# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# 215211Orig1s000

# RISK ASSESSMENT and RISK MITIGATION REVIEW(S)

**Division of Risk Management (DRM)**
**Office of Medication Error Prevention and Risk Management (OMEPRM)**
**Office of Surveillance and Epidemiology (OSE)**
**Center for Drug Evaluation and Research (CDER)**

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| **Application Type** | BLA | NDA |
| **Application Number** | 761204 | 215211 |
| **PDUFA Goal Date** | August 29, 2022 | October 29, 2022 |
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| **Reviewer Name(s)** | Courtney Cunningham, PharmD | |
| **Team Leader** | Yasmeen Abou-Sayed, PharmD | |
| **Associate Director for REMS Design and Evaluation** | Laura Zendel, PharmD, BCPS | |
| **Review Completion Date** | August 05, 2022 | |
| **Subject** | Evaluation of Need for a REMS | |
| **Established Name** | Cipaglucosidase alfa-atga in combination with miglustat | |
| **Trade Name** | Pombiliti | Opfolda |
| **Name of Applicant** | Amicus Therapeutics US, LCC | |
| **Therapeutic Class** | Cipaglucosidase alfa-atga: Recombinant human acid alpha-glucosidase (rhGAA) (enzyme replacement) | Miglustat: Glucosylceramide synthase inhibitor (enzyme stabilizer) |
| **Formulations** | Lyophilized powder for solution for intravenous infusion, 105 mg/mL | Capsule for oral administration 65 mg/capsule |
| **Dosing Regimen** | 20 mg per kg actual body weight administered every other week as an intravenous solution | (b) (4) 1 hour prior to the intravenous infusion with cipaglucosidase alfa-atga |

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## EXECUTIVE SUMMARY

This review by the Division of Risk Management (DRM) evaluates whether a risk evaluation and mitigation strategy (REMS) for Pombiliti (cipaglucosidase alfa-atga) for intravenous infusion used in combination with Opfolda (miglustat) is necessary to ensure the benefits outweigh the risks. Amicus Therapeutics US, LLC (Amicus) submitted a Biologic Licensing Application (BLA) 761204 for Pombiliti with the proposed indication for (b) (4) Amicus also submitted a New Drug Application (NDA) 215211 for Opfolda (miglustat) for oral co-administration with cipaglucosidase.[2] The serious risks associated with Pombiliti and Opfolda include hypersensitivity reactions including anaphylaxis and immune associated reactions and the potential for embryo-fetal toxicity in humans, as well as the risk of electrocardiogram changes and potential for cardiac arrhythmias. Amicus Therapeutics US, LLC did not submit a proposed REMS or risk management plan with this application.

At the time of this review, labeling negotiations were ongoing. Based on the efficacy and safety information currently available, the clinical reviewer recommends approval of Pombiliti and Opfolda for the treatment of adult patients with late onset Pompe disease (LOPD) weighing ≥ 40 kg and who are not improving on their current enzyme replacement therapy. DRM has determined that a REMS is not needed to ensure the benefits of Pombiliti and Opfolda outweigh the risks. The review team's analysis showed that the improvement in motor and lung function observed with the use of cipaglucosidase alfa coadministered with miglustat outweighs the risks when these coadministered products are used as second-line therapy according to recommendations in the approved labeling. The risk of hypersensitivity reactions (including anaphylaxis) and immune associated reactions, and the risk of acute cardiorespiratory failure in susceptible patients will be managed via a Boxed Warning as with other drugs in this class. The risk of embryo-fetal toxicity is common among this class of products; prescribers of Pombiliti and Opfolda, which include rare disease specialists and geneticists, should be aware of the risks. Additionally, the potential for cardiac arrythmias and electrocardiogram changes will be addressed by a postmarketing study.

# 1. Introduction

This review by the Division of Risk Management (DRM) evaluates whether a risk evaluation and mitigation strategy (REMS) for Pombiliti (cipaglucosidase alfa) used in combination with miglustat (cipaglucosidase/miglustat) is necessary to ensure the benefits outweigh its risks. Amicus Therapeutics US, LLC (the Applicant) submitted a Biologic License Application (BLA) 761204 for Pombiliti and a New Drug Application (NDA) 215211 for Opfolda with the proposed indication (b) (4) This application is under review in the Division of Rare Diseases and Medical Genetics (DRDMG). The Applicant did not submit a proposed REMS or risk management plan with this application.

# 2. Background

## 2.1. Product Information

Pombiliti (cipaglucosidase alfa-atga), a new molecular entity (NME), submitted as a 351(a) biological license application (BLA), is proposed as a (b) (4) enzyme replacement therapy (ERT) for the treatment of patients with Pompe disease (PD).[a] Cipaglucosidase alfa-atga (cipaglucosidase) is a recombinant human acid α-glucosidase (rhGAA) consisting of a modified form of alglucosidase alfa with higher amounts of mannose-6-phosphate-(M6P) compared to alglucosidase alfa for cellular uptake. Amicus developed Opfolda (miglustat) for oral co-administration with cipaglucosidase to ensure its stability at neutral pH and delivery of active enzyme to muscle and lysosomes. Miglustat, submitted as a new drug application (NDA), is a glucosylceramide synthase inhibitor, binds to and prevents inactivation of the rhGAA enzyme in blood, and has been approved in the US since 2003 for monotherapy for treatment of adult patients with mild/moderate type 1 Gaucher disease for whom enzyme replacement therapy is not a therapeutic option.[3]

For the treatment of Pompe disease, cipaglucosidase alfa is proposed to be available as an intravenous infusion to be administered in conjunction with the oral tablet, miglustat. Cipaglucosidase is formulated as a 15 mg/vial lyophilized powder for reconstitution to a concentration of 15 mg/mL for intravenous infusion. The recommended dosage regimen of cipaglucosidase alfa is 20 mg per kg actual body weight administered by intravenous infusion every other week for chronic use.[b] Infusion of cipaglucosidase should start 1 hour after oral administration of miglustat.[1] For miglustat, the recommended dose for patients weighing 50 kg or greater is 260 mg (4 capsules of 65 mg). For patients weighing greater than or equal to 40 kg to less than 50 kg, the recommended dose is 3 capsules (195 mg total). Miglustat should be taken on an empty stomach and patients should not eat for 2 hours before and 2 hours after taking miglustat.[1] Pombiliti and Opfolda in combination have not been approved or marketed in the United States.

## 2.2. Regulatory History

The following is a summary of the regulatory history for cipaglucosidase alfa-atga (BLA 761204) and miglustat (NDA 215211) relevant to this review:

- 09/13/2017: Orphan drug designation granted for cipaglucosidase alfa coadministered with miglustat
- 02/20/2019: Breakthrough designation granted for cipaglucosidase alfa coadministered with miglustat

[a] Section 505-1 (a) of the FD&C Act: FDAAA factor (F): Whether the drug is a new molecular entity

[b] Section 505-1 (a) of the FD&C Act: FDAAA factor (D): The expected or actual duration of treatment with the drug

- 06/30/2021: Clinical Information submitted as part of the rolling review for cipaglucosidase alfa (BLA 761204)
- 07/29/2021: The Applicant submitted the miglustat (NDA 215211) application and final portion of rolling for cipaglucosidase alfa (BLA 761204)
- 02/07/2022: Mid-Cycle Communication sent to the Applicant that states that the Agency has "currently no plan for a REMS."[4]
- 04/29/2022: The Applicant submitted data to support use in females of reproductive potential that constituted a major amendment[5]
- 05/09/2022: The Agency issued a Major Amendment Letter extending the PDUFA dates for both products by 3 months[6]

# 3. Therapeutic Context and Treatment Options

## 3.1. Description of the Medical Condition

Pompe disease (PD), is a rare inherited autosomal recessive genetic disease caused by mutations in the acid alfa-glucosidase (GAA) gene resulting in abnormal buildup of glycogen inside cells.[7] GAA is required for the break-down of lysosomal glycogen into glucose that fuels muscle function.[8,9] This buildup of glycogen results in tissue destruction and impairs the workings of different organs and tissues, especially the heart, respiratory, and skeletal muscles. In the US, PD is estimated to occur at 1 in every 40,000 births.[10] **c,d**

The severity and clinical manifestation of PD depend on the degree of enzyme deficiency. Pompe Disease has 2 forms: infantile onset and late onset. Infantile onset Pompe Disease (IOPD) is the result of complete or nearly complete deficiency of GAA. In infants with IOPD, symptoms are evident within months of birth, with feeding problems, poor weight gain, muscle weakness, floppiness, and head lag. Respiratory difficulties are often complicated by lung infections and the heart is grossly enlarged. Most infants die from cardiac or respiratory complications before their first birthday. Late onset Pompe disease (LOPD) is the result of partial deficiency in GAA and may begin anytime from late childhood to adolescence and may even present into adulthood.[11] The primary symptom of LOPD is muscle weakness progressing to respiratory weakness and death from respiratory failure after a course lasting several years.[8d]

[c] Section 505-1 (a) of the FD&C Act: FDAAA factor (A): The estimated size of the population likely to use the drug involved.

[d] Section 505-1 (a) of the FD&C Act: FDAAA factor (B): The seriousness of the disease or condition that is to be treated with the drug.

## 3.2. Description of Current Treatment Options

Enzyme replacement therapy (ERT) is the only FDA approved treatment for PD. ERT provides an exogenous source of GAA that is taken up into cells and transported into lysosomes where it hydrolyzes glycogen. Two first generation ERTs consisting of recombinant human acid alfa-glucosidase (rhGAA) (alglucosidase alfa) are currently approved for PD (Myozyme [(BLA 125141] and Lumizyme [BLA 125291]) along with a second generation rhGAA (Nexviazyme, avalglucosidase alfa, [BLA 761194]). Nexviazyme and Lumizyme are currently marketed in the US.

Nexviazyme received US approval in August 2021 for LOPD in patients 1 year of age and older.[12] Myozyme received US approval in April 2006 for IOPD based on improved ventilator-free survival in Pompe infants treated with rhGAA enzyme compared to historical, untreated controls, but the Applicant voluntarily withdraw the BLA on June 19, 2020.[13,14] Lumizyme received approval in May 2010 for LOPD patients greater than 8 years of age who do not have evidence of cardiac hypertrophy.[15] At the time of its approval, the safety and efficacy of Lumizyme had not been demonstrated in IOPD or in LOPD less than eight years of age. The Agency required a REMS with a Communication Plan, elements to assure safe use (ETASU) that included prescriber certification, healthcare setting certification, and documentation of safe use conditions as well as an implementation system, and timetable for submission of assessments. The goals of the REMS were to mitigate the potential risk of rapid disease progression in IOPD and LOPD patients less than 8 years of age, and to ensure that the known risks of anaphylaxis and severe allergic reactions including the potential risks of severe cutaneous and systemic immune mediated reaction associated with the use of Lumizyme are communicated to patients and prescribers. Based on the physiochemical comparability of Myozyme and Lumizyme, the Agency released the Lumizyme REMS in 2014 with the approval for expanded use of Lumizyme to all ages, including early-onset disease less than 8 years, as the restricted distribution under the ETASU REMS for Lumizyme was no longer necessary.[16] The certification requirement to ensure healthcare facilities appropriately monitor patients was also determined to no longer be necessary as this is a standard procedure for accredited hospitals and infusion centers to monitor and treat patients who experience severe allergic reactions including anaphylaxis. Additionally, home infusion agencies also have accreditation standards requiring policies and procedures that address these measures. Further, the REMS assessment results demonstrated completion of the communication plan and achieved acceptable levels in communicating risks to prescribers and patients.[17] All three drugs include a boxed warning (BW) for the risk of anaphylaxis, severe allergic reactions, immune-mediated reactions, and the risk of cardiorespiratory failure in patients with compromised cardiac or respiratory function due to infusion-associated reactions.

The standard dosing of Nexviazyme is 20 mg/kg every 2 weeks for ≥30 kg and 40 mg/kg every 2 weeks for <30 kg, and for Lumizyme, the standard dosing is 20 mg/kg of body weight (BW) as an intravenous (IV) infusion every two weeks for both IOPD and LOPD.[12] Although multiple first line therapies for Pompe disease exist, there is an unmet need for second-line therapy as improvements seen with first-line therapy may not be sustained.

# 4. Benefit Assessment

The efficacy and safety of cipaglucosidase with miglustat was established by a single pivotal Phase 3 Study ATB200-03 (NCT03729362). Study ATB200-03 was a randomized, double-blind, multicenter trial of 123 adult subjects with LOPD to evaluate the efficacy and safety of cipaglucosidase alfa/miglustat compared with alglucosidase alfa/placebo in adult subjects with LOPD who had previously received alglucosidase alfa (ERT-experienced) or who had never received ERT (ERT-naïve). The 123 subjects were randomized using a 2:1 ratio (85:38) to cipaglucosidase alfa 20 mg/kg IV + miglustat 195/260 mg PO or alglucosidase alfa 20 mg/kg IV + placebo PO every other week for 52 weeks.[1]

Additional safety data and supportive efficacy data was provided by data from 2 ongoing studies; Stage 3 and 4 of Study ATB200-02 (NCT02675465), an ongoing, 4-year, uncontrolled, multicenter trial of adult treatment naïve and experienced subjects with LOPD to assess safety, tolerability, and efficacy of cipaglucosidase alfa alone and with miglustat and Study ATB200-07 (NCT04138277), an ongoing, 4-year uncontrolled, randomized multicenter study of adults with LOPD who participated in Study ATB200-03.

The primary endpoint for Study ATB200-03 was change from baseline to Week 52 in 6-minute walk distance (6MWD). A key secondary efficacy endpoint is change from baseline to week 52 in sitting forced vital capacity (FVC) (% predicted). After the data-lock, the Applicant identified one subject (Subject (b) (6)) as an outlier, due to a "clinically implausible" improvement in the 6MWT, and the Agency and Applicant performed analyses to further evaluate the primary endpoint excluding the outlier, as the data "had a significant impact on the estimation and testing of the primary endpoint." The subject later revealed to the investigator that he "deliberately underperformed on the 6MWT and pulmonary function testing to ensure he would meet inclusion criteria," and had received an anabolic steroid for approximately 9 months after LOPD diagnosis and discontinued the product 2-4 weeks before study enrollment.[18]

In the primary analysis for Study ATB200-03, the mean treatment difference in change from baseline in 6MWD at week 52 was 5.33 meters ( 95% CI: -15.21, 25.88; p = 0.608). The results were significantly impacted by the outlier subject describe above (Subject (b) (6)). After exclusion of the outlier, the difference was 14 meters (95% CI: -3, 31; p =0.100).[19]

The key secondary endpoint, the mean treatment difference in change from baseline to week 52 in sitting FVC (% predicted) is 2.32% in favor of cipaglucosidase/miglustat (95% CI: 0.02, 4.62; nominal p=0.048). All other secondary endpoints also favored cipaglucosidase/miglustat.[e]

The clinical review team noted that although the primary endpoint did not reach statistical significance, an increase of 14 m walk distance is a clinically meaningful difference, and using mixed model for repeated measure analysis, (MMRM), the p-value decreases to 0.097. In the ongoing clinical review, the

[e] Section 505-1 (a) of the FD&C Act: FDAAA factor (C): The expected benefit of the drug with respect to such disease or condition.

reviewer states that, “although the results from ATB200-03 do not show statistical superiority compared to the comparator on the primary endpoint, the numerically favorable results of this endpoint and the positive results from the fist key endpoint demonstrate meaningful effectiveness of cipaglucosidase/miglustat in adult patients with LODP weighing ≥40 kg who have previously received enzyme therapy.” The clinical team also noted that the submitted nonclinical data provided evidence that miglustat increases the bioavailability of cipaglucosidase alfa (b) (4) (b) (4) As LOPD is a rare disease, the Applicant and the Division agreed during drug development that a three-arm trial would not be feasible. The review team concluded that it is reasonable to approve cipaglucosidase alfa coadministered with miglustat for chronic use (b) (4) At the time of this review, approval of cipaglucosidase/miglustat is dependent on successful site inspections, which cannot be completed due to travel restrictions from the ongoing COVID-19 pandemic. [18]

# 5. Risk Assessment & Safe-Use Conditions

The safety assessment of cipaglucosidase alfa/miglustat was based on 3 clinical studies (Studies ATB200-02, ATB200-03 and ATB200-07), with pivotal Study ATB200-03 as the focus. The combined safety population (Safety Pool 2) for this application is comprised of 151 adult subjects from these studies who received at least one dose of cipaglucosidase/miglustat. Of these 151 subjects, 34 were treatment-naïve, and 117 were treatment experienced.[20] Safety Pool 1 contained only patients from the pivotal Study ATB200-03.

The most common adverse reactions seen in ABT200-03 (≥2%) were nausea, abdominal pain/distension, flatulence, diarrhea, arthralgia, oropharyngeal pain, muscle spasms and musculoskeletal pain, asthenia, dyspnea, tachycardia, increases in blood pressure, headache, fatigue, pyrexia, chills, flushing, pruritis, rash, dysgeusia, tremor, and paresthesia.

In Study ATB200-03, 95% of patients treated with cipaglucosidase/miglustat experienced at least one treatment emergent adverse event (TEAE), as opposed to 97% of comparator treated subjects. However, serious adverse events (SAEs) and adverse events leading to discontinuation were more common in the cipaglucosidase/miglustat treated subjects with risk differences of 6.8 ( 95% CI: -1.2, 14.8) and 8.0 (95% CI: -0.3, 16.2). No deaths occurred in any study.

The serious risks associated with cipaglucosidase/miglustat are hypersensitivity reactions including anaphylaxis and infusion-associated reactions, the potential for embryo-fetal toxicity in humans, and the risk of electrocardiogram changes and potential for cardiac arrhythmias with miglustat.

In the ongoing review, the clinical review team concluded that the safety profile of cipaglucosidase/miglustat is consistent with other enzyme replacement therapies.[18]

## 5.1. Hypersensitivity Reactions Including Anaphylaxis and Infusion-Associated Reactions

Forty-one (27%) cipaglucosidase/miglustat treated subjects experienced hypersensitivity reactions. Four of the cipaglucosidase/miglustat subjects had severe hypersensitivity reactions, and an additional 4 (3%) subjects experienced anaphylaxis. Three of the four subjects who experienced anaphylaxis discontinued the study.

Forty-eight subjects (32%) who received cipaglucosidase/miglustat experienced infusion-associated reactions (IARs), most being mild to moderate, and included nausea, diarrhea, vomiting, abdominal pain/distension, chills, pyrexia, chest discomfort, dizziness, headache, cough, dysgeusia, dyspnea, pruritis, urticaria, tachycardia, increased blood pressure, fever, and rash. Four (3%) subjects reported 11 severe IARs, that included pharyngeal edema, anaphylactic reaction, urticaria, pruritus, chills, dyspnea, and flushing. IARs that led to subject discontinuation were urticaria, anaphylactic reaction, chills, and hypotension.[1]

Based on the known risk and class effect of anaphylactic reactions and infusion-associated reactions associated with alglucosidase alfa and avalglucosidase alfa, this risk will be included in a Boxed Warning and under Warnings & Precautions.

## 5.2. Risk of Acute Cardiorespiratory Failure in Susceptible Patients

Patients who use ERTs and are susceptible to fluid volume overload, such as those with acute respiratory illnesses, compromised cardiac or respiratory function such as patients with advanced Pompe disease, or those who are fluid restricted, may be at risk of a serious exacerbation during the cipaglucosidase infusion.

As with other drugs in the ERT class, this is risk is communicated in both the Boxed Warning and in warnings and precautions (Section 5.3). Instructions for increased vital sign monitoring and the potential need for prolonged observation times in these patients is also communicated in Section 5.3 of the labeling.

## 5.3. Potential Embryo-Fetal Toxicity in Humans

Both pregnant and lactating women were excluded from the cipaglucosidase/miglustat studies, therefore no data is available on human embryo-fetal toxicity. However, in rabbit studies, clusters of great vessel and cardiac malformations were seen in offspring when cipaglucosidase/miglustat was administered at 175 mg/kg and 25 mg/kg. In a rat study, increases in maternal and fetal mortality were seen at cipaglucosidase doses of 400 mg/kg, both alone and with miglustat.

Current labeling for miglustat states that it is not recommended during breast feeding, and the labeling for cipaglucosidase/miglustat will contain this as well, including a contraindication for use during pregnancy, a Warning and Precaution for risk to the fetus, recommendation for pregnancy testing as

well as information on fetal risk in Sections 2 and 8 of the label, and a recommendation to use effective contraception during treatment with cipaglucosidase/miglustat and for 60 days afterward.

### 5.4. Risk of Electrocardiogram Changes and Potential for Cardiac Arrhythmias for Miglustat at the Proposed Dosage

There is limited available data on electrocardiogram changes and potential arrhythmias with the dose of miglustat proposed by the Applicant in Pompe disease. While miglustat will be dosed less frequently than in Gaucher disease, each dose will be higher, which may result in greater acute exposure. In the studies supporting use in Gaucher disease, there was no dedicated QT study and the Applicant provided convincing data in support of the use in Pompe disease. In the studies supporting the use in Pompe disease, ECGs were performed only prior to the miglustat dose, providing no data on the QTc prolongation at peak miglustat exposure.

To better characterize this risk, the clinical review team concluded that an evaluation of miglustat's effects on the QTc interval will be required as a post marketing requirement.[18]

## 6. Expected Postmarket Use

A multidisciplinary approach is often employed in the management of patients with Pompe disease. Similar to other ERTs, specialists in rare diseases, metabolic disorders, or biochemical geneticists are likely prescribers of cipaglucosidase and miglustat. These prescribers are familiar with the risks associated with ERTs for Pompe disease including hypersensitivity reactions, anaphylaxis, and infusion associated reactions. The majority of patients will receive their infusion from an outpatient setting such as an infusion centers or from a home infusion provider, although, some patients may receive the drug in a hospital setting. All these healthcare settings and healthcare providers should be familiar with the risks of ERT infusions, have policies and procedures in place for the management of adverse events, and are specially trained in the administration, monitoring, and treatment of adverse reactions associated with ERT.

## 7. Risk Management Activities Proposed by the Applicant

The Applicant did not propose any risk management activities for cipaglucosidase and miglustat beyond routine pharmacovigilance and labeling.

## 8. Discussion of Need for a REMS

The clinical review team recommends approval of Pombiliti and Opfolda (cipaglucosidase alfa used in combination with miglustat) based on the efficacy and safety information currently available.

Depending on the degree of enzyme deficiency, symptoms of Pompe disease (PD) can begin as early as within months of birth, late childhood to adolescence, or even adulthood. There are currently three FDA-approved medical therapies for Pompe disease. The products currently manufactured for the US are Nexviazyme (avalglucosidase alfa-ngpt) and Lumizyme (alglucosidase alfas). These are useful first line therapies for Pompe disease, but there is need for additional therapies for patients whose disease progresses on these first line treatments.

The safety concerns associated with cipaglucosidase and miglustat, including the risk of hypersensitivity reactions and potential embryofetal toxicity, are similar to other ERT products, which use labeling to mitigate these risks. Proposed labeling for both cipaglucosidase-alfa and miglustat includes similar language to convey the risks of hypersensitivity reaction including anaphylaxis, infusion reactions, and risk of acute cardiorespiratory failure in susceptible patients in a Boxed Warning and in warnings and precautions (Sections 5.1 – 5.3). The risk of embryo-fetal toxicity will be communicated via warnings and precautions (Section 5.4) , as well as a contraindication for use in pregnancy, and risk information on pregnancy and fetal development in Sections 8.1 and 8.3, and an instruction to verify pregnancy status in females of reproductive potential in Section 2.1. A PMR will study the effect of the miglustat on the QTc interval.

Therefore, based on the data available and prescribing community's familiarity with how to manage the serious risks that are associated with cipaglucosidase alfa and miglustat, given that they are also expected risks with other ERT products, DRM is not recommending a REMS for Pombiliti at this time. Opfolda is currently approved without a REMS for another indication, and DRM does not believe coadministration with Pombiliti in the LOPD population changes the benefit-risk evaluation such that a REMS would be warranted.

# 9. Conclusion & Recommendations

Based on the available data, DRM and DRDMG agree that a REMS is not necessary to ensure the benefits of cipaglucosidase alfa and miglustat outweigh the risks, which will be managed via labeling. Approval of cipaglucosidase/miglustat is dependent on successful site inspections, which cannot be completed due to travel restrictions from the ongoing COVID-19 pandemic. Should DRDMG have any concerns or questions or if new safety information becomes available, please send a consult to DRM.

# 10. Appendices

## 10.1. References


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19. Amicus Therapeutics US, LLC. 2.7.3 Clinical Efficacy for Pombiliti (cipaglucosidase alfa used in combination with miglustat) February 25, 2021.
20. Amicus Therapeutics US, LLC. 2.7.4 Clinical Safety for Pombiliti (cipaglucosidase alfa used in combination with miglustat) February 25, 2021.

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COURTNEY A CUNNINGHAM
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YASMEEN I ABOU-SAYED
08/05/2022 12:52:47 PM

LAURA A ZENDEL
08/05/2022 02:37:15 PM