

**ANNEX I**

**SUMMARY OF PRODUCT CHARACTERISTICS**

## **1. NAME OF THE MEDICINAL PRODUCT**

Opfolda 65 mg hard capsules

## **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each hard capsule contains 65 mg of miglustat.

For the full list of excipients, see section 6.1.

## **3. PHARMACEUTICAL FORM**

Hard capsule

Size 2 hard capsule (6.35x18.0 mm) with a grey opaque cap and white opaque body with “AT2221” printed in black on the body, containing white to off-white powder.

## **4. CLINICAL PARTICULARS**

### **4.1 Therapeutic indications**

Opfolda (miglustat) is an enzyme stabiliser of cipaglucosidase alfa long-term enzyme replacement therapy in adults with late-onset Pompe disease (acid  $\alpha$ -glucosidase [GAA] deficiency).

### **4.2 Posology and method of administration**

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

Miglustat 65 mg hard capsules must be used in combination with cipaglucosidase alfa. The summary of product characteristics (SmPC) for cipaglucosidase alfa should be consulted before taking miglustat.

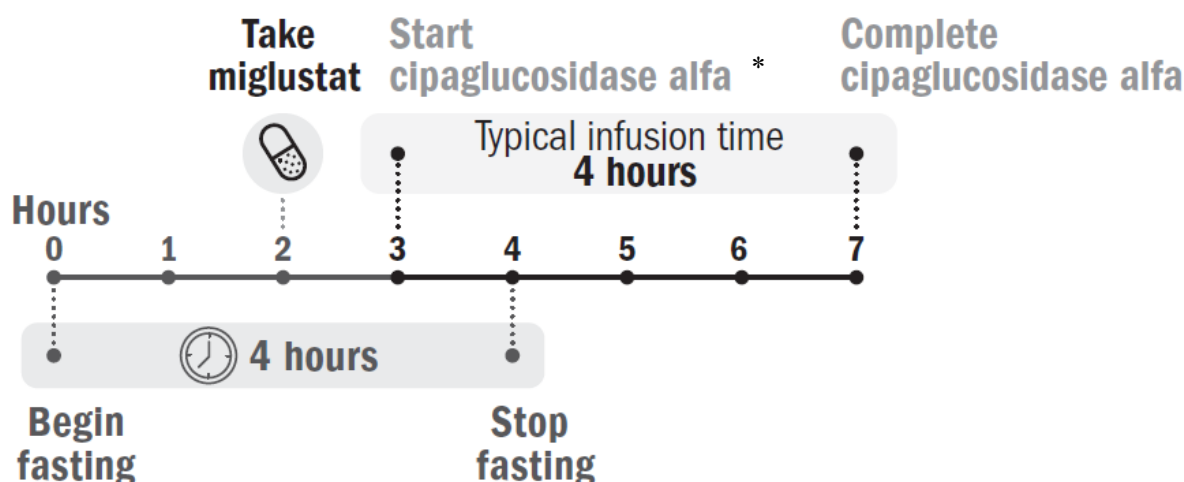
#### Posology

The recommended dose is to be taken orally every other week in adults aged 18 years and older and is based on body weight:

- For patients weighing  $\geq 50$  kg, the recommended dose is 260 mg (4 capsules of 65 mg).
- For patients weighing  $\geq 40$  kg to  $< 50$  kg, the recommended dose is 195 mg (3 capsules of 65 mg).

Miglustat 65 mg hard capsules should be taken approximately 1 hour but no more than 3 hours before the start of the cipaglucosidase alfa infusion.

**Figure 1. Dose timeline**



\* Miglustat 65 mg hard capsules should be taken approximately 1 hour but no more than 3 hours before the start of the cipaglucosidase alfa infusion.

Patient response to treatment should be routinely evaluated based on a comprehensive evaluation of all clinical manifestations of the disease. In case of an insufficient response or intolerable safety risks, discontinuation of miglustat 65 mg hard capsules in combination with cipaglucosidase alfa treatment should be considered. Both medicinal products should either be continued or discontinued.

#### *Missed dose*

If the miglustat dose is missed, treatment should occur as soon as possible. If it is not taken, do not start the cipaglucosidase alfa infusion. Cipaglucosidase alfa infusion can start 1 hour after miglustat is taken.

#### Special populations

##### *Renal and hepatic impairment*

The safety and efficacy of miglustat in combination with cipaglucosidase alfa therapy have not been evaluated in patients with renal and/or hepatic impairment. When administering every other week, increased plasma miglustat exposure as a result of moderate or severe renal or hepatic impairment is not expected to appreciably impact cipaglucosidase alfa exposures and is not anticipated to affect efficacy and safety of cipaglucosidase alfa in a clinically meaningful manner. No dose adjustment is required in patients with renal or hepatic impairment.

##### *Elderly*

There is limited experience with the use of miglustat in combination with cipaglucosidase alfa therapy in patients above the age of 65 years old. There is no dose adjustment required in elderly patients.

##### *Paediatric population*

The safety and efficacy of miglustat in combination with cipaglucosidase alfa therapy in paediatric patients less than 18 years old have not yet been established. No data are available.

#### Method of administration

Miglustat is for oral use.

Miglustat hard capsule has a crimp to prevent opening the capsule shells, and should be swallowed whole and taken on an empty stomach.

Patients should fast 2 hours before and 2 hours after taking miglustat 65 mg hard capsules (see section 5.2). 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. The patient can resume normal eating and drinking 2 hours after taking miglustat.

### **4.3 Contraindications**

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.  
Contraindication to cipaglucosidase alfa.

### **4.4 Special warnings and precautions for use**

Adverse drug reactions may occur upon the use of miglustat in combination with cipaglucosidase alfa (see section 4.8).

### **4.5 Interaction with other medicinal products and other forms of interaction**

No interaction studies have been performed related to the use of miglustat.

#### *Food interaction*

Miglustat is known to have a direct effect on the enzymatic function of major disaccharidases of the intestinal epithelium. Specifically, miglustat inhibits disaccharidases with alpha-glycosidic linkages including sucrase, maltase, and isomaltase. The strength of potential interactions can immediately interfere with digestive activity of sucrose, maltose and isomaltose leading to maldigestion, osmotic influx of water, increased fermentation, and production of irritating metabolites. Patients should fast for 2 hours before and for 2 hours after taking miglustat.

### **4.6 Fertility, pregnancy and lactation**

#### Contraception in females

Reliable contraceptive measures must be used by women of childbearing potential during treatment with miglustat in combination with cipaglucosidase alfa, and for 4 weeks after discontinuing treatment (see section 5.3). The medicinal product is not recommended in women of childbearing potential not using reliable contraception.

#### Pregnancy

There are no clinical data from the use of miglustat in combination with cipaglucosidase alfa in pregnant women. Miglustat crosses the placenta. Animal studies with miglustat alone as well as in combination with cipaglucosidase alfa have shown reproductive toxicity (see section 5.3). Miglustat in combination with cipaglucosidase alfa therapy is not recommended during pregnancy.

#### Breast-feeding

It is not known if miglustat and cipaglucosidase alfa are secreted in human breast milk (see section 5.3). Available pharmacodynamic/toxicological data in animals have shown secretion/excretion of miglustat and cipaglucosidase alfa in 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 miglustat in combination with cipaglucosidase alfa therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

#### Fertility

There are no clinical data on the effects of miglustat in combination with cipaglucosidase alfa therapy on fertility. Preclinical data in rats have shown that miglustat adversely affects sperm parameters (motility and morphology), thereby reducing fertility (see section 5.3). However, no effects on sperm

concentration, motility, or morphology were seen in 7 healthy adult men who received miglustat 100 mg, orally, twice daily for 6 weeks.

#### 4.7 Effects on ability to drive and use machines

Miglustat has no or negligible influence on the ability to drive or to use machines.

#### 4.8 Undesirable effects

##### Summary of the safety profile

The most commonly reported adverse reaction only attributable to miglustat 65 mg was constipation (1.3%).

##### Tabulated list of adverse reactions

The assessment of adverse reactions was informed by subjects treated with miglustat in combination with cipaglucosidase alfa therapy from the pooled safety analysis across the 3 clinical trials. The total mean duration of exposure was 17.2 months.

Adverse reactions from the clinical trials are listed by MedDRA system organ class in Table 1. The corresponding frequency categories are defined as follows: very common ( $\geq 1/10$ ), common ( $\geq 1/100$  to  $< 1/10$ ), uncommon ( $\geq 1/1\,000$  to  $< 1/100$ ), rare ( $\geq 1/10\,000$  to  $< 1/1\,000$ ), very rare ( $< 1/10\,000$ ), and not known (cannot be estimated from available data).

**Table 1: Summary of adverse reactions from clinical trials with miglustat-treated subjects**

| System organ class (SOC)                             | Frequency   | Adverse reaction (preferred term)  |
|--|-------------|--|
| Immune system disorders                              | Uncommon    | Hypersensitivity   |
| Nervous system disorders                             | Very common | Headache   |
|  | Common      | Tremor, dysgeusia  |
|  | Uncommon    | Balance disorder, migraine <sup>4</sup>  |
| Cardiac disorders                                    | Common      | Tachycardia <sup>6</sup>   |
| Vascular disorders                                   | Uncommon    | Hypotension, pallor  |
| Respiratory, thoracic and mediastinal disorders      | Common      | Dyspnoea   |
|  | Uncommon    | Asthma   |
| Gastrointestinal disorders                           | Common      | Diarrhoea, nausea, abdominal pain <sup>1</sup> , flatulence, abdominal distension, vomiting, constipation <sup>†</sup> |
|  | Uncommon    | Abdominal discomfort <sup>†</sup> , oesophageal spasm, oral pain   |
| Skin and subcutaneous tissue disorder                | Common      | Urticaria <sup>3</sup> , rash <sup>2</sup> , pruritus, hyperhidrosis   |
|  | Uncommon    | Skin discolouration  |
| Musculoskeletal and connective tissue disorders      | Common      | Muscle spasms, myalgia, muscular weakness  |
|  | Uncommon    | Arthralgia, flank pain, muscle fatigue, musculoskeletal stiffness  |
| General disorders and administration site conditions | Common      | Fatigue, pyrexia, chills   |
|  | Uncommon    | Asthenia, facial pain, feeling jittery <sup>†</sup> , non-cardiac chest pain, peripheral swelling                      |
| Investigations                                       | Common      | Blood pressure increased <sup>5</sup>  |
|  | Uncommon    | Lymphocyte count decreased, platelet count decreased <sup>†</sup>  |

<sup>†</sup> Reported with miglustat only

<sup>1</sup> Abdominal pain, abdominal pain upper, and abdominal pain lower are grouped under abdominal pain.

<sup>2</sup> Rash and rash erythematous are grouped under rash.

<sup>3</sup> Urticaria, urticaria rash, and mechanical urticaria are grouped under urticaria.

<sup>4</sup> Migraine and migraine with aura are grouped under migraine.

<sup>5</sup> Hypertension and blood pressure increased are grouped under blood pressure increased.

<sup>6</sup> Tachycardia and sinus tachycardia are grouped under tachycardia.

### Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in [Appendix V](#).

## **4.9 Overdose**

### Symptoms

Leukopenia, granulocytopenia, neutropenia, dizziness, and paraesthesia have been observed in human immunodeficiency virus (HIV) patients receiving miglustat at a dosage of 800 mg/day or higher.

### Management

In the event of an overdose, supportive medical care should be provided immediately. Full blood counts should be monitored for reduced white cells.

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Other alimentary tract and metabolism products, various alimentary track and metabolism products. ATC Code: A16AX06

### Mechanism of action

Miglustat is a pharmacokinetic enzyme stabiliser of cipaglucosidase alfa.

Miglustat binds selectively with cipaglucosidase alfa in the blood during infusion; thereby stabilising the conformation of cipaglucosidase alfa and minimising the loss of enzyme activity while in circulation. This selective binding between cipaglucosidase alfa and miglustat is transient with disassociation occurring in the lysosome. Miglustat alone has no effect on glycogen reduction.

### Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Opfolda in one or more subsets of the paediatric population in the treatment of glycogen storage disease Type II (Pompe disease) (see section 4.2 for information on paediatric use).

### **5.2 Pharmacokinetic properties**

#### Absorption

The rate of absorption ( $t_{max}$ ) of miglustat was approximately 2 to 3 hours. At the clinical dose, 260 mg, plasma miglustat attained a  $C_{max}$  of approximately 3000 ng/mL and an  $AUC_{0-\infty}$  of approximately 25,000 ng h/mL.

#### *Effect of food*

A significant food effect was observed and resulted in a decreased  $C_{max}$  by 36% and delayed absorption by approximately 2 hours, see section 4.2.

## Metabolism

Miglustat is largely unmetabolised with < 5% of a radiolabeled dose recovered as glucuronides.

## Elimination

The terminal elimination half-life was approximately 6 hours for miglustat. Oral clearance was approximately 10.5 L/h and terminal phase volume of distribution was approximately 90 L.

## Linearity

Miglustat demonstrated dose proportional kinetics.

## Special populations

### *Gender, elderly, and race/ethnicity*

Based on pooled population pharmacokinetic analysis, gender, age (18 to 74 years), and race/ethnicity did not have clinically meaningful effect on the exposure to miglustat in combination with cipaglucosidase alfa.

### *Hepatic impairment*

The pharmacokinetics of miglustat in combination with cipaglucosidase alfa therapy have not been evaluated in patients with hepatic impairment.

### *Renal impairment*

The AUC<sub>0-24hr</sub> of miglustat increased by 21%, 32%, and 41% in patients with mild (creatinine clearance [CLcr] 60 to 89 mL/minute, estimated by Cockcroft-Gault), moderate (CLcr 30 to 59 mL/minute), and severe (CLcr 15 to 29 mL/minute) renal impairment, respectively, compared to patients with normal renal function. The effect of end stage renal disease on the pharmacokinetics of miglustat is unknown.

## **5.3 Preclinical safety data**

Nonclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, single and repeated dose toxicity, genotoxicity, and mutagenicity.

Carcinomas in the large intestine of mice occurred occasionally following oral treatment with miglustat at 210, 420 and 840/500 mg/kg/day for a period of 2 years. These doses correspond to 8, 16, and 33/19 times a human dose of 200 mg three times per day. The relevance of these findings to humans taking miglustat is unknown at the substantially lower studied doses at 195 to 260 mg every other week for Pompe disease.

## Infertility

There was no effect of miglustat in combination with cipaglucosidase alfa therapy on spermatogenesis in animal studies; however, a decrease in sperm motility was observed in rats treated with miglustat in combination with cipaglucosidase alfa, which appeared to be associated with miglustat.

In rats, miglustat administered orally at doses of 60 mg/kg/day and above resulted in seminiferous tubule and testicular atrophy/degeneration. Decreased spermatogenesis with altered sperm morphology and motility and decreased fertility were observed in rats orally dosed with miglustat 20 mg/kg/day oral gavage 14 days prior to mating with doses at exposures less than the human therapeutic systemic exposure based on body surface area comparisons (mg/m<sup>2</sup>). Decreased spermatogenesis was reversible in rats following 6 weeks of active substance withdrawal.

## Animal toxicology and/or pharmacology

In a segment I fertility and early embryonic development study in rats, pre-implantation loss was observed in the female fertility component of the study in both miglustat alone (60 mg/kg) and the combination treatment group (cipaglucosidase alfa 400 mg/kg with oral miglustat 60 mg/kg) and was considered miglustat-related.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

#### Capsule contents

Pregelatinised starch (maize)  
Magnesium stearate (E470b)  
Microcrystalline cellulose (E460i)  
Sucralose (E955)  
Colloidal silicon dioxide

#### Capsule shell

Gelatin  
Titanium dioxide (E171)  
Black iron oxide (E172)

#### Edible printing ink

Black iron oxide (E172)  
Potassium hydroxide (E525)  
Propylene glycol (E1520)  
Shellac (E904)  
Strong ammonia solution (E527)

### **6.2 Incompatibilities**

Not applicable.

### **6.3 Shelf life**

3 years

### **6.4 Special precautions for storage**

This medicinal product does not require any special storage conditions.

### **6.5 Nature and contents of container**

40 mL high density polyethylene (HDPE) bottle with 33 mm white child resistant polypropylene cap with label. Bottle opening is sealed with an induction sealed foil liner.

Bottles of 4 and 24 capsules.

Not all pack sizes may be marketed.



## **6.6 Special precautions for disposal**

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

## **7. MARKETING AUTHORISATION HOLDER**

Amicus Therapeutics Europe Limited  
Block 1, Blanchardstown Corporate Park  
Ballycoolin Road  
Blanchardstown, Dublin  
D15 AKK1  
Ireland  
e-mail: [info@amicusrx.co.uk](mailto:info@amicusrx.co.uk)

## **8. MARKETING AUTHORISATION NUMBER(S)**

EU/1/23/1737/001  
EU/1/23/1737/002

## **9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 26 June 2023

## **10. DATE OF REVISION OF THE TEXT**

Detailed information on this medicinal product is available on the website of the European Medicines Agency <http://www.ema.europa.eu>.

## **ANNEX II**

- A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

## **A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE**

Name and address of the manufacturer responsible for batch release

Manufacturing Packaging Farmaca  
Neptunus 12, Heerenveen, Netherlands, 8448CN

## **B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

## **C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**

### **• Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

## **D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

### **• Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

**ANNEX III**  
**LABELLING AND PACKAGE LEAFLET**

**A. LABELLING**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING****OUTER CARTON****1. NAME OF THE MEDICINAL PRODUCT**

Opfolda 65 mg hard capsules  
miglustat

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

Each hard capsule contains 65 mg of miglustat.

**3. LIST OF EXCIPIENTS****4. PHARMACEUTICAL FORM AND CONTENTS**

Hard capsule

4 hard capsules

24 hard capsules

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Read the package leaflet before use.

Oral use

**6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN**

Keep out of the sight and reach of children.

**7. OTHER SPECIAL WARNING(S), IF NECESSARY**

ATTENTION: Only use Opfolda with cipaglucoasidase alfa.

**8. EXPIRY DATE**

EXP

**9. SPECIAL STORAGE CONDITIONS**

**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Amicus Therapeutics Europe Limited  
Block 1, Blanchardstown Corporate Park,  
Ballycoolin Road, Blanchardstown,  
Dublin D15 AKK1, Ireland

**12. MARKETING AUTHORISATION NUMBER(S)**

EU/1/23/1737/001 4 hard capsules  
EU/1/23/1737/002 24 hard capsules

**13. BATCH NUMBER**

Lot

**14. GENERAL CLASSIFICATION FOR SUPPLY**

**15. INSTRUCTIONS ON USE**

**16. INFORMATION IN BRAILLE**

opfolda

**17. UNIQUE IDENTIFIER – 2D BARCODE**

**18. UNIQUE IDENTIFIER - HUMAN READABLE DATA**

PC  
SN  
NN

**MINIMUM PARTICULARS TO APPEAR ON SMALL INTERMEDIATE PACKAGING****BOTTLE LABEL****1. NAME OF THE MEDICINAL PRODUCT**

Opfolda 65 mg hard capsules  
miglustat

**2. METHOD OF ADMINISTRATION**

Read the package leaflet before use

Oral use

**3. EXPIRY DATE**

EXP

**4. BATCH NUMBER**

Lot

**5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT**

Each hard capsule contains 65 mg of miglustat.

4 hard capsules  
24 hard capsules

**6. OTHER**

ATTENTION: Only use Opfolda with cipaglucosidase alfa.

Amicus Therapeutics Europe Limited  
Dublin D15 AKK1, Ireland

EU/1/23/1737/001 4 hard capsules  
EU/1/23/1737/002 24 hard capsules



**B. PACKAGE LEAFLET**

## **Package leaflet: Information for the patient**

### **Opfolda 65 mg hard capsules** miglustat

**Read all of this leaflet carefully before you take 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.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- 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 Opfolda is and what it is used for
2. What you need to know before you take Opfolda
3. How to take Opfolda
4. Possible side effects
5. How to store Opfolda
6. Contents of the pack and other information

#### **1. What Opfolda is and what it is used for**

##### **What Opfolda is**

Opfolda is a medicine that is used in the treatment of late-onset Pompe disease in adults. This medicine contains the active substance ‘miglustat’.

##### **What it is used for**

Opfolda is always used with another medicine called ‘cipaglucosidase alfa’, a type of enzyme replacement therapy (ERT). It is therefore very important that you also read the package leaflet of cipaglucosidase alfa.

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

##### **How Opfolda 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.

Opfolda binds to cipaglucosidase alfa during treatment. This makes the shape of cipaglucosidase alfa more stable, so it can be more easily absorbed from the blood by the muscle cells that are affected by Pompe disease. When in the cells, cipaglucosidase alfa works like GAA to help break down glycogen and control its levels.

#### **2. What you need to know before you take Opfolda**

##### **Do not use Opfolda**

- If you are allergic to miglustat or any of the other ingredients of this medicine (listed in section 6).
- If you are allergic to cipaglucosidase alfa.

## **Warnings and precautions**

Talk to your doctor, pharmacist, or nurse before taking Opfolda.

### Look out for serious side effects

Opfolda is used together with cipaglucosidase alfa, a type of enzyme replacement therapy (ERT), so you should also read the package leaflet of cipaglucosidase alfa. These medicines can cause side effects that you need to tell your doctor about straight away. This includes allergic reactions. Signs of allergic reactions are listed in section 4 'Allergic reactions'. These can be severe and may happen when you are being given the medicine or during the hours after.

Tell a doctor or nurse immediately if you are experiencing infusion-related or allergic reactions or think you may be experiencing them. Inform your doctor or nurse if you have ever had any such reaction with another ERT before you are given Opfolda.

## **Children and adolescents**

This medicine should not be given to patients under the age of 18 years old. This is because the effects of Opfolda in combination with cipaglucosidase alfa in this age group are not known.

## **Other medicines and Opfolda**

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.

There is no experience with the use of Opfolda in combination with cipaglucosidase alfa during pregnancy. Your doctor will discuss with you the risks and benefits of taking these medicines.

- Do not take Opfolda or receive cipaglucosidase alfa 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.
- Opfolda in combination with cipaglucosidase alfa 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**

It is advised that female patients must use reliable birth control methods prior to, while using these medicines, and for 4 weeks after stopping both medicines.

## **Driving and using machines**

Opfolda has no or negligible influence on your ability to drive or use machines. You should also read the package leaflet of cipaglucosidase alfa, as that medicine may have an impact.

## **3. How to take Opfolda**

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure how the medicine should be used.

### **How much Opfolda to take**

- Opfolda (miglustat) capsules must be used with cipaglucosidase alfa. See also the package leaflet of cipaglucosidase alfa.
- If you weigh 50 kg or more, the recommended dose is 4 capsules containing each 65 mg of miglustat.
- If you weigh between 40 kg and 50 kg, the recommended dose is 3 capsules.

### How often to take Opfolda

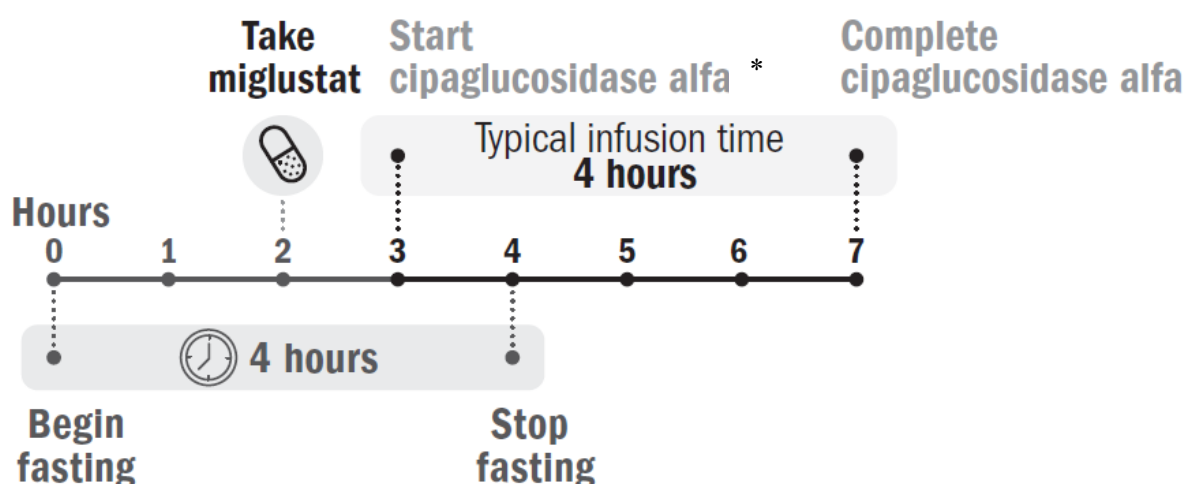
- You will receive Opfolda and cipaglucosidase alfa once every other week. Both are used on the same day.
- Take both medicines exactly as you have been told to by your doctor, see Figure 1. This is so your treatment can work as well as possible.

### Opfolda with food

You must take Opfolda by mouth on an empty stomach.

- Fast for 2 hours before and 2 hours after taking this medicine.
- During this 4-hour fasting period, water, fat-free (skimmed) cow's milk, and tea or coffee can be consumed. Do not use cream, whole/semi-skimmed cow's milk, non-dairy milks, sugar, or sweeteners. You can have fat-free (skimmed) cow's milk with your tea or coffee.
- Two hours after taking Opfolda, you can resume normal eating and drinking.

Figure 1. Dose timeline



\* Miglustat 65 mg hard capsules should be taken approximately 1 hour but no more than 3 hours before the start of the cipaglucosidase alfa infusion.

### 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 Opfolda.
- Tell your doctor when you completed your last dose.

### If you take more Opfolda than you should

Tell your doctor immediately or go to the hospital if you accidentally take more capsules than you were prescribed. You may be at increased risk of experiencing side effects with this medicine (see section 4). Your doctor will provide appropriate supportive care.

### If you forget to take Opfolda

If you miss a dose of Opfolda, please speak to your doctor or nurse. Contact your doctor or nurse immediately to reschedule miglustat in combination with cipaglucosidase alfa as soon as possible.

### If you stop taking Opfolda

Speak to your doctor if you wish to stop Opfolda 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.

Opfolda is used with cipaglucosidase alfa, and side effects can occur with either of these medicines.

The following side effects may occur:

##### 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.

Tell a doctor or nurse immediately if you are experiencing or think you may be experiencing allergic reactions. Inform your doctor or nurse if you have ever had any such reaction.

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

- Headache

**Common** (may affect up to 1 in 10 people)

- Shortness of breath (dyspnoea)
- Sudden reddening of the face, neck, or upper chest
- Rise in blood pressure
- Stomach pain
- Bloating
- Passing gas or wind
- Loose, runny stools
- Trouble passing stools
- Vomiting
- Fatigue
- Nausea
- Fever
- Very itchy hives (urticaria)
- Itchy rash, wanting to scratch (pruritis)
- Chills
- Muscle cramps, muscle pain, muscle weakness
- Involuntary shaking of one or more parts of the body
- Increased sweating
- Pain
- Altered sense of taste

**Uncommon** (may affect up to 1 in 100 people)

- Asthma
- Allergic reaction
- Uneasy stomach
- Indigestion
- Sore or irritated throat
- Painful and abnormal contractions of the throat
- Feeling of uneasiness, overall feeling of being sluggish
- Feeling jittery
- Swelling in the hands, feet, ankles, legs
- Constant feeling of being tired
- Unusual paleness of the skin

- Low blood pressure
- Decrease in platelets or a type of white blood cell – shown in tests
- Pain in joints
- Pain in the area between the hip and rib
- Muscle fatigue
- Increased rigidity of muscles
- Feeling drowsy
- Pain in one or both sides of the head, throbbing pain, aura, eye pain, sensitivity to light (migraine)
- Skin discolouration
- Balance disorder

### **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 Opfolda**

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.

This medicine does not require any special storage conditions.

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 Opfolda contains**

- The active substance is miglustat. Each hard capsule contains 65 mg of miglustat.
- The other ingredients are:

#### Capsule contents

Pregelatinised starch (maize)  
Magnesium stearate (E470b)  
Microcrystalline cellulose (E460i)  
Sucralose (E955)  
Colloidal silicon dioxide

#### Capsule shell

Gelatin  
Titanium dioxide (E171)  
Black iron oxide (E172)

#### Edible printing ink

Black iron oxide (E172)  
Potassium hydroxide (E525)  
Propylene glycol (E1520)  
Strong ammonia solution (E527)  
Shellac (E904)

## **What Opfolda looks like and contents of the pack**

Bottles of 4 and 24 capsules.

Not all pack sizes may be marketed.

Size 2 hard capsule with a grey opaque cap and white opaque body with “AT2221” printed in black on the body, containing white to off-white powder.

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### **Manufacturer**

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

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**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.