Package leaflet: Information for the patient

Pombiliti 105 mg powder for concentrate for solution for infusion
cipaglucosidase alfa

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

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

What is in this leaflet

1. What Pombiliti is and what it is used for

What Pombiliti is
Pombiliti is a type of 'enzyme-replacement therapy' (ERT) that is used in the treatment of late-onset Pompe disease in adults. It contains the active substance 'cipaglucosidase alfa'.

What it is used for
Pombiliti is always used with another medicine called miglustat 65 mg hard capsules. It is very important that you also read the package leaflet of miglustat 65 mg hard capsules.

If you have any questions about your medicines, please ask your doctor or pharmacist.

How Pombiliti works
People with Pompe disease have low levels of the enzyme acid alpha-glucosidase (GAA). This enzyme helps control levels of glycogen (a type of carbohydrate) in the body.

In Pompe disease, high levels of glycogen build up in the muscles of the body. This keeps muscles, such as the muscles that help you walk, the muscles under the lungs that help you breathe, and the heart muscle, from working properly.

Pombiliti enters the muscle cells that are affected by Pompe disease. When in the cells, the medicine works like GAA to help break down glycogen and control its levels.

2. What you need to know before you are given Pombiliti

You must not be given Pombiliti
- If you have ever had life-threatening hypersensitivity reactions to:
  - cipaglucosidase alfa
  - miglustat
  - any of the other ingredients of this medicine (listed in section 6).

- If a previous infusion had to be stopped and could not be restarted due to life threatening hypersensitivity reactions.

Warnings and precautions
Talk to your doctor, pharmacist, or nurse before using Pombiliti.

Speak to your doctor or nurse immediately if these apply to you, if you think it might apply to you or if you have ever had any such reactions with another enzyme replacement therapy (ERT):
- allergic reactions, including anaphylaxis (a severe allergic reaction) – see section 4 under 'Possible side effects', below for symptoms of life-threatening reactions.
- infusion-associated reaction while you are receiving the medicine or in the few hours afterwards - see section 4 under 'Possible side effects', below for symptoms of life-threatening reactions.

Inform your doctor if you have a history of heart or lung disease. These conditions may worsen during or immediately after your infusion with Pombiliti. Tell a doctor or nurse immediately if you are experiencing shortness of breath, cough, rapid or irregular heartbeat or any other effects from these conditions.

Also tell your doctor if you have swelling in your legs or widespread swelling of your body, severe skin rash or frothy urine when passing water. Your doctor will decide if your Pombiliti infusion should stop, and the doctor will give you appropriate medical treatment. Your doctor will also decide if you can continue receiving Pombiliti.

Pre-treatment medications
Your doctor may give you other medicines before you have Pombiliti. These medicines include:
- antihistamines and corticosteroids to prevent or help reduce infusion-related reactions.
- antipyretics to reduce fever.

Children and adolescents
This medicine should not be given to patients under the age of 18 years old. This is because the effects of Pombiliti in conjunction with miglustat in this age group are not known.

Other medicines and Pombiliti
Tell a doctor or nurse if you are using, have recently used, or will be using any other medicines. This includes medicines obtained without a prescription, including herbal medicines.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant, or are planning to have a baby, do not take this medicine but talk to your doctor or pharmacist immediately for advice before using this medicine.

There is no experience with the use of Pombiliti in combination with miglustat during pregnancy.

- You should not receive Pombiliti and / or take miglustat 65 mg hard capsules 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. There may be risks to the unborn baby.
- Pombiliti in combination with miglustat should not be given to women who are breast-feeding. A decision will need to be made whether to stop treatment or to stop breast-feeding.

Contraception and fertility
Female patients of childbearing potential must use reliable birth control methods during and for 4 weeks after stopping both medicines.

Driving and using machines
You may feel dizzy, sleepy, or have low blood pressure (hypotensive) after having Pombiliti or pre-treatment medicines. If this happens, do not drive or use any tools or machines.

Pombiliti contains sodium
This medicinal product contains 10.5 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 0.52% of the recommended maximum daily dietary intake of sodium for an adult.

3. How Pombiliti is given

Pombiliti is given to you by a doctor or nurse. It is given through a drip into a vein. This is called an intravenous infusion.

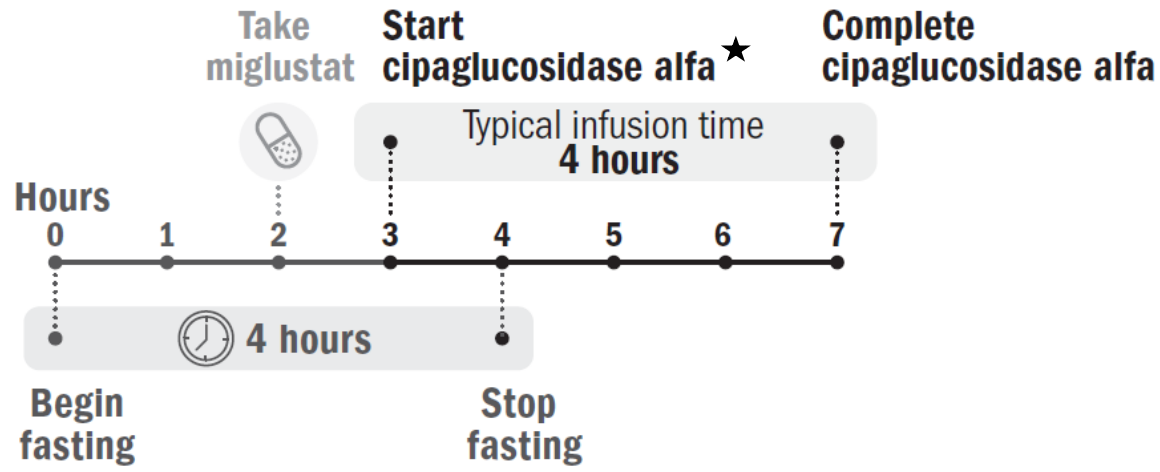
Talk to your doctor if you would like to be treated at home. Your doctor will decide upon evaluation if it is safe for you to have home infusion of Pombiliti. If you get any side effects during an infusion of Pombiliti, your home infusion staff member may stop the infusion and start appropriate medical treatment.

Pombiliti should be used in conjunction with miglustat. You can only use miglustat 65 mg capsules with cipaglucosidase alfa. Do **NOT** use miglustat 100 mg capsules (different product). Follow your doctor's instructions and read the package leaflet of miglustat 65 mg hard capsules for their recommended dose.

How much Pombiliti is given
The amount of medicine that you will be given is based on your weight. The recommended dose is 20 mg for each kg of body weight.

When and for how long Pombiliti is given
- You will be treated with Pombiliti once every other week. Miglustat 65 mg capsules are taken on the same day as Pombiliti. Refer to the package leaflet of miglustat 65 mg hard capsules for information on how to take miglustat.
- The cipaglucosidase alfa infusion should start 1 hour after taking miglustat 65 mg hard capsules.
  - In the event of a delay, the start of infusion should not exceed 3 hours from taking miglustat.
- The infusion of cipaglucosidase alfa lasts approximately 4 hours.

Figure 1. Dose timeline



★ The cipaglucosidase alfa infusion should start 1 hour after taking miglustat capsules. In the event of infusion delay, the start of infusion should not exceed 3 hours from taking miglustat.

Switching from another enzyme replacement therapy (ERT)
If you are currently being treated with another ERT:
- Your doctor will tell you when to stop the other ERT before starting Pombiliti.
- Tell your doctor when you completed your last dose.

If you are given more Pombiliti than you should
If you have difficulty breathing, feel swollen or bloated, or your heart is racing, you may have been given too much Pombiliti; tell your doctor straight away. Excessive rate of infusion of Pombiliti could result in symptoms related to too much fluid in the body, such as shortness of breath, rapid heart rate, or widespread swelling of the body.

If you miss your dose of Pombiliti
If you have missed an infusion, please contact your doctor or nurse as soon as possible to reschedule Pombiliti in combination with miglustat 24 hours after miglustat was last taken.

If you stop receiving Pombiliti
Speak to your doctor if you wish to stop Pombiliti treatment. The symptoms of your disease may worsen if you stop treatment.

4. Possible side effects

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

Pombiliti is used with miglustat, and side effects can occur with either of these medicines. Side effects were mainly seen while patients were being infused with Pombiliti (infusion-related effects) or shortly after. You must tell your doctor immediately if you get an infusion-associated reaction or an allergic reaction. Some of these reactions may become serious and life-threatening. Your doctor may give you medicines before your infusion to prevent these reactions.

Infusion-associated reactions
Most infusion-associated reactions are mild or moderate. Symptoms of infusion-associated reaction may include difficulty breathing, bloating, fever, chills, dizziness, skin redness, itchy skin, and rash.

Allergic reactions
Allergic reactions may include symptoms such as rash anywhere on the body, puffy eyes, prolonged difficulty breathing, cough, swelling of the lip, tongue, or throat, itchy skin, and hives.

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

Common (may affect up to 1 in 10 people)
- Serious life-threatening allergic reaction (anaphylactic reaction)
- Feeling dizzy
- Tremor
- Feeling sleepy
- Taste disturbance
- Sensation like numbness, tingling, pins, and needles (paraesthesia)
- Rapid heartbeat
- Reddening of the skin
- Low blood pressure
- Shortness of breath
- Cough
- Diarrhoea
- Feeling sick (nausea)
- Stomach pain
- Passing gas
- Bloating
- Vomiting

- Hives
- Itchy skin
- Rash
- Excessive sweating
- Painful muscle contractions
- Muscle pain
- Muscle weakness
- Joint pain
- Tiredness
- Fever
- Chills
- Feeling uncomfortable in chest
- Swelling in the body area where needle was inserted
- Pain
- Swelling in the hands, feet, ankles, legs
- Rise in blood pressure

Uncommon (may affect up to 1 in 100 people)
- Allergic reaction
- Cannot hold or maintain balance
- Burning sensation
- Migraine
- Feeling of near fainting
- Unusual paleness of the skin
- Asthma
- Wheezing
- Discomfort in mouth and throat
- Swollen throat
- Indigestion
- Pain or painful contractions in gullet
- Mouth pain or discomfort
- Swollen tongue
- Skin discolouration
- Swelling of the skin
- Pain in the area between the hip and rib
- Muscle tiredness
- Muscle stiffness
- Weakness
- Pain in the cheek, gums, lips, chin
- Pain in body area where needle was inserted
- Feeling generally unwell
- Pain in chest
- Swelling face
- Changes in body temperature
- Scratch or damage to the skin

Reporting of side effects

If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard
or search for MHRA Yellow Card in the Google Play or Apple App Store

5. How to store Pombiliti

Your doctor, pharmacist, or nurse is responsible for storing this medicine and disposing of any opened vials correctly. The following information is intended for healthcare professionals.

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 bottle and carton after the letters "EXP". The expiry date refers to the last date of that month.

Unopened vials: Store in the refrigerator (2°C - 8°C). Keep the vial in the outer carton in order to protect from light.

After dilution, an immediate use is recommended. However, storage of the intravenous bag with Pombiliti has been demonstrated for 6 hours at 20°C - 25°C and 24 hours at 2°C - 8°C.

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

6. Contents of the pack and other information

What Pombiliti contains
The active substance is cipaglucosidase alfa. One vial contains 105 mg of cipaglucosidase alfa. After reconstitution, the solution in the vial contains 15 mg of cipaglucosidase alfa per mL. The recommended final concentration of cipaglucosidase alfa diluted into the intravenous bag ranges 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)

What Pombiliti looks like and contents of the pack

Pombiliti is a white to slightly yellowish powder. After reconstitution, it appears as a clear to opalescent, colourless to slightly yellow solution, free of foreign particles, practically free of particles in the form of white to translucent particles. The reconstituted solution must be further diluted into an intravenous bag for infusion.

Pombiliti is a powder for concentrate for solution for infusion in a vial.

Packs of 1 vial, 10 vials, or 25 vials

Not all pack sizes may be marketed.

Marketing Authorisation Holder

Amicus Therapeutics UK Limited
One Globeside
Fieldhouse Lane
Marlow, Buckinghamshire
SL7 1HZ

Manufacturer

Manufacturing Packaging Farmaca (MPF) B.V.
Neptunus 12, Heerenveen, 8448CN, Netherlands

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Other sources of information

The following information is intended for healthcare professionals only:

Instructions for use – reconstitution, dilution, and administration

Pombiliti must be reconstituted with water for injection, then diluted with sodium chloride 9 mg/mL (0.9%) solution for injections and then administered by intravenous infusion. Reconstitution and dilution should be performed in accordance with good practice rules, particularly for the respect of asepsis.

Because this medicine is a protein, particle formation may occur in the reconstituted solution and final diluted infusion bags. Therefore, a 0.2-micron low protein binding in-line filter should be used for administration. It was demonstrated that the use of a 0.2 micron in-line filter removes visible particles and does not result in an apparent loss of protein or activity.

Determine the number of vials to be reconstituted based on the individual patient's dose regimen (mg/kg) and remove the required vials from the refrigerator in order to allow them to reach room temperature (approximately 30 minutes). Each vial of Pombiliti is for single use only.

Use aseptic technique.

Reconstitution

Reconstitute each 105 mg per vial of Pombiliti with 7.2 mL water for injections using a syringe with a needle diameter not larger than 18 gauge. Add the water for injections by slow drop-wise addition down the side of the vial and not directly onto the lyophilised powder. Tilt and roll each vial gently. Do not invert, swirl, or shake the vial. The extraction volume appears as a clear to opalescent, colourless to slightly yellow solution, free of foreign particles, and practically free of particles in the form of white to translucent particles. Perform an immediate inspection of the reconstituted vials for particulate matter and discolouration. Do not use if upon immediate inspection foreign particles other than those described above are observed, or if the reconstituted solution is discoloured. The pH of the reconstituted solution is approximately 6.0.

After reconstitution it is recommended to promptly dilute the vials (see below).

Dilution

When reconstituted as above, the reconstituted solution in the vial contains 15 mg cipaglucosidase alfa per mL. The reconstituted volume allows accurate withdrawal of 7.0 mL (equal to 105 mg) from each vial. This should then be further diluted as follows: Slowly withdraw the reconstituted solution from each vial, including less than the 7.0 mL for the partial vial, until the volume for the patient's dose is obtained using a syringe with a needle diameter not larger than 18 gauge. The recommended final concentration of cipaglucosidase alfa in the infusion bags ranges from 0.5 mg/mL to 4 mg/mL. Remove airspace within the infusion bag. Also remove an equal volume of sodium chloride 9 mg/mL (0.9%) solution for injections, that will be replaced with reconstituted Pombiliti. Slowly inject the reconstituted Pombiliti directly into the sodium chloride 9 mg/mL (0.9%) solution for injections. Gently invert or massage the infusion bag to mix the diluted solution. Do not shake or excessively agitate the infusion bag.

The final infusion solution should be administered as close to preparation time as possible.

Any unused medicine or waste material should be disposed of in accordance with local requirements.

Administration

The Pombiliti infusion should start 1 hour after taking miglustat capsules. In the event of infusion delay, the start of infusion should not exceed 3 hours from taking miglustat.

The recommended dose regimen of Pombiliti is 20 mg/kg of body weight administered once every other week as an intravenous infusion.

Infusions should be administered incrementally. It is recommended that the infusion begin at an initial rate of 1 mg/kg/hr and be gradually increased by 2 mg/kg/hr every 30 minutes if there are no signs of IARs (infusion-associated reactions) until a maximum rate of 7 mg/kg/hr is reached.