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 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:

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

As each prescribing physician is approved for entry into the EAMS scheme, they will be provided with the electronic version of the documents contained in the physician pack:

The physician pack will contain a copy of all documents being used in EAMS; i.e.:

- EAMS Information on the pharmacovigilance system and requirements for reporting safety data (this document)
- Clinicians adverse event reporting form
- EAMS Treatment Protocol – Information for Healthcare Professionals
- Instructions on entering patients into EAMS
- Physician and Patient Information Form
- Patient Information and Informed Consent form
- EAMS Treatment Protocol – Information for Patients
- Age appropriate Instructions for use
- Patient Contact Card
- Patient Dosing Card
- Patient side effect reporting form and adverse event diary

Active Pharmacovigilance:

All HCPs, (physicians, pharmacists and nurses) involved with the EAMS will be directed to report any Serious/ non serious adverse events (S/AEs), any pregnancies, lack of efficacy, occupational exposure, transmission of infectious agents, off label use or unintended drug exposure via caregiver, medication errors, overdose, misuse or abuse, drug interactions or unexpected benefit within 24 hours, as specified in the relevant documentation in the physician's pack.

Patients/caregivers will be trained by EAMS Physicians to recognise and document side effects including any adverse events of special interest [AESIs]. Training will be provided by the treating EAMS Physician at the time the patient enters the EAMS programme.

Sanofi Genzyme will allocate each patient a unique identifier upon enrolment into the dupliumab EAMS programme. This will allow tracking of patients from baseline and throughout the treatment period. This will also be used for monitoring safety information.

This identifier number should be composed of the centre code, and 3 digit patient's identifier. For example, the first patient enrolled in Southampton would have the code SO-001. This number will remain in a database of patients entered into EAMS. This identifier is required from the site when returning AE data.

Patients/caregivers will be instructed to record all side effects in a Patient Side Effects Diary throughout their treatment. They will also be trained to contact their EAMS physician immediately if they experience any of the following signs/symptoms consistent with an AESI event [anaphylactic reactions, systemic or extensive hypersensitive reactions, malignancy and helminthic infections (severe or serious or lasting ≥ 4weeks), any type of conjunctivitis (severe or serious or lasting ≥ 4weeks)],

The Patient's Diary will be reviewed by the EAMS Physician for AEs recorded during each patient's visit. In addition, any additional safety information or AE data will be solicited from the patient /caregiver by

study personnel during each patient visit. All safety information identified or recorded will be reported by the EAMS Physician to the Sanofi Pharmacovigilance team using the AE reporting form.

Pharmacovigilance data will be captured throughout the scheme including at month 1, month 3, and three monthly thereafter, until the end of EAMS for a particular patient. For patients who withdraw from the EAMS, every effort will be made to obtain follow information for up to 3 months after withdrawal.

The Sanofi Pharmacovigilance team will collect additional information, including AE of special interest [AESI], pregnancies, treatment discontinuation and/or product complaints from the participating centres. These will be recorded on a dupilumab EAMS Physician AESI/AE form. All AESIs will be notified to Sanofi Pharmacovigilance by the EAMS physician within 24 hours.

The Sanofi Pharmacovigilance team will follow up on all SAE and/or AESI information received in an expedited manner.

In accordance with Sanofi pharmacovigilance procedures and in alignment with GVP module VI guidance, all AEs received by the Sanofi pharmacovigilance team will be validated, assessed for causality and related AEs will be reported to the MHRA within 15 calendar days of day zero, if assessed as serious according to criteria for serious AEs, as per ICH E2D i.e. any untoward medical occurrence that at any dose results in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a congenital anomaly/birth defect or according to important medical events (IME) terms list.

If appropriate, all reports will be followed-up as necessary to obtain supplementary detailed information significant for the scientific evaluation of the cases. This will be particularly relevant for any event of special interest. The data management of all AE/safety information will be in accordance with Sanofi's pharmacovigilance procedures and the guidance listed in section VI. B4 of GVP module VI.
Sanofi will prepare pharmacovigilance progress reports using descriptive analysis. These reports will be provided to the MHRA every 3 months.

Training for Healthcare Professionals (HCPs)

All HCPs involved with the management of the EAMS will receive training from Sanofi in addition to the information they receive in the physician's pack upon set up.

For the main physician at each site (and any other recommended physicians), the Sanofi PV/medical team will provide training upon receipt of positive scientific opinion from the MHRA. This will include a presentation of key clinical data, product information, AE reporting and logistics of the EAMS.

The training will pay particular attention to recognising, managing and reporting adverse events.

As part of this training, the HCP receives and will be asked to provide a Patient Card to each patient at initiation of their treatment (see below).

HCPs will also be trained in how to train patients/caregivers to (self-)administer their injection at home. Detailed instructions for use will be provided for patients/caregivers.

Patient Contact Card:

This is small card for you to carry with you at all times and contains important information about the medicine you are taking and how your EAMS doctor can be contacted.

Additional information:

This provision of dupilumab through EAMS is designed to provide early access for treatment of adolescent patients ≥12 to <18 years of age with severe atopic dermatitis who have responded inadequately to at least one systemic therapy or where the available systemic therapies are not recommended or are not tolerated.

The treating physician will be requested to provide information for each patient receiving dupilumab through EAMS. Entry criteria must be met, and baseline demographic and disease severity data will be provided to Sanofi.

Contact details:

Contact details for reporting AEs: 0800 0902314

Email Address: uk-drugsafety@sanofi.com

Facsimile Transmission: +44(0)8004716122

Telephone Contact: Sanofi Medical Information number (including out of hours): Tel: 0845 372 7101

Contact email for Sanofi Medical Information: uk-medicalinformation@sanofi.com

Contact email for the EAMS programme: GB-EAMS@sanofi.com