

B. PACKAGE LEAFLET

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
2. What you need to know before you are given Pombiliti
3. How Pombiliti is given
4. Possible side effects
5. How to store Pombiliti
6. Contents of the pack and other information

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.

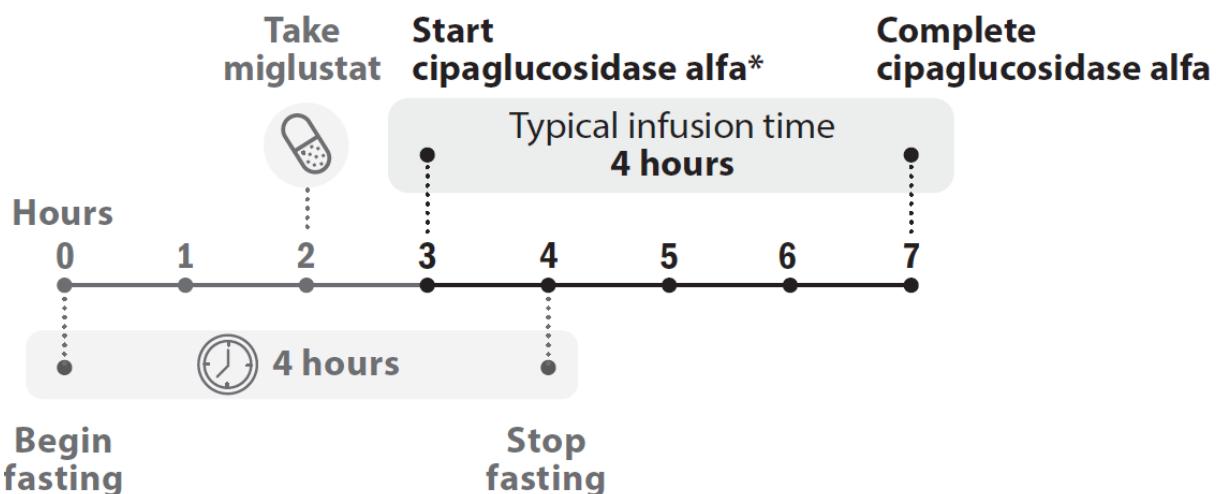
How much Pombiliti is given

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, pharmacist, or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in [Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

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 Europe Limited
Block 1, Blanchardstown Corporate Park
Ballycoolin Road
Blanchardstown, Dublin
D15 AKK1
Ireland
Tel: +353 (0) 1 588 0836
Fax: +353 (0) 1 588 6851
e-mail: info@amicusrx.co.uk

Manufacturer

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

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien

Amicus Therapeutics Europe Limited
Tél/Tel: (+32) 0800 89172
e-mail: MedInfo@amicusrx.com

България

Amicus Therapeutics Europe Limited
Тел.: (+359) 00800 111 3214
имейл: MedInfo@amicusrx.com

Česká republika

Amicus Therapeutics Europe Limited
Tel.: (+420) 800 142 207
e-mail: MedInfo@amicusrx.com

Danmark

Amicus Therapeutics Europe Limited
Tlf.: (+45) 80 253 262
e-mail: MedInfo@amicusrx.com

Deutschland

Amicus Therapeutics GmbH
Tel: (+49) 0800 000 2038
E-Mail: MedInfo@amicusrx.com

Eesti

Amicus Therapeutics Europe Limited
Tel: (+372) 800 0111 911
e-post: MedInfo@amicusrx.com

Lietuva

Amicus Therapeutics Europe Limited
Tel: (+370) 8800 33167
El. paštas: MedInfo@amicusrx.com

Luxembourg/Luxemburg

Amicus Therapeutics Europe Limited
Tél/Tel: (+352) 800 27003
e-mail: MedInfo@amicusrx.com

Magyarország

Amicus Therapeutics Europe Limited
Tel.: (+36) 06 800 21202
e-mail: MedInfo@amicusrx.com

Malta

Amicus Therapeutics Europe Limited
Tel: (+356) 800 62674
e-mail: MedInfo@amicusrx.com

Nederland

Amicus Therapeutics BV
Tel: (+31) 20 235 8510 / (+31) 0800 022 8399
e-mail: MedInfo@amicusrx.com

Norge

Amicus Therapeutics Europe Limited
Tlf: (+47) 800 13837
e-post: MedInfo@amicusrx.com

Ελλάδα

Amicus Therapeutics Europe Limited
Τηλ: (+30) 00800 126 169
e-mail: MedInfo@amicusrx.com

España

Amicus Therapeutics S.L.U.
Tel: (+34) 900 941 616
e-mail: MedInfo@amicusrx.com

France

Amicus Therapeutics SAS
Tél: (+33) 0 800 906 788
e-mail: MedInfo@amicusrx.com

Hrvatska

Amicus Therapeutics Europe Limited
Tel: (+385) 0800 222 452
e-pošta: MedInfo@amicusrx.com

Ireland

Amicus Therapeutics Europe Limited
Tel: (+353) 1800 936 230
e-mail: MedInfo@amicusrx.com

Ísland

Amicus Therapeutics Europe Limited
Sími: (+354) 800 7634
Netfang: MedInfo@amicusrx.com

Italia

Amicus Therapeutics S.r.l.
Tel: (+39) 800 795 572
e-mail: MedInfo@amicusrx.com

Κύπρος

Amicus Therapeutics Europe Limited
Τηλ: (+357) 800 97595
e-mail: MedInfo@amicusrx.com

Latvija

Amicus Therapeutics Europe Limited
Tel: (+371) 800 05391
e-pasts: MedInfo@amicusrx.com

This leaflet was last revised in**Other sources of information**

Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu>. There are also links to other websites about rare diseases and treatments.

Österreich

Amicus Therapeutics Europe Limited
Tel: (+43) 0800 909 639
E-Mail: MedInfo@amicusrx.com

Polska

Amicus Therapeutics Europe Limited
Tel.: (+48) 0080 012 15475
e-mail: MedInfo@amicusrx.com

Portugal

Amicus Therapeutics Europe Limited
Tel: (+351) 800 812 531
e-mail: MedInfo@amicusrx.com

România

Amicus Therapeutics Europe Limited
Tel.: (+40) 800 476 561
e-mail: MedInfo@amicusrx.com

Slovenija

Amicus Therapeutics Europe Limited
Tel.: (+386) 0800 81794
e-pošta: MedInfo@amicusrx.com

Slovenská republika

Amicus Therapeutics Europe Limited
Tel: (+421) 0800 002 437
e-mail: MedInfo@amicusrx.com

Suomi/Finland

Amicus Therapeutics Europe Limited
Puh/Tel: (+358) 0800 917 780
sähköposti/e-mail: MedInfo@amicusrx.com

Sverige

Amicus Therapeutics Europe Limited
Tfn: (+46) 020 795 493
e-post: MedInfo@amicusrx.com