Medicines and Healthcare products Regulatory Agency (MHRA): Early Access to Medicines Scheme (EAMS)

Summary of operational arrangements for idebenone (Raxone [R]) in NHS Scotland.

The aim of the MHRA 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. More information about the scheme can be found here: http://www.mhra.gov.uk/Howweregulate/Innovation/EarlyaccesstomedicinesschemeEAMS/index.htm


The SO includes the public assessment report, treatment protocols for patients and healthcare professionals and a treatment protocol on the pharmacovigilance system. Information is provided on how the product is used and how it works, a summary of the key clinical studies, the risks and benefits of the product, the reason for the positive EAMS scientific opinion, any uncertainties, information about ongoing clinical studies and measures in place to monitor and manage risk. The documents are also appended at the end of this summary.

Idebenone is made available free of charge for patients via EAMS during the EAMS period. This document summarises how the medicine can be accessed and used in Scotland.

Medicine

Idebenone 150mg film-coated tablets

Indication/ patient population

Raxone is indicated for slowing the decline of respiratory function in patients with Duchenne Muscular Dystrophy (DMD) from the age of 10 years who are currently not taking glucocorticoids. The decline of respiratory function must be confirmed by repeated measurements of pulmonary function prior to initiation of treatment. Raxone can be used in patients previously treated with glucocorticoids or in patients in whom glucocorticoid treatment is not tolerated or is considered inadvisable.

Supply arrangements
1. The clinician prescribing this medicine as part of EAMS should be the prescribing clinician responsible for the patient’s care and be a specialist trained and accredited in the use of clinical management of patients with DMD, and idebenone within the EAMS scheme.

2. Clinicians wishing to access treatment for their patients need to contact the Santhera UK Limited EAMS team on Tel: 020 3434 5740 / Fax: 0845 805 0772 or by email at EAMS@santhera.com

3. The Santhera UK Limited team will confirm the additional requirements (forms and training) in accordance with the terms of the Scientific Opinion provided by the MHRA.

4. In order to initiate enrolment of patients, clinicians will be required to fully complete and return a patient access request form.

5. If access is approved following a Santhera UK Limited medical review* prescribing clinicians will be provided with a complete prescribing clinician pack and drug supply will be arranged. All clinicians wishing to prescribe idebenone will be required to undergo training prior to supply. The purpose of the training is to instruct clinicians on the data collection and safety reporting that is required as part of the idebenone EAMS. Santhera UK Limited will contact prescribing clinicians to ensure this is conducted.

6. Pharmacy Departments will be required to complete a patient resupply form for each individual patient to ensure ongoing supply. Close liaison with prescribing clinicians will be required to obtain patient details and if a unique patient identifier has been provided by the pharmaceutical company, this will be required in all correspondence. Pharmacy Departments may wish to co-ordinate all correspondence with the manufacturer to ensure clear and accurate communication. The prescribing clinician will also be required to complete an individual prescription to be sent to the Pharmacy Departments for each patient prescribed idebenone. Idebenone may be supplied directly to a registered hospital pharmacy or community pharmacy. This may be important if the patient has difficulty in travelling to an expert site to collect the medicine.

7. One bottle of 180 tablets of idebenone will be provided for each patient at each supply. Each patient will have a unique EAMS patient identification number assigned by Santhera against which each order must be placed. Orders will be placed via an EAMS Order Form emailed to order@santhera.com.

8. Continuation of supply will need to be requested every month in line with the standard resupply process which will be communicated by Santhera upon initial patient registration.

*to check that all criteria are met and also to ensure that centres which have access to a trial site are directed there in preference to EAMS in keeping with the MHRA view that EAMS should not be a substitute to the conduct of clinical trials.

As for all unlicensed medicines, individual NHS boards will have local governance arrangements in place to authorise medicines supplied via EAMS. This review should be expedited as a rigorous risk/benefit assessment has already been conducted by MHRA and can be accessed in the Public Assessment Report (PAR) (appended) or from the relevant link at https://www.gov.uk/government/collections/early-access-to-medicines-scheme-eams-scientific-opinions.
Patient information and informed consent

Prescribing clinicians should advise and explain to patients the risks and benefits of treatment with the medicine, including the fact that the medicine is unlicensed. The clinician should also advise the patient on how the medicine should be taken and obtain informed consent from the patient before treatment is initiated. Patients should be supplied with a patient alert card (provided by Santhera) which they must carry with them at all times. This card summarises the symptoms of the most important potential risks of idebenone and gives advice on what to do if these symptoms develop. The card also alerts other healthcare professionals that the patient is receiving idebenone and provides contact details for their prescribing clinician and the company’s contact details.

Patient information for this medicine can be found in the Treatment Protocol for Patients (appended).

Pharmacovigilance, monitoring and data collection

Clinicians are required to report to www.mhra.gov.uk/yellowcard and also to Santhera using specific documentation and recording mechanisms:

Mandatory reporting (baseline patient data and adverse events) are as follows:

• Confirmation of the condition which the medicine is being used for (DMD with respiratory decline)
• Patient date of birth and age
• Patient gender (likely to be male in every case)
• Patient height (and/or ulna length) and weight
• Date of glucocorticoid initiation and discontinuation dates and reason for discontinuation.
  (Patients will not be enrolled unless glucocorticoids were stopped over three months previously. This requirement may be exempted if specific adverse events on steroids are reported)
• Dose and duration of Raxone treatment (standard dose to be used)
• Important underlying comorbidities
• Concomitant medications
• Adverse events (including hospitalisations for any reason) and events of special interest that require reporting.

Events of special interest in this EAMS have been determined to help to ensure that timely ventilatory support will be provided where clinically indicated, and are the following:

– Non ambulatory patients with any of the following:
  signs or symptoms of hypoventilation,
  or FVC <50% predicted,
  or current use of ventilation: end tidal CO2 levels should be measured by capnography and reported, and monitored annually thereafter
– In any patient with either acute respiratory illness if PCF is <270 L/min, or if at any time PCF is<160L/min: pulse oximetry should be measured at home and reported
– In any patient in whom hypo-ventilation is suspected: a formal assessment of gas exchange during sleep should be conducted and reported
– Any patient with FVC<40% predicted, and/or awake baseline blood or ETCO2 >45mm Hg, and/or awake baseline SpO2 < 95%: formal assessment of gas exchange during sleep should be conducted and reported
– In a patient who is a teenager or older with FVC < 1.25L: a formal assessment of gas exchange during sleep should be conducted and reported
– A change in ventilatory status should be reported

More detailed information on pharmacovigilance, monitoring and data collection can be found at
Clinical monitoring of patients enrolled in EAMS is at the discretion of the prescribing clinician. Clinicians must satisfy themselves that the nature of the monitoring allows them to complete the safety assessment accurately. Santhera will not provide further supplies of the medicine unless the completed re-supply form has been returned.

Prescribing clinicians will have either been provided with the appropriate adverse event forms, directed to the source where they can be obtained or informed of alternative mechanisms of reporting adverse events. Where written (or electronic) forms are used, they should be completed with all available information and then faxed to Santhera on 0845 805 0774 (or emailed to Santhera@PI-ARM.co.uk) within the stipulated timelines. It is also good practice for prescribing clinicians to complete a Yellow Card for any adverse events experienced by the patient.

In some cases, may contact prescribing clinicians regarding AE monitoring proactively.

All Prescribing clinicians and healthcare professionals involved in the prescribing, supply or administration are reminded to include the unique patient identification number with all correspondence.

Should new information become available which leads the treating physician, Santhera, or the MHRA to feel it is in the patient’s best interest to discontinue, treatment may be halted early and with a limited notice period.
EAMS termination arrangements/ exit strategy

The Early Access to Medicine Scheme (EAMS) makes free-of-charge idebenone for use in slowing the decline of respiratory function in patients with DMD available to Health Boards (subject to approval by Santhera UK Limited) provided that the following conditions are met:

I. The patient (who is the subject of each order for EAMS idebenone) is a patient with respiratory decline associated with Duchenne muscular dystrophy who is currently not taking glucocorticoids and aged from 10 years.

II. The Health Board does not have any policies, guidelines or procedures in place which prohibit the acceptance of EAMS medicines.

III. While a valid positive EAMS opinion is in place (Marketing Authorisation expected in 2017).

Following Marketing Authorisation of idebenone for the treatment of patients with respiratory decline associated with Duchenne Muscular Dystrophy who are not taking glucocorticoids, the EAMS scheme will close in line with the MHRA regulations and no new patients will be allowed to enrol onto the scheme to access free of charge supply. Free of charge supply will however continue for patients already enrolled in the EAMS.

Access to idebenone for new patients would be via local board processes from the point of licensing until SMC accepted advice is issued.

The provision of idebenone, free of charge via EAMS for any one patient shall end, on the earliest of the following to occur:

A. In the event that SMC accepted advice is issued for this medicine and indication,
   I. 30 days after the publication of SMC accepted advice on the SMC website

OR

B. In the event that SMC not recommended advice is issued
   I. For a minimum of 12 months as Santhera may receive SMC accepted advice for this medicine and indication (e.g. after a resubmission). Should Santhera discontinue the scheme at any time after the 12 months and stop free of charge supply of Raxone for any reason, all prescribers will receive a minimum of three months’ notice of any decision prior to the supply being stopped.
   II. until such time as the clinician believes that the disease has progressed to a point where the patient no longer derives clinical benefit (e.g. disease progression or unacceptable toxicity).

OR

C. In the event that Negative Marketing Authorisation is issued;
   I. until such time as Santhera may receive positive Market Authorisation.
   II. until such time as the clinician believes that the disease has progressed to a point where the patient no longer derives clinical benefit (disease progression or unacceptable toxicity).
Other issues

Communication with primary care professionals.

It is expected that supply of idebenone during the EAMS period will be via secondary care. It is advisable that prescribing clinicians ensure that the GP of patients prescribed idebenone via EAMS are aware of the arrangement.

Supporting documents

Documents from MHRA website are appended below for ease of access:

1. Public assessment report
2. Treatment protocol for patients
3. Treatment protocol for healthcare professionals
4. Treatment protocol for patients in the pharmacovigilance system
5. Raxone - background information for medical directors

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