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

Risdiplam is indicated for the treatment of patients 2 months of age and older with type 1 and type 2 spinal muscular atrophy (SMA) who are not suitable for authorised treatments.

Information on the Pharmacovigilance system

After the Risdiplam Early Access to Medicines Scheme (EAMS 00031/0011) (Protocol number: AL42513) is open, neurologists will be able to request information about the EAMS by writing to: welwyn.risdiplameams@roche.com.
The following steps will then occur in parallel:
A - Neurologists will be able to request any details they require in relation to the scheme, e.g. benefit-risk profile, which will allow them to understand if the EAMS is suitable for their patient.
B - Roche will provide all the EAMS documents needed (e.g. the Application Form and Initial Drug Supply Prescription, Treatment Protocols and Informed Consent Form, etc) to the neurologist, allowing them to discuss the scheme with their patients.
C - Roche will provide a copy of the Institution Agreement to be signed by the Trust.
D - Roche will arrange for Adverse Event training to be provided to the neurologist (and other members of the hospital team if required).

The Trust will return a signed copy of the Institution Agreement to Roche, the neurologist will return a signed copy of the Application Form and Initial Drug Supply Prescription to Polar Speed (service provider carrying out hospital and homecare delivery on behalf of Roche) and the neurologist will complete the safety training. This can be done in any order. However, patients cannot be enrolled onto the EAMS until each of these steps is complete.

An assessment will be made regarding the patient's eligibility for the scheme. The neurologist will be notified of the outcome. Eligible patients will be provided with a unique EAMS ID number.

Adverse event/Adverse drug reaction reporting

All Healthcare Professionals (HCPs) involved in the care of patients on EAMS will be instructed to report all adverse events (AE) (including serious, non-serious, and special situations (SS) whether or not there is an associated AE) within one business day of awareness as specified in the EAMS documents and HCP training.

The SS may include the following:

- Use of a medicinal product during pregnancy and breastfeeding
- Overdose
- Misuse
- Abuse
- Off-label use
- Medication error
- Occupational exposure
- Lack of therapeutic efficacy
- Disease progression
- Suspected Transmission of Infectious Agent (STIAMP)
- Drug Interactions
- Class action lawsuits
- Death cases
- Product Complaints with associated AEs/SSs
- Product Complaints without associated AEs/SSs

The AE reporting forms are provided in a link on the first email Roche will send to the physician with all of the documentation. HCPs can download the document. Additionally, they can always request copies of this AE reporting form by sending an email to welwyn.risdiplamEAMS@roche.com.

All AEs reported will be entered into the Roche safety database which will form part of the EAMS Drug Registry and will be linked to the patient by the specific EAMS protocol number and unique EAMS patient number.

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 healthcare professionals

Training for adverse events will be provided to all relevant HCPs prior to commencement of patient treatment, focusing on recognising and reporting AEs during the scheme. Equally, the HCP's obligation to keep their patients fully informed on their treatment will be emphasised. AE reporting forms and the below additional risk minimisation materials will be provided to facilitate this activity.

Additional risk minimisation materials

The following risk minimisation materials will be utilised as part of the EAMS Drug Registry:

- EAMS dosing guidance for HCPs and the instructions for use for patients/parents and caregivers
- Patient Alert Card – This will be given to all patients before they start treatment. It is a wallet-sized card to be carried at all times to show at all medical visits to HCPs (e.g. emergency HCPs). It has contact details of the treating physician and it alerts other HCPs that the patient is treated with risdiplam. It highlights the importance of notifying the treating physician immediately if adverse events occur and also the importance of not attempting to self-treat any symptoms without consulting with an HCP first.

Additional information

Drug registry

Mandatory data

The neurologist will be requested to provide the following information by completing an EAMS Application Form and Initial Drug Supply Prescription for each patient to be enrolled on to the programme for eligibility assessment.
The following information will need to be collected for all EAMS products:

- Initials
- Gender
- Year of Birth (YYYY)
- Age (months)
- Weight (Kg)
- SMA Type
- Patient suitable for an authorised treatment? (yes/no)
- Comorbidities
- Concomitant medications
- All side effects
- SMN2 copy number (if available)
- Dose and duration of treatment

Additional data

There will also be additional data elements included within the EAMS Application Form and Initial Drug Supply Prescription. This data is being collected by Roche to understand how risdiplam will be used in

clinical practice, particularly for patients who have previously received a targeted SMA treatment. The additional data elements are as follows:

- Date of SMA diagnosis (DD/MM/YYYY)
- Patient's previous targeted SMA treatment prior to receiving risdiplam (if applicable)
- Duration of previous targeted SMA treatment (if applicable)
- Reasons for switching/stopping SMA treatment (if applicable)

Upon receipt of the completed Application form, Polar Speed (on behalf of Roche) will confirm eligibility and assign a unique EAMS Patient number to the patient. This unique EAMS patient number assigned will be communicated back to the physician to be used in all future communications including re-ordering drug supplies and reporting adverse events. All data collected will be recorded under this number, making it anonymous for the purpose of this programme.

The EAMS Application Form and Initial Drug Supply Prescription document includes the Treating Physician Responsibilities and Safety Obligations and Roche contacts.

Upon receipt of fully signed documents and confirmation of safety training, Roche will arrange initial drug shipment for the patient.

Patient withdrawal

For patients withdrawing from the EAMS, the HCP needs to send an email to the Roche Drug Supply Team (welwyn.risdiplamEAMS@roche.com) or to Polar Speed (psd.homecare@nhs.net) within 1 business day of awareness. Please provide the reason for discontinuation and last date of treatment. If the reason for discontinuation is due to an AE, this should also be reported to Roche Drug Safety (welwyn.uk_dsc@roche.com) within 1 business day of awareness.

For patients approved under this scheme and requiring ongoing drug supply, the HCPs will be required to complete the Drug Re-supply Prescription provided in the initial email sent by Roche. The HCPs will also be asked for confirmation that they understand and agree to comply with their obligations to report all AEs and SSs to Roche and that they are complying with this requirement. They will be also asked to confirm that all AEs and SSs experienced since the last re-supply request have been reported and there are no new AEs to report. Roche will produce a quarterly line-listing for all single case reports received in the preceding time period and send this to the Physician. Once received, the Physician will confirm receipt and completeness of the line-listing **within five (5) business days**. This process is referred to as 'Case Transmission Verification (CTV)' in the physician agreement.

HCPs should also report AEs to the MHRA via the Yellow Card scheme, www.mhra.gov.uk/yellowcard and reporters are requested to state the manufacturer and that the product is unlicensed on the AE report. In addition to this, the EAMS patient ID number should be provided in the report narrative to help the MHRA identify that AE is related to EAMS product and to help Roche link the AE report to the correct EAMS patient.

Periodic reports

A 3-monthly periodic report will be submitted to the MHRA to summarise data on safety, efficacy/effectiveness data and usage of risdiplam under the scheme.

Contact details

Contact details for reporting Adverse Events and Special Situations:
Name: UK Drug Safety Centre

SAE Email Address: welwyn.uk_dsc@roche.com

SAE Facsimile Transmission: 01707 367582

SAE TELEPHONE CONTACT: 01707 367554 (The number is available at all times. During working hours 9.00 to 16.00, it is answered by members of the team. Outside of these hours a voicemail message can be left which is checked the next working day by a team member).

Contact email for the EAMS programme (excluding AE reporting):
welwyn.risdiplamEAMS@roche.com