Neighborhood Health Plan OF RHODE ISLAND™
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Pombiliti™ (cipaglucosidase alfa-atga, intravenous) & Opfolda™ (miglustat, oral)

Effective Date: 07/01/2024
Review Date: 05/08/2024, 02/26/2025
Scope: Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

I. Length of Authorization

Coverage will be initially provided for 6 months and may be renewed for 6 months

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Pombiliti 105 mg single-dose vial (dosed as 20 mg/kg): 22 vials every 14 days
- Opfolda 65 mg oral capsules: 4 capsules every 14 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- Pombiliti: 2300 mg every 14 days
- Opfolda: 260 mg every 14 days

III. Summary of Evidence:

Pombiliti (cipaglucosidase alfa-atga) is a hydrolytic lysosomal glycogen-specific enzyme indicated, in combination with Opfolda, an enzyme stabilizer, 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 (ERT). LOPD, or lysosomal acid alpha-glucosidase (GAA) deficiency, affects approximately 1 in 40,000 people in the United States. Pombiliti was evaluated in a randomized, double-blind, active-controlled, multi-center, phase 3 clinical trial (PROPEL). There were 123 adult patients randomized 2:1 to receive a combination of Pombiliti and Opfolda, or an alglucosidase alfa product not available in the United States for 52 weeks. Of the 123 patients in the trial, 77% were ERT experienced (defined as ≥2 years; average 7.4 years of treatment prior to the study). Results showed numerically favorable results for the primary endpoint of the study, improvement in a 6-minute walk test capered to baseline, but these results were determined to not be statistically superior. Pombiliti has a Boxed Warning for severe hypersensitivity reactions, infusion-associated reactions, and risk of acute cardiorespiratory failure in susceptible patients. The most common adverse reactions of Pombiliti are headache, diarrhea, fatigue, nausea, abdominal pain, and pyrexia.

IV. Initial Approval Criteria [1,4]

Coverage is provided in the following conditions:

- Patient age is at least 18 years of age; **AND**
- Patient has measurable signs of Pompe disease such as impairment in pulmonary function or motor weakness**; AND**

- Documented baseline values for percent predicted forced vital capacity (FVC) and 6-minute walk test (6MWT) are submitted that demonstrate a FVC of ≥30% of the predicted value for healthy adults and 6MWT distance of ≥75 meters; **AND**
- Females of reproductive potential have a negative pregnancy test prior to initiating therapy and will use effective methods of contraception during treatment; **AND**
- Patient is experiencing an inadequate response or intolerance to their current enzyme replacement therapy [i.e., alglucosidase-alfa (Lumizyme), avalglucosidase-alfa (Nexviazyme)]; **AND**

Universal Criteria [1]

- Will not be used in combination with other enzyme replacement therapies [i.e., alglucosidase-alfa (Lumizyme), avalglucosidase-alfa (Nexviazyme)] ; **AND**
- Pombiliti will be used in combination with the enzyme stabilizer formulation miglustat (Opfolda ™) as outlined in the Dosage/Administration information below; **AND**
- Patients susceptible to fluid volume overload or those with an acute underlying respiratory illness or compromised cardiac or respiratory function, will be closely monitored for exacerbation of their cardiac or respiratory status during infusion; **AND**
- Patient has an actual body weight of at least 40 kilograms; **AND**
- Patient does not require the use of invasive or noninvasive ventilation support for >6 hours per day while awake**; AND**

Pompe Disease (Acid Alpha-Glucosidase (GAA) deficiency) † Φ [1,4]

- Diagnosis has been confirmed by one of the following:
  - Deficiency of acid alpha-glucosidase (GAA) enzyme activity; **OR**
  - Detection of biallelic pathogenic variants in the *GAA* gene by molecular genetic testing; **AND**
- Patient has a diagnosis of late-onset (non-infantile) disease

MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements

† FDA Approved Indication(s); **‡** Compendia Recommended Indication(s); **Φ** Orphan Drug

V. Renewal Criteria [1,4]

Coverage can be renewed based on the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: anaphylaxis and severe hypersensitivity reactions, severe infusion-associated reactions, acute cardiorespiratory failure, etc.; **AND**
- Patient has demonstrated a beneficial response to therapy compared to pretreatment baseline in one or more of the following: stabilization or improvement in FVC and 6-MWT; **AND**
- Patient is being monitored for antibody formation (including neutralizing antibodies)

VI. Dosage/Administration [1]

Indication	Dose
Pompe Disease	Pombiliti - Administer 20 mg/kg (of actual body weight) every two weeks as an intravenous infusion over approximately 4 hours. Opfolda - Administer 260 mg for patients weight ≥50 kg - Administer 195 mg for patients weighing ≥40 kg to <50 kg Pombiliti & Opfolda - Patients must weigh ≥40 kg. - Pombiliti must be administered in combination with Opfolda (see PI for both products for dosing timeline). If the Opfolda dose is missed, Pombiliti should not be administered. - Prior to Pombiliti administration, consider pretreating with antihistamines, antipyretics, and/or corticosteroids. If premedication was used with previous enzyme replacement therapy (ERT), prior to Pombiliti administration, pretreat with antihistamines, antipyretics, and/or corticosteroids. - Start Pombiliti in combination with Opfolda two weeks after the last ERT dose. - Initiate Pombiliti ~1 hour after oral administration of Opfolda. If the Pombiliti infusion cannot be started within 3 hours of oral administration of Opfolda, reschedule Pombiliti in combination with Opfolda at least 24 hours after Opfolda was last taken.

VII. Billing Code/Availability Information

HCPCS Code(s):

- J1203: Injection, cipaglucosidase alfa-atga, 5 mg
- J1202: Miglustat, oral, 65 mg

NDC:

- Pombiliti 105 mg single-dose vial as a powder for injection: 71904-0200-xx
- Opfold 65 mg oral capsules: 71904-0300-xx

VIII. References

1. Pombiliti [package insert]. Philadelphia, PA; Amicus Therapeutics, LLC.; November 2024. Accessed February 2025.
2. Cupler EJ, Berger KI, Leshner RT, et al. Consensus treatment recommendations for late-onset Pompe disease. Muscle Nerve. 2012 Mar; 45(3):319-33. doi: 10.1002/mus.22329. Epub 2011 Dec 15.
3. Kishnani PS, Steiner RD, Bali D, et al. Pompe disease diagnosis and management guidelines. *Genet Med* 2006; 8:267-88.
4. Nancy L, Bailey L. Pompe Disease. GeneReviews. www.ncbi.nlm.nih.gov/books/NBK1261/. Initial Posting: August 31, 2007; Last Update: November 2, 20237. Accessed on January 03, 2024.
5. Tarnopolsky M, Katzberg H, Petrof BJ, et al. Pompe Disease: Diagnosis and Management. Evidence-Based Guidelines from a Canadian Expert Panel. Can J Neurol Sci. 2016 Jul;43(4):472-85.

6. Kishnani PS, Hwu WL, et al. Introduction to the Newborn Screening, Diagnosis, and Treatment for Pompe Disease Guidance Supplement. Pediatrics 2017 Jul:(1):S1-S3.
7. Schoser B, Roberts M, Byrne BJ, et al. Safety and efficacy of cipaglucosidase alfa plus miglustat versus alglucosidase alfa plus placebo in late-onset Pompe disease (PROPEL): an international, randomised, double-blind, parallel-group, phase 3 trial [published correction appears in Lancet Neurol. 2023 Oct;22(10):e11]. *Lancet Neurol.* 2021;20(12):1027-1037. doi:10.1016/S1474-4422(21)00331-8.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
E74.02	Pompe disease

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Policy Rationale:

Pombiliti and Opfolda were reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Pombiliti and Opfolda according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will

help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For INTEGRITY (Medicare-Medicaid Plan) members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.