treatment as outlined in the treatment protocol, Information for the Patients. Patients will be required to sign an Informed Consent Form to acknowledge their understanding and consent to eligibility information being shared with Alnylam. In addition to pharmacovigilance data, additional data may be collected on efficacy and quality of life, which will require additional consent.

The prescribing physician, will request access by completing a Physician Declaration and Patient Access Form for each individual patient. Following confirmation of eligibility by Alnylam, physicians will work with Alnylam, or designated third party (Medpace), to activate the site and provide the necessary EAMS-related materials to the site for the physician. These materials include the EAMS Adverse Event Reporting Guideline, adverse event (AE) reporting forms (EAMS Adverse Event Reporting Form, the EAMS Exposure in Utero Form and the EAMS Exposure in Utero Follow-up Form), the EAMS Discontinuation Form and contact details.

In addition, physicians and healthcare professionals will receive comprehensive training on the appropriate use and administration of patisiran-LNP and the recognition and reporting of adverse events.

Patients should 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 free phone 0800 731 6789 (10am to 2pm Monday-Friday only).*

- Physicians are responsible for reporting all AEs, including the following special situations to Medpace Safety:
  - Overdose
  - Misuse
  - Abuse
  - Lack of effect
  - Medication error
  - Occupational exposure
  - Off label use
  - Exposure during pregnancy or lactation

The above special situations should be reported within 24 hours of awareness regardless of whether the special situation is associated with an AE or not.

All non-serious AEs observed or reported by the patient after administration of the first dose of patisiran-LNP through 28 days after the last dose of patisiran-LNP should be reported as soon as possible.

Any AEs characterized as intermittent require documentation of the start and stop of each incidence.

An assessment of severity should be made for each AE as well as an assessment of causality. All AEs should be reported regardless of causality assessment. All AEs should be followed up by the physician until resolution or stabilization of the event.

The physician is responsible for reporting AEs assessed as Serious that are observed or reported by the patient after administration of the first dose of patisiran-LNP through 28 days after the last dose of patisiran-LNP within 24 hours of awareness. An assessment of severity should be made for each Serious Adverse Event (SAE) as well as an assessment of causality.

The physician should utilise a paper AE reporting form throughout the program. Non-serious AEs and SAEs should be documented on the Adverse Event Reporting Form. When reporting SAEs, any available medical records supporting the event should also be forwarded along with the AE form. The EAMS number will be reference in the safety database.
The physician should report details of any pregnancies or partner pregnancies on a paper Exposure in Utero Form within 24 hours of awareness. Details of pregnancies will be collected during treatment with patisiran-LNP through 28 days after the last dose of Patisiran-LNP.
The pregnancy should be followed until completion. At the completion of the pregnancy, the physician/HCP will document the outcome of the pregnancy. If the outcome of the pregnancy results in a postpartum complication, spontaneous abortion, stillbirth, neonatal death, or congenital anomaly, then the physician should follow the procedures for reporting an SAE. The EAMS number will be referenced in the safety database.

The prescribing physician is also requested to report if a patient discontinues treatment by completing a Discontinuation Form with the last date of treatment and the reason for discontinuation. If the reason for discontinuation is due to an adverse event, this should also be reported as per the procedures for reporting an AE/SAE.

All paper reporting forms should be reported to Medpace Clinical Safety using the contact details provided below. Within 24 hours of receipt of additional information, the physician must provide follow-up information on the paper reporting forms and any other additional diagnostic information that will assist in the understanding of the events e.g. hospital discharge summary.

A periodic safety report will be submitted, every 3 months to the MHRA to summarize data on safety and usage of patisiran under the scheme.

Contact details:

All reporting forms should be reported to Medpace Clinical Safety using the reporting details below:

Medpace Clinical Safety Europe

SAE Hotline: +49 89 89 55 718 44 (p)
Safety Fax: +49 89 89 55 718 104 (f)

Medpace Clinical Safety: Medpace-safetynotification@medpace.com
General EAMS related enquiries: EAPalnylam.com