YOUR GUIDE TO RECONSTITUTING AND ADMINISTERING
POMBILITI AND OPFOLDA

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

TREATMENT DAY CHECKLIST[1,2]

PRODUCTS

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

INFUSION SUPPLIES & EQUIPMENT

- ☐ **Sterile water** for injection at room temperature
- ☐ **Sodium chloride 9 mg/mL (0.9%) solution** for injection at room temperature—choose a bag size based on the patient's body weight
- ☐ **Additional supplies** per institution protocol

*Patients with moderate or severe renal impairment may require alternate dosing of OPFOLDA. See page 3 for additional details.

INDICATION

POMBILITI in combination with OPFOLDA is indicated for the treatment of adult patients with late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency) weighing ≥40 kg and who are not improving on their current enzyme replacement therapy (ERT).

IMPORTANT SAFETY INFORMATION

WARNING: SEVERE HYPERSENSITIVITY REACTIONS, INFUSION-ASSOCIATED REACTIONS, and RISK OF ACUTE CARDIORESPIRATORY FAILURE IN SUSCEPTIBLE PATIENTS

See full prescribing information for complete boxed warning

Hypersensitivity Reactions Including Anaphylaxis

Appropriate medical support measures, including cardiopulmonary resuscitation equipment, should be readily available. If a severe hypersensitivity reaction occurs, POMBILITI should be discontinued immediately and appropriate medical treatment should be initiated.

Infusion-Associated Reactions (IARs)

If severe IARs occur, immediately discontinue POMBILITI and initiate appropriate medical treatment.

Risk of Acute Cardiorespiratory Failure in Susceptible Patients

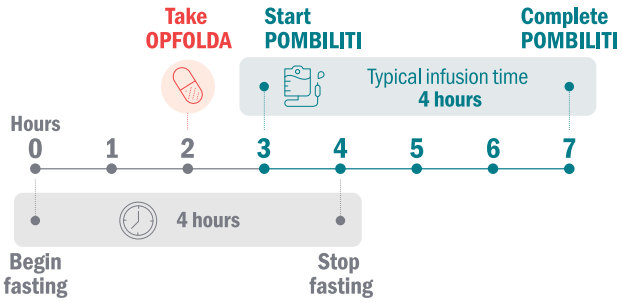
Patients susceptible to fluid volume overload, or those with acute underlying respiratory illness or compromised cardiac or respiratory function, may be at risk of serious exacerbation of their cardiac or respiratory status during POMBILITI infusion.

Please see additional Important Safety Information throughout and on page 8, and full Prescribing Information, including BOXED WARNING, for POMBILITI and full Prescribing Information for OPFOLDA, also available at PombilitiOpfoldaHCP.com.

TIMELINE FOR ADMINISTRATION

POMBILITI must be administered in combination with OPFOLDA[1,2]

TREATMENT DAY SCHEDULE

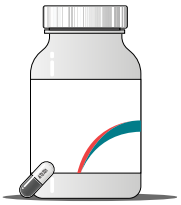


When switching from another ERT, treatment with POMBILITI + OPFOLDA can be started 2 weeks after the last ERT dose. Prior to POMBILITI administration, consider pretreating with antihistamines, antipyretics, and/or corticosteroids, especially if premedication was used with the patient's previous ERT.

Double-check the following:

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

Taking OPFOLDA:



- Patients are required to **fast for 2 hours before and 2 hours after taking OPFOLDA**
- OPFOLDA should be taken **approximately 1 hour before the start of POMBILITI infusion**
  - If the infusion cannot be started within 3 hours of oral administration of OPFOLDA, reschedule POMBILITI in combination with OPFOLDA to at least 24 hours after OPFOLDA was last taken. If both medications are missed, re-start treatment as soon as possible
- OPFOLDA should be swallowed whole with unsweetened beverages, including water, tea, or coffee with no cream, sugar, or other sweeteners. These beverages can be consumed during this 4-hour fasting period
- 2 hours after taking OPFOLDA, the patient can resume normal eating and drinking

For female patients:

- POMBILITI in combination with OPFOLDA is contraindicated in pregnancy
- Verify the pregnancy status in females of reproductive potential prior to initiating treatment with OPFOLDA in combination with POMBILITI
- Advise females of reproductive potential to use effective contraception during treatment with OPFOLDA in combination with POMBILITI and for at least 60 days after the last dose

IMPORTANT SAFETY INFORMATION (continued)

HYPERSENSITIVITY REACTIONS INCLUDING ANAPHYLAXIS

Patients treated with POMBILITI have experienced life-threatening hypersensitivity reactions, including anaphylaxis. Appropriate medical support measures, including cardiopulmonary resuscitation equipment, should be readily available during POMBILITI administration. If a severe hypersensitivity reaction (e.g., anaphylaxis) occurs, POMBILITI should be discontinued immediately, and appropriate medical treatment should be initiated. In patients with severe hypersensitivity reaction, desensitization measures to POMBILITI may be considered. The risks and benefits of readministering POMBILITI following severe hypersensitivity reaction should be considered. If mild or moderate hypersensitivity reaction occurs, the infusion rate may be slowed or temporarily stopped. Prior to POMBILITI administration, consider pretreating with antihistamines, antipyretics, and/or corticosteroids.

Please see additional Important Safety Information throughout and on page 8, and full Prescribing Information, including BOXED WARNING, for POMBILITI and full Prescribing Information for OPFOLDA, also available at PombilitiOpfoldaHCP.com.

HELPFUL INFORMATION FOR DOSING

Dosing for both POMBILITI and OPFOLDA is based on actual body weight[1,2]

Patients should be weighed at every visit to calculate the correct dose.

Calculating the dose

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

Weight-based dosing

Recommended dosage:

20 mg/kg of actual body weight administered every other week as an intravenous solution

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

Weight-based dosing

Recommended dosage for patients weighing:

- ≥50 kg = 260 mg (4 capsules of 65 mg)
- ≥40 kg to <50 kg = 195 mg (3 capsules of 65 mg)

Patients with moderate or severe renal impairment may require alternate dosing of OPFOLDA*

Recommended OPFOLDA dosage in patients with moderate or severe renal impairment:

- ≥50 kg = 195 mg (3 capsules of 65 mg)
- ≥40 kg to <50 kg = 130 mg (2 capsules of 65 mg)

For patients with mild renal impairment, the recommended OPFOLDA dosage is the same as for patients with normal renal function.

*Renal function is classified by creatinine clearance (CLcr) based on the Cockcroft-Gault equation. Mild renal impairment is CLcr 60-89 mL/min, moderate renal impairment is CLcr 30-59 mL/min, and severe renal impairment is CLcr 15-29 mL/min.

	Calculation	Example	
Dose	Patient's actual body weight (kg) x dose (20 mg/kg)	75 kg x 20 mg/kg = 1500 mg total dose	
Vials to reconstitute	Total dose (in mg) divided by 105 (mg/vial) Round up to the nearest whole vial	1500 mg / 105 mg/vial = **14.29 vials** 14.29 vials → 15 vials	
Total extraction volume	Number of vials x 7.0 mL/bottle extraction volume	**14** vials x 7.0 mL = **98 mL**	**0.29** vial x 7.0 mL ≈ **2.0 mL**
		98 mL + 2.0 mL = **100 mL extraction volume**	

Note that each vial requires 7.2 mL of sterile water to reconstitute, but should only yield 7.0 mL of solution for the infusion bag.

Dosage and administration modifications may be necessary due to hypersensitivity reactions (including anaphylaxis) and/or infusion-associated reactions. Please consult the full Prescribing Information for instructions on appropriate dose modifications before administration.

IMPORTANT SAFETY INFORMATION (continued)

INFUSION-ASSOCIATED REACTIONS

Patients treated with POMBILITI have experienced severe IARs. If severe IARs occur, immediately discontinue the POMBILITI infusion, initiate appropriate medical treatment, and assess the benefits and risks of readministering POMBILITI following severe IARs. If mild or moderate IARs occur regardless of pretreatment, decreasing the infusion rate or temporarily stopping the infusion may ameliorate the symptoms. IARs may still occur in patients after receiving pretreatment.

Patients with an acute underlying illness at the time of POMBILITI infusion may be at greater risk for IARs. Patients with advanced Pompe disease may have compromised cardiac and respiratory function, which may predispose them to a higher risk of severe complications from IARs.

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PREPARING FOR RECONSTITUTION AND DILUTION

Before POMBILITI can be administered to the patient, it must be reconstituted and diluted[1]

Items needed for reconstitution and dilution:

POMBILITI 105-mg vials

Sterile water for injection at room temperature

Sodium chloride 9 mg/mL (0.9%) solution for injection at room temperature
– Choose a bag size based on the patient's actual body weight

RECONSTITUTING

Reconstituting the lyophilized powder[1]:

1.

Remove vials from the refrigerator and set aside for approximately 30 minutes to allow vials to come to room temperature.

2.

Reconstitute each vial by slowly adding 7.2 mL of sterile water for injection down the inside wall of each vial to avoid foaming. Avoid forceful impact of sterile water for injection on the lyophilized powder and avoid foaming.

3.

Roll and tilt each vial to allow the lyophilized powder to dissolve completely. This typically takes 2 minutes. Do not invert, swirl, or shake.

4.

Visually inspect the reconstituted vials for particulate matter and discoloration. The reconstituted solution appears as a clear to opalescent, colorless to yellowish solution, essentially particle free.

- Discard if foreign matter is observed or the solution is discolored
- Each reconstituted vial should yield a concentration of 15 mg/mL

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

Storing the reconstituted solution

If the reconstituted POMBILITI vials are not used immediately, store refrigerated at 2 °C to 8 °C (36 °F to 46 °F) for up to 24 hours. Do not freeze.

IMPORTANT SAFETY INFORMATION (continued)

CONTRAINDICATION

POMBILITI in combination with OPFOLDA is contraindicated in pregnancy.

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DILUTING

Diluting the solution[1]:

Remove airspace within a bag of 0.9% sodium chloride injection. Remove an equal volume of 0.9% sodium chloride injection that will be replaced by the total volume (mL) of reconstituted POMBILITI.

Slowly withdraw 7 mL of reconstituted solution from each of the vials until the patient's dose is obtained. Discard any remaining reconstituted solution in the last vial.

Slowly inject reconstituted POMBILITI directly into the infusion bag.

To prevent foaming, gently invert the infusion bag to mix the solution.

- Avoid vigorous shaking or agitation
- Do not use a pneumatic tube to transport the infusion bag. Each reconstituted vial should yield a concentration of 15 mg/mL

- **Administer the diluted solution at room temperature without delay**
- **If the diluted solution is not administered immediately, store refrigerated at 2 °C to 8 °C (36 °F to 46 °F) for up to 16 hours. Storage at room temperature is not recommended. Do not freeze**

See section 2.4 of the POMBILITI Prescribing Information for instructions for handling diluted solution that has been refrigerated.

ADMINISTERING THE INFUSION[1]

1. The infusion solution should be administered at room temperature. If the infusion solution has been refrigerated, allow solution to equilibrate to room temperature for 30 minutes prior to infusion.
2. Prior to administration, inspect the infusion bag for foaming. If foaming is present, let foam dissipate before administering POMBILITI.
3. Infusion of POMBILITI should start **approximately 1 hour after oral administration of OPFOLDA.**
4. 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.
5. The initial recommended infusion rate is 1 mg per kg per hour.
6. The infusion rate may be increased by 2 mg per kg per hour every 30 minutes, if there are no signs of hypersensitivity or infusion-associated reactions (IARs), until a maximum rate of 7 mg/kg/hour is reached; then, maintain the infusion rate at 7 mg/kg/hour until the infusion is complete. **Do not infuse POMBILITI in the same intravenous line with other products.**

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

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

IMPORTANT SAFETY INFORMATION (continued)

RISKS ASSOCIATED WITH POMBILITI AND OPFOLDA

POMBILITI and OPFOLDA must be administered in combination.

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For more information on dosing, please visit PombilitiOpfoldaHCP.com

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HYPERSENSITIVITY REACTIONS INCLUDING ANAPHYLAXIS

Patients treated with POMBILITI have experienced life-threatening hypersensitivity reactions, including anaphylaxis. Appropriate medical support measures, including cardiopulmonary resuscitation equipment, should be readily available during POMBILITI administration. If a severe hypersensitivity reaction (e.g., anaphylaxis) occurs, POMBILITI should be discontinued immediately, and appropriate medical treatment should be initiated. In patients with severe hypersensitivity reaction, desensitization measures to POMBILITI may be considered. The risks and benefits of readministering POMBILITI following severe hypersensitivity reaction should be considered. If mild or moderate hypersensitivity reaction occurs, the infusion rate may be slowed or temporarily stopped. Prior to POMBILITI administration, consider pretreating with antihistamines, antipyretics, and/or corticosteroids.

INFUSION-ASSOCIATED REACTIONS (IARs)

Patients treated with POMBILITI have experienced severe IARs. If severe IARs occur, immediately discontinue the POMBILITI infusion, initiate appropriate medical treatment, and assess the benefits and risks of readministering POMBILITI following severe IARs. If mild or moderate IARs occur regardless of pretreatment, decreasing the infusion rate or temporarily stopping the infusion may ameliorate the symptoms. IARs may still occur in patients after receiving pretreatment.

Patients with an acute underlying illness at the time of POMBILITI infusion may be at greater risk for IARs. Patients with advanced Pompe disease may have compromised cardiac and respiratory function, which may predispose them to a higher risk of severe complications from IARs.

RISK OF ACUTE CARDIORESPIRATORY FAILURE IN SUSCEPTIBLE PATIENTS

Patients susceptible to fluid volume overload, or those with acute underlying respiratory illness or compromised cardiac or respiratory function for whom fluid restriction is indicated may be at risk of serious exacerbation of their cardiac or respiratory status during POMBILITI infusion. More frequent monitoring of vitals should be performed during POMBILITI infusion in such patients.

CONTRAINDICATION

POMBILITI in combination with OPFOLDA is contraindicated in pregnancy.

EMBRYO-FETAL TOXICITY

Based on findings from animal reproduction studies, POMBILITI in combination with OPFOLDA may cause embryo-fetal harm when administered to a pregnant female and is contraindicated during pregnancy. Verify the pregnancy status in females of reproductive potential prior to initiating treatment with POMBILITI in combination with OPFOLDA. Advise females of reproductive potential to use effective contraception during treatment with POMBILITI in combination with OPFOLDA and for at least 60 days after the last dose.

RISKS ASSOCIATED WITH POMBILITI AND OPFOLDA

POMBILITI and OPFOLDA must be administered in combination.

ADVERSE REACTIONS

The most common adverse reactions (≥5%) reported in the pooled safety population of patients treated with POMBILITI in combination with OPFOLDA in the 3 clinical trials were headache, diarrhea, fatigue, nausea, abdominal pain, and pyrexia.

To report SUSPECTED ADVERSE REACTIONS, contact Amicus Therapeutics at 1-877-4AMICUS or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

LACTATION

Advise females that breastfeeding is not recommended while on treatment with POMBILITI in combination with OPFOLDA.

INDICATION

POMBILITI in combination with OPFOLDA is indicated for the treatment of adult patients with late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency) weighing ≥40 kg and who are not improving on their current enzyme replacement therapy (ERT).

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References: 1. POMBILITI. Prescribing information. Amicus Therapeutics US, LLC; 2024. **2.** OPFOLDA. Prescribing information. Amicus Therapeutics US, LLC; 2024
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