Early Access to Medicines Scheme – Treatment protocol – Information for patients

Introduction

The aim of the Early Access to Medicines Scheme (EAMS) is to provide earlier availability of promising new unlicensed medicines (medicines that do not have a marketing authorisation or are used outside their licence) to UK patients that have a high unmet clinical need. The medicines included in the scheme after they have received a positive scientific opinion 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 information below is intended for you, the patient, and is provided by the pharmaceutical company (called scientific opinion holder) that manufactures the EAMS medicine. This medicine, which does not yet have a drug licence or is used outside its licence, may also be used in combination with other medicines. More information about medicines licensing can be found here: http://www.nhs.uk/conditions/medicines-information

This medicine can be prescribed for individual patients to meet specific needs provided they are given sufficient information about the medicine to make an informed decision. Your physician will be responsible for giving you all the information you need to make this decision and for obtaining informed consent from you prior to treatment. You will be asked to sign a form to confirm that you are providing informed consent to receiving the EAMS treatment. Information on consent can be found here:
https://www.nhs.uk/conditions/Consent-to-treatment

The information below is provided to help you decide with your physician on whether to use the EAMS medicine and helps explain how to use it in accordance with the pharmaceutical company's instructions for safe and proper use. 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.

The information below may change during the time you are using the medicine if more data become available. Your physician will highlight to you any changes that you need to be aware of.

Whilst you are using this medicine, data will be collected on the use and safety profile of the medicine, to ensure that the benefits of taking the medicine continue to outweigh any potential risks. Your physician will answer all your questions during and after the treatment and will provide you with contact details that you should use in case of any events or problems.

Each patient enrolled in the scheme will continue to receive the EAMS product until the end of the treatment in line with prescribing and NHS guidance and as long as benefit is seen. In rare cases where the EAMS treatment may not be available anymore, your physician will discuss other options with you.

Information for the patient

Cipaglucosidase alfa 105 mg powder for concentrate for solution for infusion
and
Miglustat 65 mg hard capsules

Read all of this leaflet carefully before you are given each medicine because each contains important information for you.
- Keep this leaflet. You may need to read it again.
- It is important that you keep the Alert Card with you during treatment.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What cipaglucosidase alfa is, what miglustat is, and what they are used for

What cipaglucosidase alfa is

Cipaglucosidase alfa is an enzyme replacement therapy that mimics the naturally occurring enzyme (alpha-glucosidase) which is lacking in late-on-set Pompe disease.

What miglustat is

Miglustat is a medicine that helps the cipaglucosidase alfa enzyme be absorbed more readily be absorbed more readily by the cells in your body that are affected by late-onset Pompe disease.

Cipaglucosidase alfa is used in conjunction with miglustat is to treat symptomatic adults who have a confirmed diagnosis of late-onset Pompe disease (acid alpha-alglucosidase [GAA] deficiency) who have received enzyme replacement therapy with alglucosidase alfa for ≥ 2 years.

What they are used for

People with late onset Pompe disease have low levels of an enzyme called alpha-glucosidase. This enzyme helps the body control levels of glycogen (a type of carbohydrate) within the cells. Glycogen provides the body with energy. However, in late-onset Pompe disease the levels of glycogen can get too high, causing a build-up of glycogen in the muscles of the body which prevents them from working properly.

2. What you need to know before you are given cipaglucosidase alfa in conjunction with miglustat

You must not be given cipaglucosidase alfa or miglustat if:

- You have a history of life-threatening infusion-associated or allergic (hypersensitivity) reactions to alglucosidase alfa, cipaglucosidase alfa, miglustat, or other iminosugars, or to any of the other ingredients of this medicine (listed in section 6). Symptoms of life-threatening infusion-associated, or allergic reactions include, but are not limited to anaphylaxis, and severe cutaneous reactions.

Tell a doctor or nurse immediately if you have had any of these reactions with cipaglucosidase alfa and/or miglustat or have a prior history of any such reactions with another enzyme replacement therapy (ERT).

Warnings and precautions

Only take the miglustat that has been provided to you in this programme. **65 mg** miglustat capsules should only be used with cipaglucosidase alfa. Do not use 100 mg miglustat capsules with cipaglucosidase alfa.

Allergic (hypersensitivity) and infusion-associated reactions - If you are treated with cipaglucosidase alfa, you may experience an infusion-associated or allergic (hypersensitivity) reaction while you are being given the medicine or during the hours following the infusion. Such a reaction may include different symptoms like low blood pressure, very fast heart rate, chest discomfort, throat tightness, swelling of the tongue, lips and or throat (pharyngeal oedema), hives (urticaria), dizziness, rash, itchy skin, nausea, vomiting, and cough (see section 4 for an overview of all infusion-associated reactions). An allergic or infusion-associated reaction can sometimes be very severe. If you experience a reaction like this, you should **tell your doctor immediately**. You may need to be given pre-treatment medicines to prevent an allergic reaction (e.g. antihistamines and/or corticosteroids) or to reduce fever (antipyretics).

Immune-mediated reactions – Immune-mediated reactions (side effects that occur due to high levels of antibodies to enzyme replacement therapy) have been reported with other enzyme replacement therapies. These have included severe skin reactions, joint inflammation, and kidney disease. These symptoms have not been reported with cipaglucosidase alfa and miglustat in clinical trials.

Your doctor will monitor you for signs or symptoms related to these types of side effects, such as rash, high fever, joint pain or swelling, and abnormalities in urine testing. If you experience an immune-mediated reaction, your doctor may decide to stop treating you with cipaglucosidase alfa and miglustat and/or may give you additional medications.

Children and adolescents
This medicine is not to be taken by patients under the age of 18 years old. This is because the effects of cipaglucosidase alfa in combination with miglustat in this age group are not known.

Other medicines and cipaglucosidase alfa in conjunction with miglustat

Tell a doctor or nurse if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription, including herbal medicines.

Contraception, pregnancy, breast-feeding, and fertility

There is limited experience of the use of cipaglucosidase alfa/miglustat in pregnant women. Your doctor will discuss with you the risks and benefits of taking this medicine.

- It is advised that male and female patients should use reliable birth control methods while taking both medicines.
- Do not take miglustat or receive cipaglucosidase alfa if you are pregnant. Be sure to tell your doctor immediately if you get pregnant, think that you may be pregnant, or if you are planning to become pregnant.
- Stop breast-feeding when you are taking miglustat or given cipaglucosidase alfa.

If you are pregnant or breastfeeding, think you may be pregnant, or are planning to have a baby, talk to your doctor for advice before using this medicine.

Driving, cycling and using machines

Take care when driving or using any tools or machines shortly after receiving cipaglucosidase alfa/miglustat, since you may experience dizziness.

3. How miglustat and cipaglucosidase alfa are given

Your doctor who is experienced in the treatment of late-onset Pompe disease will determine how much miglustat and cipaglucosidase alfa are given to you.

If you are currently being treated on another enzyme replacement therapy (ERT), the other ERT must be stopped before starting miglustat and cipaglucosidase alfa ERT.

Talk to your doctor about when to begin taking miglustat in conjunction with cipaglucosidase alfa if you have been treated with another ERT.

Both medicines are given to you once every 2 weeks. Miglustat must be taken first.

How much miglustat is given

The recommended dose regimen in adults 18 years and older is based on body weight:

- For patients weighing at least 50 kg, the recommended dose is 4 capsules (260 mg total).
- For patients weighing greater than or equal to 30 kg to less than 50 kg, the recommended dose is 3 capsules (195 mg total).

Swallow miglustat capsules whole: do not cut, crush, or chew the capsules. Do not use a broken or cracked (damaged) capsule.

You should not eat for 2 hours before and 2 hours after taking miglustat. Miglustat capsule should be taken by mouth on an empty stomach 1 hour before the start of the cipaglucosidase alfa infusion.

Water, carbonated water, tea or coffee may be consumed. Two hours after taking miglustat, you can resume normal eating and drinking.

If you miss a dose of miglustat

If you miss a dose of miglustat, please speak to your doctor or nurse. If your infusion of cipaglucosidase alfa is delayed, the start of infusion should not exceed 3 hours from when you have taken miglustat.

If you take more miglustat than you should

If you accidentally take more capsules than you were prescribed, you may be at increased risk of experiencing side effects with this medicine (see section 4 of this leaflet**). Contact your doctor immediately or go to the hospital and show your patient information card.**

How much cipaglucosidase alfa is given

The dose you receive is based on your body weight. The recommended dosage of cipaglucosidase alfa is 20 mg per kg of body weight. Cipaglucosidase alfa is given into a vein (by intravenous infusion). It is supplied as a powder which will be mixed with sterile water and then diluted into the IV bag before it is given.

If you miss a dose of cipaglucosidase alfa

If you may miss or have missed the time by which the infusion was supposed to be started, please speak to your doctor or nurse.

If you stop receiving miglustat and cipaglucosidase alfa

If you have any further questions on the use of these medicines, ask a doctor, nurse, or pharmacist.

4. Possible side effects

Like all medicines, these medicines can cause side effects, although not everybody gets them.

Side effects were mainly seen while patients were being given the medicine or shortly after (infusion related effects). Most of the infusion-related reactions were mild or moderate. Some of these infusion-related or allergic side effects were serious..

Common (may affect up to 1 in 100 people)
- Difficulty breathing
- Itchy skin
- Rapid pulse
- Feeling dizzy
- Rash or hives
- Anaphylactic reaction

Uncommon (may affect up to 1 in 100 people)
- Swelling of the face, lip, tongue or throat
- Pale skin
- Wheezing
- Low blood pressure

Speak to a doctor or nurse immediately if you get the side effects listed above. **Show your patient alert card** and this package leaflet to any doctor or nurse who treats you, not only to your treating doctor.

Other side effects

Very common (may affect more than 1 in 10 people)

- Headache
- Dizziness
- Diarrhoea
- Nausea
- Fatigue
- Joint pain
- Abdominal pain
- Muscle spasm
- Muscle pain
- Fever

Common (may affect up to 1 in 100 people)

- Difficulty breathing, swelling of neck and or face, skin rash, itching, rapid or weak pulse, nausea, vomiting, fainting (one or more of the following symptoms – anaphylactic reaction
- Difficulty breathing which may trigger coughing, a whistling sound (wheezing) when you breathe out, and shortness of breath (asthma)
- Fast heart rate
- Flushing
- Difficulty or trouble breathing
- Cough
- Chest discomfort
- Flatulence (wind)
- Swelling by injection site
- Pain by the injection site
- Rash
- Severe itchy skin
- Hives
- Increased sweating
- Trouble passing stool
- Altered sense of taste
- Vomiting
- Feeling jittery
- Blood pressure increased
- Low blood pressure
- Pain
- Mouth or jaw pain
- Chills
- Involuntary shaking (tremor) of one or more parts of the body
- Bloating
- Indigestion
- Unpleasant or painful sensation in the belly
- Burning sensation
- Pain in one or both sides of the head, throbbing pain, aura, eye pain, sensitivity to light (migraine)
- Tingling or prickling sensation* (paraesthesia)
- Feeling of near fainting (presyncope)
- Feeling of uneasiness, doldrums
- Feeling weak all-over
- Muscle weakness, tiredness

- Body aches, stiffness, and pains
- Swelling in the hands, arms, feet, ankles, legs
- Pain in chest
- Pain in areas around the sides of your body from upper abdomen to your back (flank pain)
- Damage to skin
- Feeling drowsy
- Platelet count decreased – decrease in thrombocytes

Uncommon (may affect up to 1 in 1000 people)
- Wheezing
- Swelling of the throat
- Oral pain or discomfort
- Swelling of the lips and or tongue
- Spasms / pain in the throat
- Unsteady dizziness (balance disorder)
- Pale skin
- Difficulty swallowing or feeling something caught in throat or chest
- Feeling unwell (malaise)
- Skin discoloured
- Pain in the face
- Skin appears swollen
- Lymphocyte count decreased- decrease in a type of white blood cell
- Changes in body temperature

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.
You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
Alternatively, you can call Freephone 0808 100 3352 (available between 10am – 2pm Monday – Friday), or email: drugsafety@amicusrx.com.

By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store cipaglucosidase alfa and miglustat

Do not use this medicine after the expiry date which is stated on the label after 'EXP'. The expiry date refers to the last day of that month.

Cipaglucosidase alfa

Store in a refrigerator at 2°C to 8°C. After dilution, an immediate use is recommended. The reconstituted product can be stored up to 24 hours when refrigerated at 2°C to 8°C and diluted product can be stored up to 24 hours when refrigerated at 2°C to 8°C when protected from light.

Do not freeze.

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.

Do not throw away any medicines via wastewater or household waste. Ask your doctor, pharmacist or nurse how to throw away medicines you no longer use. These measures will help protect the environment.

Miglustat

Keep this medicine out of the sight and reach of children.

Store below 30°C in the original container.

This product does not require special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What cipaglucosidase alfa and miglustat contain

Cipaglucosidase alfa

The active substance is cipaglucosidase alfa. One vial contains 105 mg of cipglucosidase alfa. After reconstitution, the solution contains 15 mg of cipglucosidase alfa per mL and after dilution the concentration varies from 0.5 mg/mL to 4 mg/mL.

The other ingredients are:
- Sodium citrate dihydrate (E331)
- Citric acid monohydrate (E330)
- Mannitol (E421)
- Polysorbate 80 (E433)

Miglustat

The active substance is miglustat.
Each capsule contains 65 mg miglustat.

The other ingredients are
- Capsule contents: pregelatinised starch (maize), magnesium stearate (E470b), microcrystalline cellulose (E460i), sucralose (E955), colloidal silicon dioxide

  Capsule shell: gelatin, titanium dioxide (E171), black iron oxide (E172)

  Edible Printing ink: black iron oxide (E172), shellac (E904)

What cipaglucosidase alfa and miglustat look like and contents of the pack

Cipaglucosidase alfa

Cipaglucosidase alfa is a powder for concentrate for solution for infusion in a vial (105 mg/vial). Each pack contains 1, 10 or 25 vials. Not all pack sizes may be marketed.

The powder is white to pale yellow. After reconstitution it is a clear, colourless to pale yellow solution, which may contain particles or translucent fibres. The reconstituted solution must be further diluted.

Miglustat

Miglustat is 65 mg hard capsule with a grey opaque cap and white opaque body with “AT2221” printed in black on the body.

The capsules are provided in a high-density polyethylene (HDPE) bottle with closure. Each pack contains 24 hard capsules.

Scientific Opinion Holder and manufacturer

Amicus Therapeutics Europe Limited
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Ireland
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Additional information

Informed consent

You will have the Early Access to Medicines Scheme explained to you using the informed consent form. A copy of the signed consent form will be given to you to keep. Upon providing your permission, you will undergo certain therapy, medical procedures, and diagnostics as a participant in the EAMS registry.

Patient alert card

You will be given a patient alert card before you start treatment with miglustat and cipaglucosidase alfa. You should carry this alert card with you at all times during the treatment and for at least 12 months after completing your treatment. You should show this card to any physician or nurse treating you. The card summarises that you are currently receiving miglustat and cipaglucosidase alfa. This card contains important information such as contact details of your doctor, out of hours contact information, company contact details and safety reporting for which you should seek assistance.

Contact information

Contact details for reporting Adverse Events/Special Situations

YellowCard: https://yellowcard.mhra.gov.uk alternatively you can call Freephone 0808 100 3352 (available between 10am-2pm Monday – Friday), or
Email: drugsafety@amicusrx.com

Contact details for EAMS programme and Medical Information

Marlow, United Kingdom telephone: 01753 888567
Email: info@amicusrx.co.uk