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

**A two-component therapy for adults with late-onset Pompe disease (LOPD) weighing 88 lbs or more who are not improving on their current enzyme replacement therapy (ERT).**

## POMBILITI + OPFOLDA

# improvement is possible

**If you and your doctor are considering a different treatment, it could be helpful to see study results in adults with LOPD who were switched from their previous ERT.**

Learn more at **improvementispossible.com**

**EMMA & MADDIE**
SIBLINGS DIAGNOSED WITH LOPD IN 2009

**In a clinical trial, ERT-experienced adults who received POMBILITI + OPFOLDA experienced improvements in walking ability and breathing function compared to those who received the Comparator***

*An alglucosidase alfa product not approved in the US + placebo.

### What are POMBILITI and OPFOLDA?

POMBILITI and OPFOLDA are prescription medicines used in combination for the treatment of adults with late-onset Pompe disease weighing 88 pounds (40 kg) or more and who are not improving on their current enzyme replacement therapy (ERT).

It is not known if POMBILITI in combination with OPFOLDA is safe and effective in children with late-onset Pompe disease.

### IMPORTANT SAFETY INFORMATION

**Warning: Hypersensitivity Reactions (including Anaphylaxis), Infusion-Associated Reactions (IARs), and Risk of Acute Cardiorespiratory Failure**

**POMBILITI in combination with OPFOLDA may cause serious side effects, including:**

- **Hypersensitivity reactions (including anaphylaxis):** Severe and potentially life-threatening allergic-type reactions related to the infusion have been reported during and after POMBILITI in combination with OPFOLDA treatment. Your doctor will inform you of the signs and symptoms of hypersensitivity reactions which may include: difficulty breathing or swallowing; rash or hives; low blood pressure; swelling of lips, tongue, throat, or face. Seek medical care immediately should signs and symptoms occur. If a severe reaction occurs, your doctor may decide to immediately discontinue the infusion and provide medical care. Appropriate medical support measures may be administered, and you may require close observation during and after POMBILITI infusion.

**Please see Important Safety Information throughout and on page 10, and full Prescribing Information, including BOXED WARNING, for POMBILITI and full Prescribing Information and Patient Information for OPFOLDA, also available at improvementispossible.com.**

# What is late-onset Pompe disease (LOPD)?

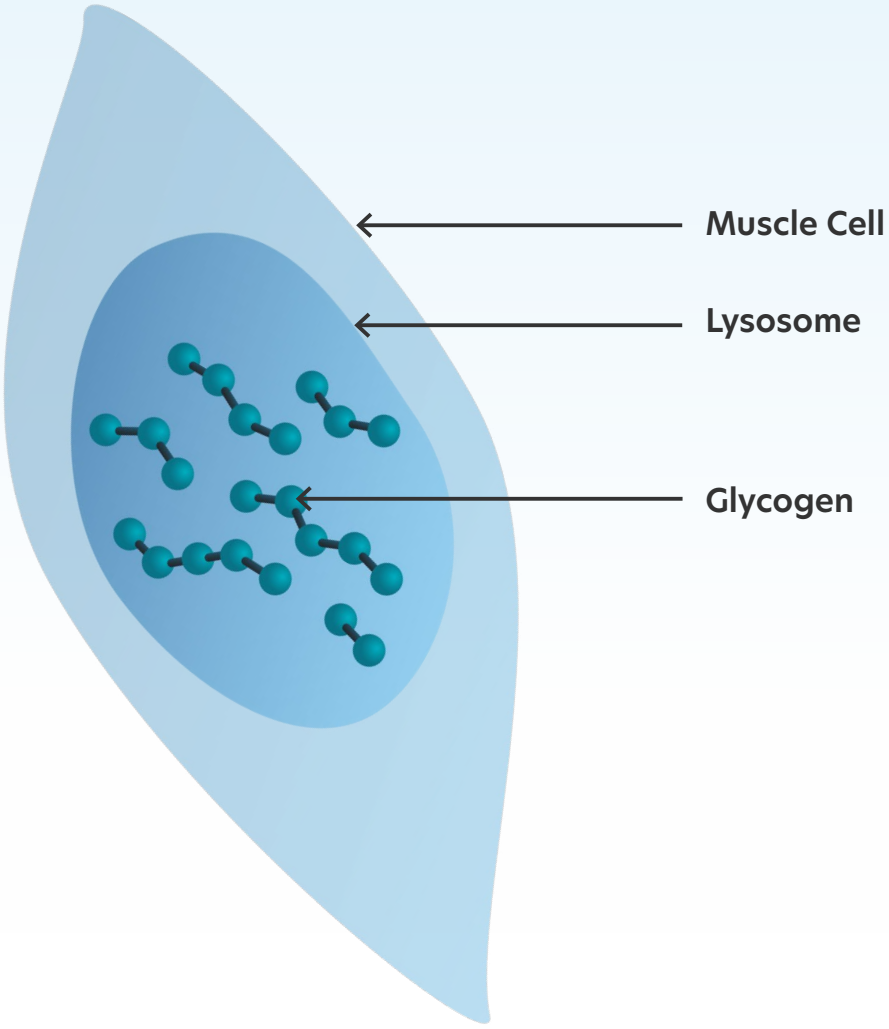
**LOPD is a rare lysosomal disease** that's caused by deficiencies in the acid alpha-glucosidase enzyme, also known as GAA.

**GAA is responsible for breaking down glycogen, a type of sugar, into glucose.** This occurs within a part of the muscle cells called the lysosomes. But when there's not enough active GAA available in the lysosomes, excess glycogen buildup may cause irreparable damage to the muscles responsible for walking and breathing.

Enzyme replacement therapy (ERT) replaces the natural GAA that people with LOPD lack. But it can become vulnerable and lose function once infused into the bloodstream.

### LOPD Treatment Challenges

Many people who received ERT alone began experiencing declines 3-5 years after starting therapy.



# A purposeful partnership for LOPD

**POMBILITI® (cipaglucosidase alfa-atga)** is a bis-M6P–enriched enzyme replacement therapy (ERT) that was **designed to deliver active GAA enzyme directly to the muscle cells** for improved binding and effective uptake

**OPFOLDA® (miglustat)** is the first and only oral enzyme stabilizer designed for LOPD. OPFOLDA **stabilizes POMBILITI within the bloodstream**

## Words you need to know

**Acid alpha-glucosidase (GAA) enzyme**
Protein that breaks down glycogen into glucose, which is used for energy.

**Bis-M6P**
POMBILITI contains bis-M6P (bis-mannose 6-phosphate). Bis-M6P is a type of sugar that contains 2 phosphates. These phosphates help POMBILITI bind more strongly to receptors on the muscle cells compared with M6P, which contains only 1 phosphate.

**Enzyme replacement therapy**
Enzyme replacement therapy, or ERT, is a prescription medicine that is infused intravenously to replace missing or deficient GAA enzymes in people with LOPD.

**Enzyme stabilizer**
When ERT is infused, the pH of the blood can cause it to lose function. OPFOLDA helps stabilize POMBILITI and prevent it from becoming inactive while in the blood.

## SELECT IMPORTANT SAFETY INFORMATION (continued)

**POMBILITI in combination with OPFOLDA may cause serious side effects, including:**

- **Infusion-Associated Reactions (IARs):** Severe IARs related to the infusion have been reported during or after POMBILITI in combination with OPFOLDA. Your doctor will inform you of the signs and symptoms of hypersensitivity reactions which may include: hives, itching, shortness of breath, flushing, chills, and low blood pressure. Seek medical care immediately should signs and symptoms occur. If severe IARs occur during infusion, your doctor may decide to immediately discontinue the infusion and provide appropriate medical care. If you have an acute underlying illness at the time of POMBILITI infusion you may be at greater risk for IARs. If you have advanced Pompe disease you may have compromised heart and breathing function, which may put you at a higher risk of severe complications from IARs.

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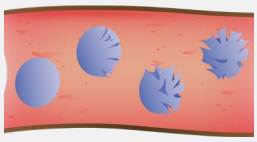
# Here's how it works

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

## IN THE BLOOD



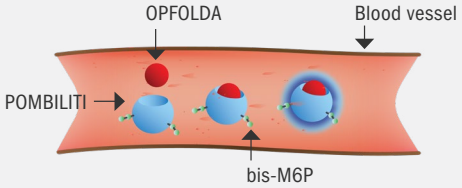
The enzymes used in enzyme replacement therapy (ERT) can become vulnerable and lose function in the blood before reaching your muscle cells, which limits the amount of ERT available to enter the cell and break down glycogen.

**1**

OPFOLDA is specifically designed to stabilize **POMBILITI, a bis-M6P-enriched enzyme**, and help it maintain function as it travels in the blood.

POMBILITI + OPFOLDA dosing is determined by your actual body weight and kidney function. Your healthcare provider will prescribe the dosage that is appropriate for you.

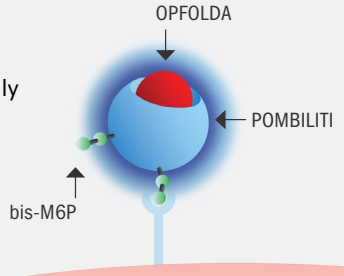
**2**




OPFOLDA binds to and stabilizes POMBILITI as it travels through the bloodstream to maximize the amount of enzyme available for uptake into the muscle.

**3**

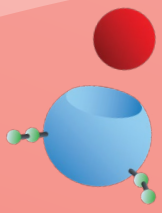
Now, POMBILITI + OPFOLDA can bind strongly to receptors that help guide POMBILITI into the lysosome, the cell's recycling center.




Muscle Cell

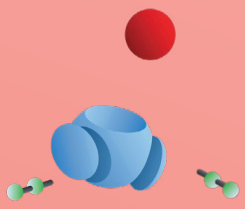
## IN THE LYSOSOME

**4**



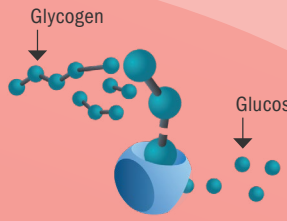
Once inside the lysosome of the muscle cell, OPFOLDA separates from POMBILITI.

**5**



POMBILITI is then processed into the most active form of GAA.

**6**




POMBILITI begins working like a GAA enzyme normally produced by the body, which means it has a similar ability to break down glycogen into glucose.

To learn more about how POMBILITI + OPFOLDA work together to treat LOPD, visit **improvementispossible.com**.

## SELECT IMPORTANT SAFETY INFORMATION (continued)

**POMBILITI in combination with OPFOLDA may cause serious side effects, including:**

- **Risk of Acute Cardiorespiratory Failure:** If you are likely to develop fluid volume overload or have an acute breathing condition or heart and/or breathing problems that require fluid restriction, you may be at risk of worsening of your heart or breathing status during POMBILITI infusion. Your doctor may decide that close observation during and after POMBILITI administration may be necessary.

**Do not take POMBILITI in combination with OPFOLDA if you are pregnant.**

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# OPFOLDA increased levels of POMBILITI in the blood

A study was conducted to measure the levels of POMBILITI in the blood 24 hours after administration. ERT-experienced adults with LOPD were administered POMBILITI 20 mg/kg alone (11 people) or with a single dose of OPFOLDA 260 mg (10 people).

**This study found that 29% more POMBILITI was available in the blood with the addition of OPFOLDA. It is not known if these results provide a clinical benefit.**

**The Total Amount of POMBILITI Available in the Blood**


**POMBILITI is not approved for use without OPFOLDA**

## SELECT IMPORTANT SAFETY INFORMATION (continued)

**Before taking POMBILITI in combination with OPFOLDA, tell your healthcare provider about all of your medical conditions, including if you:**

- have kidney problems
- are pregnant or plan to become pregnant. POMBILITI in combination with OPFOLDA may cause harm to your unborn baby.

  **Females who are able to become pregnant:**
  - Your healthcare provider will check if you are pregnant before you start treatment with POMBILITI in combination with OPFOLDA.
  - You should use effective birth control (contraception) during treatment with POMBILITI in combination with OPFOLDA and for at least 60 days after the last dose.
  - Tell your healthcare provider right away if you become pregnant or think you might be pregnant during treatment with POMBILITI in combination with OPFOLDA.
- are breastfeeding or plan to breastfeed. It is not known if OPFOLDA alone or in combination with POMBILITI passes into your breast milk. **Do not** breastfeed during treatment with POMBILITI in combination with OPFOLDA. Talk to your healthcare provider about the best way to feed your baby during this time.

**Tell your healthcare provider about all the medicines you take,** including prescription and over-the-counter medicines, vitamins, and herbal supplements.

**POMBILITI and OPFOLDA must be taken in combination. POMBILITI in combination with OPFOLDA will be given to you 1 time every other week.**

**The most common side effects of POMBILITI in combination with OPFOLDA include:** headache, diarrhea, tiredness, nausea, stomach area pain, and fever.

**Please see Important Safety Information throughout and on page 10, and full Prescribing Information, including BOXED WARNING, for POMBILITI and full Prescribing Information and Patient Information for OPFOLDA, also available at improvementispossible.com.**

# POMBILITI + OPFOLDA was shown to improve walking distance and breathing function

## vs the Comparator* in ERT-experienced adults

**POMBILITI + OPFOLDA was evaluated in a randomized, controlled clinical study vs the Comparator* over 52 weeks.**

**123 PEOPLE TOTAL IN THE STUDY, INCLUDING:**

**ERT-experienced**
People in this group were on an ERT for at least 2 years

**ERT-naïve†**
People in this group had never received an ERT

**85 people received POMBILITI + OPFOLDA**

**38 people received the Comparator**

- The study's primary endpoint (goal) was to see how much farther people who received POMBILITI + OPFOLDA could walk in 6 minutes, using the **6-Minute Walk Test (6MWT)‡**
- **Forced vital capacity (FVC)**, a test of breathing ability, was a key secondary endpoint (goal) of the study
- ERT-experienced people were on treatment for an average of 7.4 years before the study

*An alglucosidase alfa product not approved in the US + placebo.
†POMBILITI + OPFOLDA is not approved for use in ERT-naïve people.
‡Results of the 6MWT were numerically favorable but did not meet the primary endpoint of statistical superiority for the full study population.

## SELECT IMPORTANT SAFETY INFORMATION (continued)

POMBILITI in combination with OPFOLDA may cause fertility problems in females and males, which may affect the ability to have children. Talk to your healthcare provider if you have concerns about fertility.

**These are not all the possible side effects of POMBILITI and OPFOLDA.** Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

**Warning: Hypersensitivity Reactions (including Anaphylaxis), Infusion-Associated Reactions (IARs), and Risk of Acute Cardiorespiratory Failure**
**POMBILITI in combination with OPFOLDA may cause serious side effects, including:**

- **Hypersensitivity reactions (including anaphylaxis):** Severe and potentially life-threatening allergic-type reactions related to the infusion have been reported during and after POMBILITI in combination with OPFOLDA treatment. Your doctor will inform you of the signs and symptoms of hypersensitivity reactions which may include: difficulty breathing or swallowing; rash or hives; low blood pressure; swelling of lips, tongue, throat, or face. Seek medical care immediately should signs and symptoms occur. If a severe reaction occurs, your doctor may decide to immediately discontinue the infusion and provide medical care. Appropriate medical support measures may be administered, and you may require close observation during and after POMBILITI infusion.

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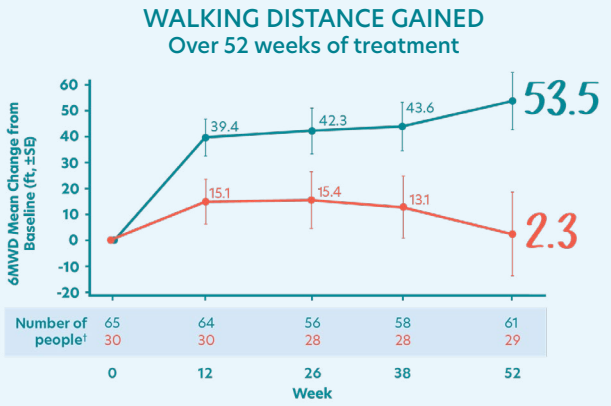
# Walking and breathing results for ERT-experienced adults

**RESULTS FOR ERT-EXPERIENCED ADULTS**

POMBILITI + OPFOLDA (65 people) | Comparator (30 people)

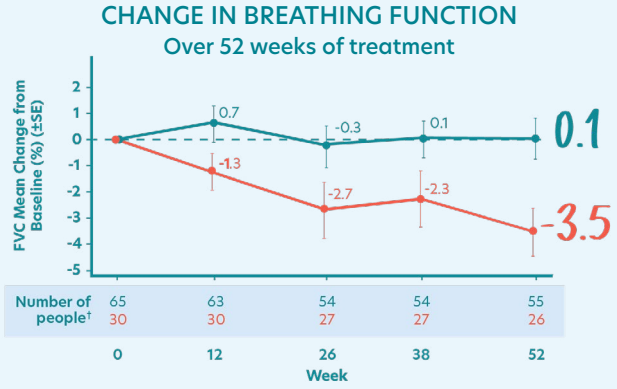
**ERT-experienced adults receiving POMBILITI + OPFOLDA had IMPROVED WALKING DISTANCE versus adults who received the Comparator***

- People who received POMBILITI + OPFOLDA **walked an average of 53.5 feet farther** from the start of the study
- People who received the Comparator **walked an average of 2.3 feet farther** from the start of the study




**ERT-experienced adults receiving POMBILITI + OPFOLDA had IMPROVED BREATHING FUNCTION versus adults who received the Comparator***

- People who received POMBILITI + OPFOLDA saw their breathing **increase by an average of 0.1%** from the start of the study
- People who received the Comparator saw their breathing **decline by an average of 3.5%** from the start of the study




*Results of the 6MWT and FVC for the ERT-experienced group were numerically favorable but were not tested to determine statistical superiority of POMBILITI + OPFOLDA vs the Comparator.

†The number of people for each time point in the chart changed because some people missed some of the tests and some people did not complete the study.

## SELECT IMPORTANT SAFETY INFORMATION (continued)

**POMBILITI in combination with OPFOLDA may cause serious side effects, including:**

- **Infusion-Associated Reactions (IARs):** Severe IARs related to the infusion have been reported during or after POMBILITI in combination with OPFOLDA. Your doctor will inform you of the signs and symptoms of hypersensitivity reactions which may include: hives, itching, shortness of breath, flushing, chills, and low blood pressure. Seek medical care immediately should signs and symptoms occur. If severe IARs occur during infusion, your doctor may decide to immediately discontinue the infusion and provide appropriate medical care. If you have an acute underlying illness at the time of POMBILITI infusion you may be at greater risk for IARs. If you have advanced Pompe disease you may have compromised heart and breathing function, which may put you at a higher risk of severe complications from IARs.

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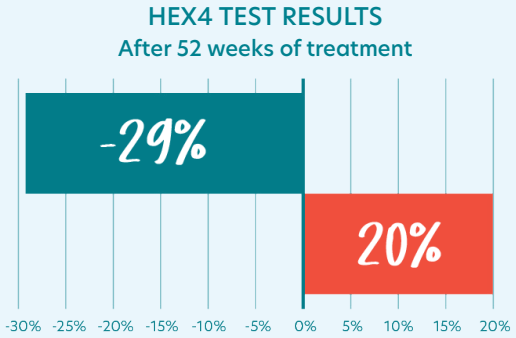
# Biomarker data: improvements in measures of glycogen buildup

**BIOMARKER MEASUREMENT**

POMBILITI + OPFOLDA (64 people) | Comparator (30 people)

**ERT-experienced adults receiving POMBILITI + OPFOLDA had IMPROVED MEASURES OF GLYCOGEN BUILDUP**

- Lower test results in Hex4 are a sign that there is less glycogen buildup
- People receiving POMBILITI + OPFOLDA saw **an average reduction of 29% in Hex4** vs **an average increase of 20%** with the Comparator




## Select Safety Information

### Information about side effects with POMBILITI + OPFOLDA

The most common side effects (≥5%) reported during the clinical study were headache and diarrhea.

The most common side effects reported in at least 5% of participants treated with POMBILITI + OPFOLDA across 3 clinical trials were headache, diarrhea, fatigue, nausea, abdominal pain, and fever.

Serious adverse reactions reported in 2 or more people treated with POMBILITI + OPFOLDA were severe allergic reaction and hives. A total of 5 people treated with POMBILITI + OPFOLDA permanently discontinued POMBILITI due to side effects, including 4 who discontinued the treatment because of a serious side effect.

**Additional side effects**

Side effects reported in at least 2% of adults treated with POMBILITI + OPFOLDA across 3 clinical trials included:

- muscle aches
- joint pain
- increased blood pressure
- pain
- tremors (shaking)
- indigestion
- weakness
- constipation
- infusion site swelling
- flank (side) pain
- feeling unwell
- burning or pins and needles feeling
- drowsiness
- decreased platelet count

Please see additional safety information on page 10, including the BOXED WARNING for Hypersensitivity Reactions (including Anaphylaxis), Infusion-Associated Reactions (IARs), and Risk of Cardiorespiratory Failure.

**These are not all of the possible side effects of POMBILITI in combination with OPFOLDA. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.**

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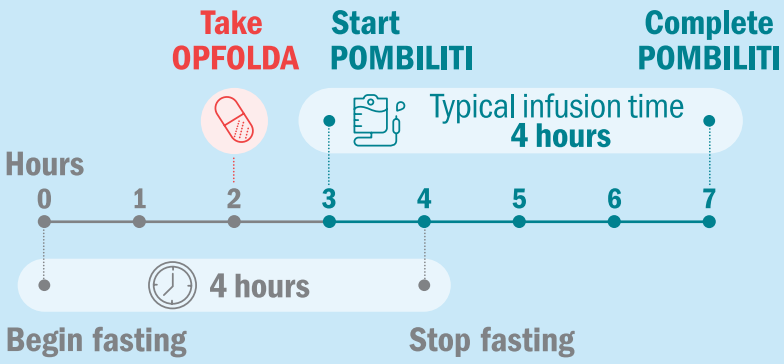
# Treatment day at a glance

**A regular routine every 2 weeks**

**Take OPFOLDA orally approximately 1 hour before each POMBILITI infusion begins**

**Have POMBILITI administered intravenously at a hospital or infusion center**

## A typical treatment day should look like this:




### POMBILITI + OPFOLDA dosing is determined by your actual body weight

You will take 3 or 4 OPFOLDA capsules depending on the dosage that your healthcare provider determines is right for you.

### Switch without delay

When switching to POMBILITI + OPFOLDA, you can start POMBILITI + OPFOLDA on your next scheduled treatment day (2 weeks after your last ERT dose).

Your doctor may recommend taking medicine such as an antihistamine, antipyretic (fever reducer), or corticosteroid before your POMBILITI infusion, especially if you took a medication with your previous ERT. Always take your medication exactly as directed by your healthcare provider.

### A note on fasting:

Avoid food and most liquids (you can drink unsweetened beverages like water, tea, or coffee with no cream, sugar, or other sweeteners) 2 hours before and 2 hours after taking OPFOLDA.

OPFOLDA must be taken while you are fasting to be able to bind to POMBILITI in your bloodstream when your infusion begins. You can resume drinking and eating 2 hours after taking OPFOLDA.

### Track your treatment

Keep track of your upcoming appointments, plan your fasting schedule, and more with the MyDay Pompe™ app. Scan the QR code to download it from the App Store or Google Play.

MyDay Pompe

Download on the App Store

GET IT ON Google Play



## SELECT IMPORTANT SAFETY INFORMATION (continued)

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- **Risk of Acute Cardiorespiratory Failure:** If you are likely to develop fluid volume overload or have an acute breathing condition or heart and/or breathing problems that require fluid restriction, you may be at risk of worsening of your heart or breathing status during POMBILITI infusion. Your doctor may decide that close observation during and after POMBILITI administration may be necessary.

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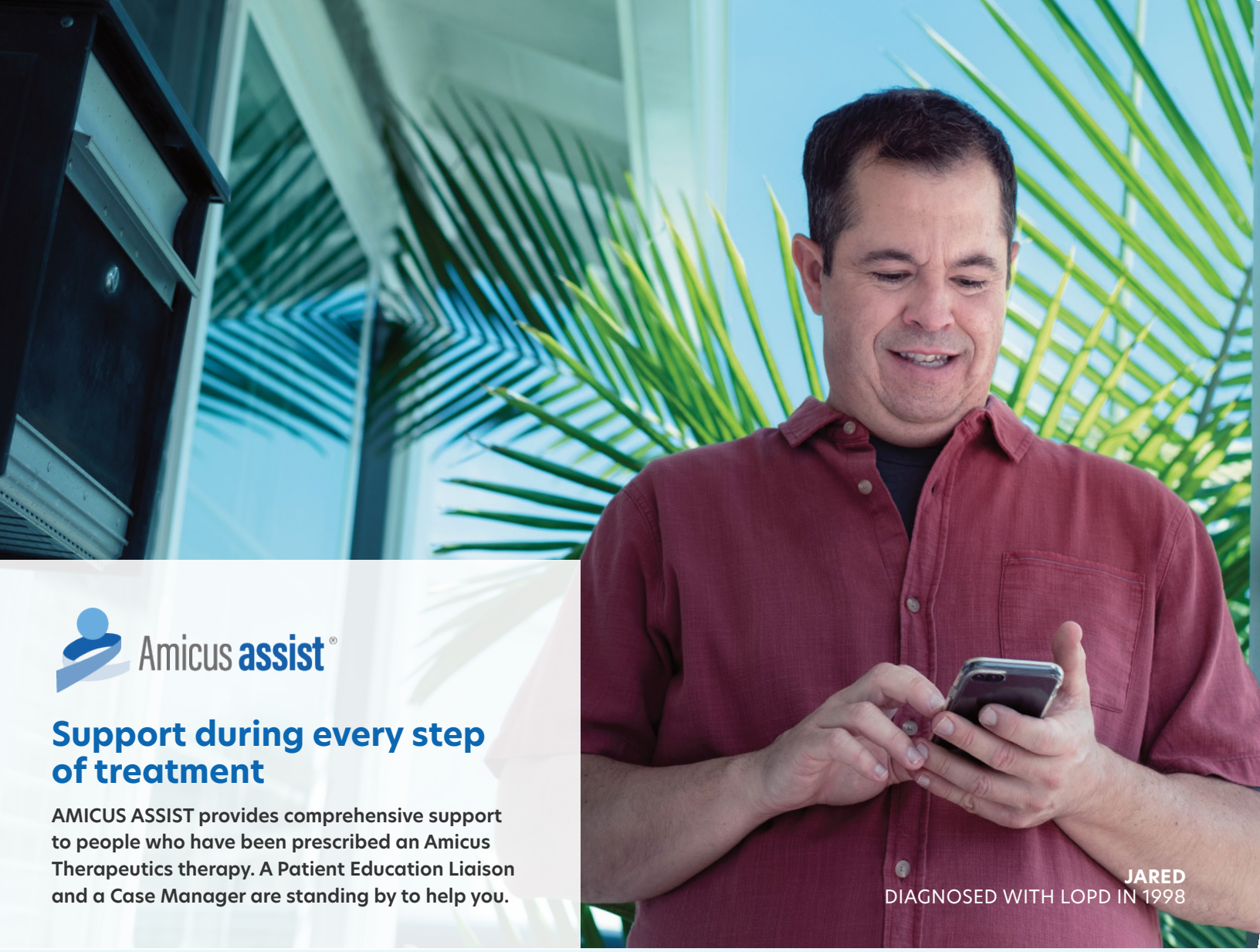


Amicus assist®

# Support during every step of treatment

**AMICUS ASSIST provides comprehensive support to people who have been prescribed an Amicus Therapeutics therapy. A Patient Education Liaison and a Case Manager are standing by to help you.**

**Your Patient Education Liaison (PEL)** is available to answer your treatment questions, educate you on how to prepare for infusions, and assist you in having more productive conversations with your care team.

**Your Case Manager** can help you navigate your insurance coverage, coordinate your prescription deliveries, find possible sources of financial assistance, and more.

Please remember, while your PEL and Case Manager are available to provide support throughout your treatment, they do not provide medical advice. Your healthcare provider is your go-to resource for any questions related to your care.

**You can contact AMICUS ASSIST Monday through Friday from 8AM to 8PM ET at 1-833-AMICUS-A (1-833-264-2872).**



Amicus Therapeutics®