

## **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](http://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 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 given a link to a private, password protected Sanofi-run website that has copies of the documents contained in the physician pack:

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

- Instructions on entering patients into EAMS
- Physician form for inclusion criteria and request for EAMS product
- Treatment Protocol for Health Care Professional (HCP)
- Treatment Protocol for Patients (Information for patients)
- Instructions for Use
- Dosing Card
- Patient Alert Card
- Adverse Event Report Form (for HCP)
- Patient Side Effects Reporting {Adverse Event} Diary
- Patient Consent Form

#### 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 parent, medication errors, overdose, misuse or abuse, drug interactions, benefit within 24 hours as specified in the relevant documentation in the physicians pack.

Patients 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.

The treating physician will allocate each patient a unique identifier upon enrolment into the dupilumab 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, patient initials and 3 digit patient's identifier. For example, the first patient enrolled in Southampton would have the code SO-XX001, where XX is the patient'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.

Patients 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, helminthic infections, suicide-related events, blepharitis (severe or serious or lasting  $\geq$  4weeks), any type of conjunctivitis (severe or serious or lasting  $\geq$  4weeks)].

The Patient Diary will be reviewed by the EAMS Physician during each patient visit for AEs recorded. In addition, any additional safety information or AE data will be solicited from the patient 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 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 serious criteria 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 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 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 pack upon set up.

For the main physician at each site (and any other recommended physicians), the Sanofi medical team will provide training upon receipt of positive scientific opinion. 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 Alert Card to each patient at initiation of their treatment (see below).

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

**Patient Alert Card:**

Before treatment starts, all patients will have the scheme explained to them by the physician and will be given a Patient Alert Card.

This is a wallet-card sized and patients must be instructed to carry it with them at all times. It summarises the important side effects which they need to seek assistance for. In addition it alerts any other healthcare professional that may treat the patient that they are receiving dupilumab through an early access scheme, and provides information about their dermatologist, out of hours contact details and the Company's contact information.

**Additional information:**

This provision of dupilumab through EAMS is designed to provide early access to this medicine to adult patients with severe atopic dermatitis who have failed to respond, or who are intolerant of, or ineligible for all approved therapies, where there is a clear unmet need, prior to licensing of the product in the UK. 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](mailto: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](mailto:uk-medicalinformation@sanofi.com)

Contact email for the EAMS programme: [GB-eams@sanofi.com](mailto:GB-eams@sanofi.com)