DEVELOPED BY AMICUS THERAPEUTICS UK LTD.
INTENDED FOR HEALTHCARE PROFESSIONALS
IN THE UK AND IRELAND

YOUR GUIDE TO RECONSTITUTION AND ADMINISTRATION

Pombiliti®▼ (cipaglucosidase alfa) + Opfolda® (miglustat) 65 mg capsules

TREATMENT DAY CHECKLIST

PRODUCTS

- ☐ **POMBILITI® 105 mg vials** (20 mg/kg body weight administered every other week)
- ☐ **OPFOLDA® 65 mg capsules** (for patients ≥50 kg, 4 capsules [260 mg total]; for ≥40 kg to <50 kg, 3 capsules [195 mg total])
- ☐ Premedications as prescribed
- ☐ Adequate contraception as applicable

INFUSION SUPPLIES & EQUIPMENT

- ☐ **Sterile water** for injection at room temperature of 20°C to 25°C
- ☐ **Sodium chloride 9 mg/mL (0.9%) solution** for injection at room temperature of 20°C to 25°C – Choose a bag size based on the patient's body weight
- ☐ **A needle that has a diameter of 18 gauge or less**
- ☐ **Additional supplies** per institution protocol

Always consult the full SmPC and risk management materials before prescribing and administering POMBILITI® + OPFOLDA®.

INDICATION

Pombiliti® (cipaglucosidase alfa) is a long-term enzyme replacement therapy used in combination with the enzyme stabiliser miglustat for the treatment of adults with late-onset Pompe disease (acid α-glucosidase [GAA] deficiency).
Opfolda® (miglustat) is an enzyme stabiliser of cipaglucosidase alfa long-term enzyme replacement therapy in adults with late-onset Pompe disease (acid α-glucosidase [GAA] deficiency).

ADVERSE EVENT REPORTING

Adverse events should be reported.

In the UK, reporting forms and information can be found at **yellowcard.mhra.gov.uk**. Adverse events should also be reported to Amicus on 0808 234 6864 or via email to **drugsafety@amicusrx.com**.

In Ireland, reporting forms and information can be found at **www.hpra.ie**. Adverse events in Ireland should also be reported to Amicus on 1800936230 or via email to **drugsafety@amicusrx.com**.

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

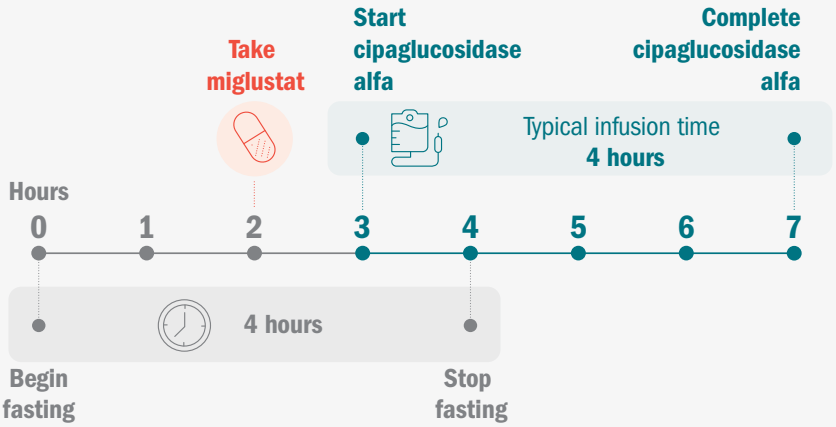
Prescribing information and adverse event reporting information are available at the end of this document.

TIMELINE TO ADMINISTRATION[1,2]

POMBILITI® must be used in combination with OPFOLDA®

The use of OPFOLDA® with any other rhGAA enzyme replacement therapy has not been studied.

WHAT THE INFUSION DAY SHOULD LOOK LIKE



If the patient is switching from another enzyme replacement therapy (ERT), treatment with POMBILITI® + OPFOLDA® can be started at the next scheduled dosing time—approximately 2 weeks after the last ERT administration. Patients who have switched from another ERT to POMBILITI® + OPFOLDA® therapy should be advised to continue with any premedications used with the previous therapy to minimize infusion-associated reactions (IARs).

Note that dosing for both POMBILITI® + OPFOLDA® is based on weight. Double-check the following:

- The patient has taken the OPFOLDA® capsules approximately 1 hour before the infusion is due to begin
- They've been fasting for 2 hours before and 2 hours after taking OPFOLDA®

Taking OPFOLDA® :

- Capsules should be swallowed whole and taken on an empty stomach
- The patient should **fast 2 hours before and 2 hours after taking OPFOLDA®**
  - During this 4-hour fasting period, water, fat-free (skimmed) cow's milk, and tea or coffee with no cream, sugars, or sweeteners can be consumed.
- Capsules should be taken approximately **1 hour before the start of POMBILITI® infusion**
  - In the event of infusion delay, the start of infusion should not exceed 3 hours from the oral administration of OPFOLDA®
- Two hours after taking OPFOLDA® , the patient can resume normal eating and drinking

rhGAA, recombinant human acid alpha-glucosidase.

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HELPFUL INFORMATION FOR DOSING[1,2]

Dosing for both POMBILITI® + OPFOLDA® is based on body weight

If the patient's weight has changed since their last infusion, or if you haven't administered POMBILITI® + OPFOLDA® to the patient before, you will need to weigh the patient.

Calculating the dose

POMBILITI® is administered to the patient by intravenous infusion every other week in combination with the oral medication OPFOLDA® .

Weight-based dosing

Recommended dosage:
20 mg/kg of total body weight administered once every other week as an intravenous infusion

OPFOLDA® capsules of 65 mg are administered every other week in combination with the intravenous infusion POMBILITI®.

Weight-based dosing

Recommended dosage:
- ≥ 40 kg to < 50 kg = 3 capsules
- ≥ 50 kg = 4 capsules

	Calculation	Example	
Dose	Patient's body weight (kg) x dose (20 mg/kg)	65 kg x 20 mg/kg = 1300 mg total dose	
Number of vials	Patient's dose (in mg) divided by 105 (mg/vial)	1300/105 mg per vial = **12.38 vials**	
	Round up to the nearest whole vial	12.38 vials → 13 vials	
Calculate extraction volume	Number of full vials x 7.0 mL/bottle extraction volume	**12** vials x 7.0 mL = **84 mL**	**0.38** vial x 7.0 mL = **2.7 mL**
		84 mL + 2.7 mL = **86.7 mL extraction volume**	

PREPARING FOR RECONSTITUTION[1]

Before POMBILITI® can be administered to the patient, it must be reconstituted

- Once you know how many vials you'll be using, take them out of the refrigerator and let them stand for about 30 minutes to reach room temperature of 20°C to 25°C
- Each vial of Pombiliti® is for single use only
- Use aseptic technique

Items needed for reconstitution and dilution:

POMBILITI® 105 mg vials

Sterile water for injection at room temperature of 20°C to 25°C

Sodium chloride 9 mg/mL (0.9%) solution for injection at room temperature of 20°C to 25°C
- Choose a bag size based on the patient's body weight

A needle with a diameter of 18 gauge or less

Inspect each vial carefully.

Clear to opalescent, colourless to slightly yellow, and appears almost free of particles, but may contain white-to-translucent particles.

Do not use if foreign particles are observed or if the solution is discoloured.

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RECONSTITUTING[1]

Reconstituting the lyophilised powder:

1.

Remove vials from the refrigerator (2°C to 8°C) and allow to come to room temperature (ie, approximately 30 minutes at 20°C to 25°C).

2.

Reconstitute each vial by slowly adding 7.2 mL sterile water for injection dropwise down onto the lyophilised powder. Avoid forceful impact of sterile water for injection on the lyophilised powder and avoid foaming.

3.

Tilt and roll each vial gently to dissolve the powder. Do not invert, swirl or shake. Reconstitution of the lyophilised powder typically takes 2 minutes.

4.

Perform an inspection of the reconstituted vials for particulate matter and discolouration. The reconstituted 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.

- Do not use if upon immediate inspection foreign particles other than those described above are observed, or if the reconstituted solution is discoloured
- Each reconstituted vial should yield a concentration of 15 mg/mL with an extractable volume of 7.0 mL

5. **Repeat the above steps for the number of vials needed for dilution.**

DILUTING[1]

Diluting the solution:

1.

Select an intravenous (IV) bag with sufficient volume to achieve a final target concentration range of 0.5 mg/mL to 4 mg/mL for the diluted POMBILITI® solution for IV infusion.

2.

Remove airspace within the infusion bag. Remove an equal volume of sodium chloride 9 mg/mL (0.9%) solution for injection that will be replaced by the total volume (mL) of reconstituted POMBILITI®.

3.

The reconstituted volume allows accurate withdrawal of 7.0 mL (equal to 105 mg) from each vial. Slowly withdraw the reconstituted solution from the vials until the patient's dose is obtained. Avoid foaming in the syringe. Discard any remaining reconstituted solution in the last vial.

4.

Slowly inject reconstituted POMBILITI® directly into the sodium chloride 9 mg/mL (0.9%) solution for injection bag. Do not add directly into the air space that may remain within the infusion bag.

5.

Gently invert or massage the bag to mix the diluted solution.

- Do not shake or excessively agitate the bag for infusion
- Do not use a pneumatic tube to transport the infusion bag

6.

Repeat steps on remaining infusion bag(s) to achieve the total volume (mL) of reconstituted cipaglucosidase alfa required for the patient's dose.

- **POMBILITI® should be administered as stated in the Summary of Product Characteristics**
- **The infusion solution should be administered as close to after dilution preparation as possible at room temperature**
- **An intravenous administration set should be used with an inline low protein binding 0.2 micron filter. If the intravenous line blocks during infusion, change the filter**
- **If immediate use is not possible, the reconstituted solution may be stored for up to 24 hours under refrigeration at 2°-8° C**

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ADMINISTERING THE INFUSION[1]

Now you're ready to begin the infusion

The infusion will take approximately 4 hours.

Treatment should be supervised by a physician experienced in the management of patients with Pompe disease or other inherited metabolic or neuromuscular diseases.

Recommended Infusion Volumes and Rates

Patient Weight Range (kg)	Total Infusion Volume (mL)	Step 1 1 mg/kg/hr	Step 2 3 mg/kg/hr	Step 3 5 mg/kg/hr	Step 4 7 mg/kg/hr
		Infusion rate in mL/hr			
40–50	250	13	38	63	88
50.1–60	300	15	45	75	105
60.1–100	500	25	75	125	175
100.1–120	600	30	90	150	210
120.1–140	700	35	105	175	245

1. The infusion solution should be administered at room temperature.
2. Total volume of infusion is determined by body weight and typically administered over approximately 4 hours, if tolerated.
3. Infusion of POMBILITI® should start approximately **1 hour after oral administration of OPFOLDA® .**
4. In the event of infusion delay, the **start of infusion should not exceed 3 hours from the oral administration of OPFOLDA® .**
5. Infusion should be administered in a stepwise manner.
6. The initial infusion rate of 1 mg per kg per hour is recommended.
7. The infusion rate may be gradually increased by 2 mg per kg per hour every 30 minutes, if there are no signs of infusion-associated allergic reactions (IARs), until a maximum rate of 7 mg per kg per hour is reached.

The infusion rate may be slowed or temporarily stopped in the event of mild-to-moderate IARs.
In the event of severe allergic, anaphylaxis, serious or severe IARs, immediately stop the infusion and initiate appropriate medical treatment.

Disposal

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

SAFETY[1-3]

Always consult the full SmPC and risk management materials before prescribing and administering POMBILITI® + OPFOLDA®.

Contraindications

- **POMBILITI** is contraindicated in patients with life-threatening hypersensitivity to the active substance, or to any of the excipients listed in the SmPC, when rechallenge was unsuccessful
- **OPFOLDA** is contraindicated in patients with a hypersensitivity to the active substance, or to any of the excipients as listed in the SmPC

Immunogenicity

- Overall, there was **no apparent association between immunogenicity** and safety, PK, or PD effects
- **Patients should be monitored** for signs and symptoms of systemic immune complex-related reactions

Most commonly reported adverse reactions (≥ 1/10)

- **POMBILITI: The most commonly reported adverse reactions** only attributable to cipaglucosidase alfa were dizziness (2.6%), flushing (2.0%), somnolence (2.0%), chest discomfort (1.3%), cough (1.3%), infusion site swelling (1.3%), and pain (1.3%).
- **OPFOLDA: The most commonly reported adverse reaction** only attributable to miglustat 65 mg was constipation (1.3%).

Infusion-associated reactions (IARs)

- In the Phase 3 study, the following IARs were reported during or within 2 hours after completion of the POMBILITI infusion: abdominal distension, chills, pyrexia, dizziness, dysgeusia, dyspnoea, pruritus, rash, and flushing
- 0.7% of patients receiving POMBILITI + OPFOLDA experienced a serious adverse reaction of anaphylaxis (characterised by generalised pruritus, dyspnoea, and hypotension) during the Phase 3 trial. 1.3% of patients receiving POMBILITI + OPFOLDA discontinued treatment due to IARs (anaphylaxis and chills). Most IARs were mild or moderate in severity and transient in nature

Risk management information

FERTILITY, PREGNANCY AND LACTATION

- Reliable contraceptive measures must be used by women of childbearing potential during and for 4 weeks after stopping treatment. POMBILITI + OPFOLDA is not recommended for use in women of childbearing potential not using reliable contraception.
- POMBILITI + OPFOLDA is not recommended for use during pregnancy.
- It is not known whether POMBILITI + OPFOLDA are excreted in human breast milk. A risk to new-borns/infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from POMBILITI + OPFOLDA taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.
- There are no clinical data on the effects of POMBILITI + OPFOLDA on fertility.
- Please consult the SmPC.

PD, pharmacodynamics; PK, pharmacokinetics.

PRESCRIBING INFORMATION

Pombiliti® ▼
(cipaglucosidase alfa)

Click here or scan the QR code for UK POMBILITI prescribing information

ADVERSE EVENTS SHOULD BE REPORTED

In the UK, reporting forms and information can be found at **yellowcard.mhra.gov.uk**. Adverse events should also be reported to Amicus on 0808 234 6864 or via email to **drugsafety@amicusrx.com.**

Click here or scan the QR code for Ireland POMBILITI prescribing information

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▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.
See section 4.8 of SmPC for how to report adverse reactions.

Opfolda®
(miglustat) 65 mg capsules

Click here or scan the QR code for UK OPFOLDA prescribing information

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REFERENCES

1. Amicus Therapeutics. Pombiliti 105 mg powder for concentrate for solution for infusion SmPC.
2. Amicus Therapeutics. Opfolda 65 mg hard capsules SmPC.
3. Schoser B, Roberts M, Byrne BJ, et al. Safety and efficacy of cipaglucosidase alfa plus miglustat versus alglucosidase alfa plus placebo in late-onset Pompe disease (PROPEL): an international, randomised, double-blind, parallel-group, phase 3 trial. Lancet Neurol. 2021;20(12):1027-1037. doi:10.1016/S1474-4422(21)00331-8

Pombiliti® (cipaglucosidase alfa) + Opfolda® (miglustat) 65 mg capsules

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