

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 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 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:

The prescribing physician will be requested to provide the eligibility information by completing an Initial Application and Drug Supply Request for each patient to be enrolled on to the programme. Upon review of the individual request and fulfilment of the eligibility criteria, Akcea will provide EAMS training and relevant materials which will include information on the collection and reporting of adverse events.

All Healthcare Professionals (HCP's) involved in the care of patients on EAMS will be instructed to report all adverse events (AE), special situations (SS) (whether or not there is an associated AE) and any pregnancies within 24 hours of awareness. The adverse event reporting form is also included in the physician pack. Healthcare Professional can request additional copies of this AE reporting form by sending email to EAMS@caligorrx.com. Additional follow-up may be requested on all reports received to obtain further information. Contact details for reporting Adverse Events/Special Situations/Pregnancies are provided below:

Email: drugsafety@pharsafer.com

Tel number: +44 1483 212150

Fax number: +44 1483 212178

All adverse events reported will be entered into the Akcea safety database and will be linked to the patient by the specific EAMS protocol number and unique patient number.

Training for Healthcare Professionals (HCPs)

In addition to the Physician Pack, a comprehensive AE and SS training will be provided to all relevant HCP's prior to commencement of patient treatment, focusing on recognising, managing and reporting AE/SS/pregnancies during the scheme. Equally, the HCP's obligation to keep their patients fully informed on their treatment will be emphasized. Pertinent patient related supporting documents such as the Patient Alert Card will be provided to facilitate this activity.

Additional information:

Provision of Volanesorsen through the EAMS is designed to provide early access to this medicine as an adjunct to diet for the treatment of patients with familial chylomicronemia syndrome (FCS) prior to licensing the product in the UK for this indication.

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:

- Patient's initials
- Year of birth
- Gender
- Diagnosis
- Genetically Confirmed FCS (Yes/No)
- Age at diagnosis
- Platelet count at the time of application
- Triglyceride levels at the time of application
- History of pancreatitis (Yes/No)
- Previous treatment history
- Comorbidities
- Concomitant medications

Upon receipt of the completed Application form, Akcea will confirm eligibility and assign a unique EAMS Patient number to the patient. This unique patient number assigned by Akcea will be communicated back to the prescribing physician to be used in all future communications including

re-ordering drug supplies and reporting adverse events. All data collected will be recorded under this number, making it anonymous for the purpose of this programme.

Akcea will arrange safety training and delivery of the program materials to the healthcare professional (HCPs). The safety training will contain the instructions on recognising, managing and reporting AEs.

Upon completion of safety training, Akcea will arrange initial drug shipment to cover 1-month of treatment for the patient.

In addition, following materials will be provided to all treating physicians:

- **AE reporting form**
- **Patient Alert Card** – This passport sized card will be given to all patients before they start treatment. Patients should be instructed to carry it with them at all times to show at all medical visits with HCPs other than the prescribers (e.g. emergency HCPs). It has contact details of the treating physician and it alerts other physicians that the patient is treated with Volanesorsen. It also contains information on the main symptoms of the important adverse reactions and highlights the importance of notifying the treating physician immediately if symptoms occur, persist or worsen and also the importance of not attempting to self-treat any symptoms without consulting with an HCP first.
- **Physician Educational Materials**

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 1-month of treatment. The HCPs will also be asked for confirmation that they understand and agree with the obligations to report all adverse events to Akcea and that they are complying with this requirement. They will be also asked to confirm that all adverse events experienced since the last re-supply request have been reported and there are no new adverse events to report. In addition, the HCPs will be asked to provide the results of routine platelets monitoring test at the time of drug re-supply requests. HCPs will also be advised to report platelet count reductions to $<140, \times 10^9/L$ as an AE.

The prescribing HCP is also requested to inform Akcea if a patient discontinues treatment by emailing EAMS@caligorr.com with the last date of treatment and the reason for discontinuation. If the reason for discontinuation is due to an adverse drug reaction, this should also be reported to Akcea within 24 hours of awareness. Contact details for reporting Adverse Events/Special Situations/Pregnancies are provided below:

Email: drugsafety@pharsafer.com

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A 3-monthly periodic safety report will be submitted to the MHRA to summarize data on safety and usage of Volanesorsen under the scheme

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Contact email for the EAMS programme (excluding AE reporting):

EAMS@caligorr.com