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 medicines and medicines used outside their license, 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 license 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 enrol 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. The description below 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
Dostarlimab is indicated in combination with platinum-containing chemotherapy for the treatment of adult patients with mismatch repair deficient (dMMR) / microsatellite instability-high (MSI-H) primary advanced or recurrent endometrial cancer (EC) and who are candidates for systemic therapy.

Information on the Pharmacovigilance system:

When a Healthcare professional requests entry into the dostarlimab EAMS by contacting ukeams.request@gsk.com, the physician or pharmacist (HCP) will be asked to register for a web-portal Inceptua Medical Access Portal (IMAP) at https://portal.inceptua.com/#/login The company (Inceptua) supporting GSK with the implementation of the EAMS will validate the HCP's credentials and enable the HCP to register and create a profile on the IMAP portal.

Once the HCP has been qualified on the portal, they will be able to initiate the process to submit a request for dostarlimab for an individual patient. Patients will need to meet certain criteria to be eligible for the EAMS. Once the completed patient access form is submitted, a unique patient ID specific to GSK's EAMS will be assigned to the patient and used to track the status of the request, manage drug orders and supply, and for adverse event (AE) reports.

The GSK medical team will log into the IMAP portal and review the patient's details for eligibility and approve or reject the request. Once a request has been approved, all the mandatory information provided, site training completed, and the HCP has signed off the HCP's declarations, Inceptua will organise for drug to be shipped to site. Re-supply orders will also be submitted via the IMAP portal and fulfilled by Inceptua if all the re-supply conditions are met.

A core set of EAMS materials for Healthcare Professionals and patients will be accessible via the portal including information on reporting of adverse events (AEs), as follows:

- Dostarlimab EAMS instructions for HCPs on how to register and enrol patients.
- Dostarlimab EAMS – Real World Data Collection Protocol
- Dostarlimab EAMS – Treatment Protocol – Information for Healthcare Professionals (HCPs)
- Dostarlimab EAMS – Treatment Protocol – Information for Patients
- Dostarlimab EAMS – Treatment Protocol – Information on the Pharmacovigilance (PV) System and requirements for reporting safety data
- Dostarlimab EAMS – Informed Consent Form (ICF)
- Dostarlimab EAMS – Patient Alert Card
- Dostarlimab EAMS – Adverse Event Report Form
- Dostarlimab EAMS – Pregnancy Report Form

Adverse event/Adverse drug reaction reporting:

All HCPs (physicians, pharmacists, and nurses) involved with the EAMS are instructed to report any adverse events (AEs) (serious or non-serious) occurring in patients receiving dostarlimab via this EAMS programme to GSK, within 1 business day (24 hours) (or 3 calendar days whichever is sooner) of becoming aware of the event(s), using the Dostarlimab EAMS Adverse Event Report Form available on the IMAP portal.

For the purposes of this EAMS, an AE/human safety information (HSI) is defined as any untoward medical occurrence in an EAMS participant administered the EAMS medicinal product and which does not necessarily have to have a causal relationship with this treatment.

An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (either onset of new illness or exacerbation of pre-existing medical conditions) temporally associated with the use of the EAMS medicinal product, whether or not considered related to the medicinal product. AEs and safety information may also include: Failure to produce expected benefits (i.e. lack of efficacy); Off-label use; Medication errors or misuse, including drug over-dose whether accidental or intentional; Drug abuse or effects of drug withdrawal; Occupational exposure; Patient taking the GSK EAMS product while

pregnant (see below) or breastfeeding; Paternal exposure to a GSK product before and during pregnancy; Transmission of an infectious agent via a medicinal product; Safety information received as part of a product quality complaint (PQC); Drug interaction; Unexpected therapeutic benefit (i.e. an unexpected improvement in a concurrent condition other than the one being treated).

Any pregnancy in a patient which occurs during the EAMS (from the start of the first dose of dostarlimab) should be reported to GSK within 1 working day (24 hours) of learning of the pregnancy. The Dostarlimab EAMS Pregnancy Notification Form should be used for this purpose.

Patients should be educated by their EAMS healthcare professional on what side effects they might expect during treatment with dostarlimab. An EAMS-specific Patient Card that lists potential side effects, particularly immune-mediated adverse events, that may occur in association with dostarlimab treatment is required to be provided to patients. These cards will be distributed to requesting physicians to pass onto patients.

AEs may be volunteered spontaneously by patients or identified by an EAMS HCP during patient's outpatient appointments or treatment visits which take place every 3 weeks for 6 cycles and then every 6 weeks thereafter. Patients should be instructed to contact their EAMS healthcare professionals between hospital visits should they need to discuss any side effects they are experiencing.

The Dostarlimab EAMS AE Reporting Form requires the EAMS healthcare professional to categorise events by seriousness (serious or nonserious) and include an assessment of causality where possible.

Seriousness criteria definition for the purpose of this EAMS is: an adverse reaction which results in death, is life-threatening, requires in-patient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, is a congenital anomaly/birth defect, possible drug-induced liver injury, or other important medical event.

The causal relationship to the GSK product under the EAMS programme should be determined by the EAMS physician and be used to assess all AEs, as follows:

- Related: A causal relationship between the GSK product and the AE is a reasonable possibility
- Not related: A causal relationship between the GSK product and the AE is a not a reasonable possibility (i.e., there is no temporal relationship between the GSK product and the event, and an alternative aetiology is more plausible).

An assessment of intensity for each AE and SAE reported should also be made by the EAMS physician (based on the general guideline: Grade 1/Mild, Grade 2/Moderate, Grade 3/Severe, Grade 4/Life-threatening, Grade 5/Death).

Following submission to GSK, all EAMS AE/HSI reports will be entered into the GSK safety database and linked to the patient by the unique ID (assigned following the completion of the Dostarlimab EAMS Patient Access Form (PAF) on the IMAP portal) and the EAMS number. If only limited information is provided initially, EAMS AE reports may be followed-up to obtain additional / missing information relevant for the evaluation of the case, according to GSK standard procedures for handling AE cases.

The Scientific Opinion Holder is required to send all AEs/HSI related to the GSK EAMS product to the MHRA within the agreed timelines.

Where AEs/HSI are considered related to the chemotherapy agents (carboplatin and/or paclitaxel) used in combination with dostarlimab under the EAMS programme, HCPs should report these events to the MHRA via the Yellow Card scheme, https://yellowcard.mhra.gov.uk. Reporters should include the manufacturer of the chemotherapy agent(s) if known, the EAMS number, and the unique patient ID when reporting to the MHRA.

HCPs involved in the EAMS are instructed to collect and report all AEs/HSI information whilst a patient continues to receive treatment with dostarlimab under this EAMS programme. If a patient permanently discontinues treatment with dostarlimab, the HCP is requested to inform GSK/Inceptua. If the reason(s) for discontinuing dostarlimab is due to an adverse event(s), this should be reported in line with the instructions provided above.

Additionally, any AEs/HSI that are considered related to dostarlimab in a period of 30 days post last dose, post-discontinuation, should be reported in line with the instructions provided in this document up until the point of Marketing Authorisation (MA) for the EAMS indication mentioned above. Once MA has been granted for the EAMS indication, AE/safety information for dostarlimab should be reported to the GSK Safety team by emailing OAX37649@gsk.com or by calling 0800 221 441 (option 3).

Training for Healthcare Professionals (HCPs)
Once the prescribing oncologist has registered their intent to participate in the dostarlimab EAMS, the GSK medical team will arrange delivery of training for all HCPs at each centre likely to be involved in the EAMS programme, which will include the process for reporting AEs/HSI together with information on recognising and managing AEs associated with dostarlimab treatment. HCPs will also be made aware of the Patient Card and instructed to provide it to patients at initiation of treatment (see below).

Additional risk minimisation materials: Patient Card
Before treatment starts, all patients will have the scheme explained to them by the treating EAMS physician and will be given a Patient Card. This is a wallet sized card, and the patient must be instructed to always carry it with them. An electronic version can be viewed via the IMAP portal. A physical copy will be shipped with each initial dostarlimab drug request and a supply of these Patient Cards will be left at the site at the time of training. The card summarises what patients should do if they experience any side effects, particularly immune-related adverse events, while being treated or after treatment with dostarlimab. In addition, it serves to inform any other healthcare professional that may manage the patient that they are receiving dostarlimab through an early access scheme. Further it provides information about their oncologist's out of hours contact details and the Company's contact information.

Additional information

EAMS drug registry/real-world data collection
The treating EAMS physician will be requested to provide information for each patient enrolled in the programme. The Dostarlimab EAMS Patient Access Form (PAF) on the IMAP portal permits the capture of the mandatory baseline information required by the EAMS as follows:

The following information will need to be collected for all patients enrolled in EAMS.

Baseline:
- Condition for which the product is being used
- Demographic details (including Age, Gender, Race)
- Disease details (such as Endometrial cancer [EC] histology, Stage, Grade, Mismatch repair (MMR) status)
- ECOG performance status
- Details of prior treatment for the disease (e.g., surgery, systemic, radiation therapy)
- Underlying co-morbidities
- Concomitant medications

Treatment:
- Dose and duration of dostarlimab treatment
- Dose and duration of carboplatin and paclitaxel treatment
- All adverse events/safety information.

The provision of the following information is not mandated but can be collected and provided on a voluntary basis as part of routine care. This data collection will be subject to additional patient consent and the decision not to provide this data will not exclude the patient from receiving EAMs treatment.

- Assessment of patient's benefit from the EAMS treatment

All data being collected, and their use are described in detail in the “Informed consent form”.

Periodic reports
Data on the safety and usage of the GSK EAMS product will also be provided to the MHRA via periodic reports which will be prepared and submitted according to the frequency agreed with the MHRA.

Contact details:

Contact details for reporting AEs
Tel: 0800 221 441 (option 3)
Email Address: OAX37649@gsk.com

Medical Information (including out of hours):
Tel: 0800 221 441
Email address: ukmedinfo@gsk.com

EAMS programme Contact details
Email: ukeams.request@gsk.com