



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

For the purpose of EAMS, dupilumab is being made available to children 6 to 11 years of age with severe atopic dermatitis who are candidates for systemic therapy and where existing systemic therapies are not advisable.

Information on the Pharmacovigilance system

When a prescribing dermatologist 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@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)
- Instructions for Use
- Dosing Card
- Patient's Card
- Adverse Event Report Form (for HCP)
- Patient Side Effects Reporting (Adverse Event) Diary
- Patient's Carer/Parent/Legal Guardian Consent Form

Adverse event/Adverse drug reaction reporting

All HCPs, (physicians, pharmacists and nurses) 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 Adverse Event Report Form (for HCPs) included in the physician's pack.

The patient's parent/guardian will be trained by the EAMS Physicians to recognise side effects and document them in the patient's diary provided upon enrolment in to the EAMS.

Upon enrolment into the dupilumab EAMS, the treating physician 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, doctor's initials and 3-digit patient's identifier. For example, the first patient enrolled in Southampton would have the code SO-XX-001, where XX is the doctor's initials. This number will remain in a database of patients entered into EAMS. This identifier is required from the site when returning AE data.

The Patient and their parent(s)/guardian(s) will be instructed to record all side effects in a Patient's Diary throughout the treatment period. They will also be trained to contact the EAMS physician immediately if the patient experiences any of the following signs/symptoms: (Systemic hypersensitivity reactions including events associated with immunogenicity and conjunctivitis related events).

For recorded AEs the Patient's Diary will be reviewed by the EAMS Physician during each patient's visit. In addition, any additional safety information or AE data will be solicited from the patient and/or their parent/ guardian by study personnel during each patient's 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 4 weeks, and 8 weeks after initiation of treatment and then 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-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 a dupilumab EAMS Physician AE form. All AEs will be notified to Sanofi Pharmacovigilance by the EAMS physician within 24 hours of their awareness.

In accordance with Sanofi pharmacovigilance procedures and in alignment with the EMA GVP module VI guidance, all AEs received by the Sanofi pharmacovigilance team will be validated, assessed for causality and reported to the MHRA within 15 calendar days of day zero if appropriate.

All AE reports will be followed-up 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.

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 physicians

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 physician will be trained by the Sanofi medical team. This will include a non-promotional presentation of key clinical data, focussing on ensuring safe use of the product, product information, and the logistics of the EAMS. The Training also will pay particular attention to ensuring that the physician can recognise, manage and appropriately report adverse events using the EAMS specific AE reporting form. The training at each site will be documented and participation sheets(s) kept on record by Sanofi.

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

Detailed instructions for use will be provided to the patient's parent(s)/guardians(s). The instructions for use will be used if the treating physician decides to train the patient's parent(s)/guardian(s) in administration of dupilumab to the patient at home.

Additional information

Patient Card:

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

Drug registry

Safety data on all patients enrolled onto the EAMS are captured as described above, and other data will be captured as follows.

Mandatory data

The following information will need to be collected for all EAMS patients, at baseline:

- Age
- Gender
- Height
- Weight

- History of Atopic Dermatitis (severity, duration of disease, main manifestations)
- Diagnosis
- Eczema area and severity index (EASI)
- Investigator's global assessment (IGA)
- Children's dermatology life quality index (cDLQI)
- EQ across 5 dimensions (youth), ED-5D-Y

- Dose and duration of previous treatment
- Previous medical history
- Underlying co-morbidities
- Concomitant medications including dose and duration

during EAMS:

- Dose and duration of dupilumab
- Additional concomitant medications including dose and duration
- All medically confirmed adverse events

Additional data

No additional prospective data are required by MHRA. Subsequent real-world data collection is voluntary and not mandatory for the participation in EAMS

Periodic reports

Sanofi will produce a 3 monthly periodic report of all AE reports received via the EAMS. The first data lock point (DLP) will be 3 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 the end of the EAMS with 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@sanofi.com