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 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

Voxelotor is indicated for the treatment of haemolytic anaemia (haemoglobin ≤ 10.5 g/dL) due to sickle cell disease (SCD) in adults and paediatric patients 12 years of age and older as monotherapy or in combination with hydroxycarbamide.

## Information on the Pharmacovigilance system

The following steps indicate how a physician accesses and registers a patient in the voxelotor EAMS programme:

1. All physicians interested in participating in the EAMS programme will have to register on the Inceptua IMAP portal (electronic) (https://portal.inceptua.com/).
   - The first time they visit the portal, they need to go to the 'Not registered' link to start the registration process.
   - Here they will be asked to provide their e-mail address, title, name, telephone number, job title, role, professional registration number, country and select a password for their account.
   - They will also be asked to confirm the 'Data Protection Notice and Terms of Use'.
   - Once they click "Submit", they will receive an e-mail from Inceptua with a confirmation link to verify their e-mail address.
   - Clicking the e-mail verification link will take them to the 'complete registration' page.
2. On the Inceptua IMAP portal the physician can then complete the registration process by adding all relevant information.
3. During this process the physician will be contacted by a representative of GBT´s Medical Affairs department offering support.
4. Inceptua will review the information provided by the HCP. If the qualification criteria are met, the physician will receive an email notification confirming the registration process is complete. If additional information is needed to complete the process, Inceptua will send an e-mail requesting the information needed to complete the registration process. Once all information is complete and approved, the physician will receive a link that allows them to log back into the IMAP portal and place the order.
5. The physician logs in on the Inceptua IMAP portal for the EAMS programme and fills in the mandatory information on the patient access form (PAF) required in order to request voxelotor for the individual patient.
   - Instructions for safety reporting as well as the safety reporting form will be available for download on the IMAP portal once a physician has registered. Additionally, the following documents will also be available on the Inceptua IMAP portal: Physician information document, Patient information document, Informed consent form and the Blueteq form.
6. The physician confirms that counselling to the patient has been performed, that the informed consent has been taken and that the Blueteq form has been completed (for England and Wales). For sites in Scotland and Northern Ireland please look at contact information shared on MHRA website regarding Blueteq alternative.
7. The physician submits the order on the Inceptua IMAP portal.
8. A unique patient ID specific to GBT´s EAMS programme will be provided by Inceptua once the completed patient access form (PAF) is submitted.
9. The submitted form requesting voxelotor for an individual patient will be reviewed by a representative of GBT´s Medical Affairs department. Approval/rejection/ more information needed will be conveyed to the physician by Inceptua/GBT.

10. The first order of voxelotor will be limited to a one-month supply; resupply request can be for a three month supply
11. For resupply, mandatory information will have to be entered in the Inceptua IMAP portal and will be reviewed by a representative of GBT´s Medical Affairs department prior to further processing of the request.
12. If all resupply information is provided and is in accordance with the programme definitions, Inceptua will proceed to send the requested supply of voxelotor.

## Adverse event/Adverse drug reaction reporting

In accordance with GBT pharmacovigilance procedures, all safety information received by the GBT pharmacovigilance team will be validated, assessed for causality and reported via Eudravigilance database to the appropriate health authorities.

All HCPs, (physicians, pharmacists and nurses) involved with the EAMS programme will be directed to report any adverse events (AEs), any pregnancies/drug exposure, lack of efficacy, unintended beneficial effect, medication errors, overdose, misuse, abuse, within 1 working day using the voxelotor EAMS Adverse Event Report Form (for HCPs) available on the Inceptua IMAP portal (see attachment 1).

The treating physician will assess the severity for each AE and SAE reported during the patient's participation in EAMS and assign it to one of the following categories:

- Mild: An event that is easily tolerated by the patient, causing minimal discomfort, and not interfering with everyday activities.
- Moderate: An event that causes sufficient discomfort to interfere with normal everyday activities.
- Severe: An event that prevents normal everyday activities. An AE that is assessed as severe should not be confused with an SAE. Severe is a category utilised for rating the intensity of an event, and both AEs and SAEs can be assessed as severe.

All adverse events will be captured, with transmission to the MHRA as appropriate. Reporting of safety data will categorise events by seriousness (serious or nonserious) and include an assessment of causality where possible.

All SAEs will be notified to GBT Pharmacovigilance directly by the EAMS physician to globalbloodtherapeutics@parexel.com within 1 working day of their awareness.

All AE reports will be followed-up with the physician 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 GBT pharmacovigilance procedures.

All AEs received by the GBT pharmacovigilance team will be reported to MHRA within 15 calendar days of day zero for serious cases and 90 calendar days of day zero for non-serious cases if appropriate.

Adverse Events of Interest
For this EAMS, the following are defined as AEs of interest:
• Rash
• Diarrhoea
• Headache
• AEs leading to voxelotor dose modification or discontinuation

Any adverse events (AEs) regardless of seriousness (Please note this includes any AEs listed in the treatment protocol),

• Use in pregnancy or lactation
• Lack of efficacy
• Overdose
• Drug misuse or abuse
• Medication errors
• Abnormal laboratory findings
• Unintended beneficial effects

### Training for healthcare professionals

All HCPs involved with the management of the EAMS programme will have access to all relevant documents on the Inceptua IMAP portal and may contact GBT for additional information or clarification. Physicians will be contacted by a representative of GBT´s Medical Affairs department after they have registered their interest in participating in the EAMS programme.
The Inceptua IMAP portal will contain all documents which will be used in the EAMS programme:
- 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)
- Voxelotor EAMS Adverse Event Report Form (for HCP)

Physicians will receive training on AE reporting process including the form to be used. They will also be informed that they should report AEs to MHRA using the yellow card system.
https://yellowcard.mhra.gov.uk/

### Additional information

### Data collection

The following data will be collected:

### Mandatory data

The following information will be collected for all patients receiving voxelotor in EAMS:

- Demography (Age, Gender)
- Underlying co-morbidities
- Concomitant medications / treatments (incl. blood transfusions)
- All medically confirmed adverse events
- Markers of haemolytic anaemia (Haemoglobin, reticulocyte count, total bilirubin)
- Crisis requiring treatment and/or hospital admission
- Therapy discontinuation

### Additional data

- Patient Ethnicity
- Other markers of haemolysis (% reticulocyte, LDH, indirect bilirubin)

The additional data is being collected on a voluntary basis and is subject to patient consent. The decision not to provide this data will not exclude the patient from receiving EAMS treatment.

### Periodic reports

Periodic reports describing the safety and usage of Voxelotor under the scheme will also be provided to the MHRA every three month within 30 days of the data lock point, or as agreed with the MHRA, as per the EAMS periodic update/renewal template up until the point of Marketing Authorisation as per the required EAMS process.

#### Reporting Pregnancy

If a patient or a partner pregnancy is identified during the course of the study (retrospective or prospective review) while taking voxelotor, the pregnancy should be reported to GBT pharmacovigilance (globalbloodtherapeutics@parexel.com) immediately.

Voxelotor will be discontinued immediately.

Reported pregnancy of a patient or a patient's partner, while participating in EAMS, will be monitored for the full duration of the pregnancy and/or followed through a definitive outcome (i.e. birth or spontaneous or elective abortion), if a patient or a patient's partner consent for follow-up. The child born to a female patient or partner of a male patient exposed to voxelotor will be followed for 3 months after delivery.

**Contact details**

**EAMS Programme:**
To request access to EAMS: access@inceptua.com
Or log in using the IMAP portal: https://portal.inceptua.com/

**Medical Information:**
Contact email for GBT Medical Information: EAMSinquiry@gbt.com
Medical Information Web address: https://www.gbt.com/ex-us-contact-form-medical-information/

**Pharmacovigilance:**
Email Address for reporting AEs: globalbloodtherapeutics@parexel.com