

Clinical Policy: Cipaglucosidase Alfa-atga + Miglustat (Pombiliti + Opfolda)

Reference Number: PA.CP.PHAR.567

Effective Date: 02/2024

Last Review Date: 01/2024

Description

Cipaglucosidase alfa-atga + miglustat (Pombiliti™ + Opfolda™) is a combination therapy of hydrolytic lysosomal glycogen-specific recombinant human α -glucosidase (rhGAA) enzyme (cipaglucosidase alfa-atga) with an enzyme stabilizer (miglustat).

FDA Approved Indication(s)

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

Opfolda is indicated for use in combination with Pombiliti for the treatment of adult patients with late-onset Pompe disease (lysosomal GAA deficiency) weighing \geq 40 kg and who are not improving on their current ERT.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Pombiliti + Opfolda is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Pompe Disease (must meet all):

1. Diagnosis of late-onset Pompe disease confirmed by one of the following (a or b):
 - a. Enzyme assay confirming low GAA activity;
 - b. DNA testing;
2. Age \geq 18 years;
3. Member weighs \geq 40 kg;
4. Pombiliti and Opfolda are prescribed together;
5. Pombiliti and Opfolda are not prescribed concurrently with Lumizyme® or Nexviazyme®;
6. Dose does not exceed any of the following (a or b):
 - a. Members weighing \geq 50 kg: Pombiliti 20 mg/kg + Opfolda 260 mg (or 4 capsules) every other week;
 - b. Members weighing \geq 40 kg to $<$ 50 kg: Pombiliti 20 mg/kg + Opfolda 195 mg (or 3 capsules) every other week.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Pompe Disease (must meet all):

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy as evidenced by improvement in the individual member's Pompe disease manifestation profile (*see Appendix D for examples*);
3. Pombiliti and Opfolda are prescribed together;
4. Pombiliti and Opfolda are not prescribed concurrently with Lumizyme[®] or Nexviazyme[®];
5. If request is for a dose increase, new dose does not exceed any of the following (a or b):
 - a. Members weighing ≥ 50 kg: Pombiliti 20 mg/kg + Opfolda 260 mg (or 4 capsules) every other week;
 - b. Members weighing ≥ 40 kg to < 50 kg: Pombiliti 20 mg/kg + Opfolda 195 mg (or 3 capsules) every other week.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.

Approval duration: Duration of request or 12 months (whichever is less); or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

- A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

6MWT: 6-minute walk test

ERT: enzyme replacement therapy

FDA: Food and Drug Administration

GAA: acid alpha-glucosidase

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): pregnancy
- Boxed warning(s): (*Pombiliti only*) severe hypersensitivity reactions, infusion-associated reactions, and risk of acute cardiorespiratory failure in susceptible patients

Appendix D: Measures of Therapeutic Response

- Pompe disease manifests as a clinical spectrum that varies with respect to age at onset*, rate of disease progression, and extent of organ involvement. Patients can present with a variety of signs and symptoms, which can include cardiomegaly, cardiomyopathy, hypotonia, muscle weakness, respiratory distress (eventually requiring assisted ventilation), and skeletal muscle dysfunction.
- While there is not one generally applicable set of clinical criteria that can be used to determine appropriateness of continued therapy, clinical parameters that can indicate therapeutic response to Pombiliti + Opfolda include improved or maintained forced vital capacity, and improved or maintained 6-minute walk test (6MWT) distance.

**Although infantile-onset disease typically presents in the first year of life, age of onset alone does not necessarily distinguish between infantile- and late-onset disease since juvenile-onset disease can present prior to 12 months of age.*

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Pompe disease	<ul style="list-style-type: none"> • Members weighing ≥ 50 kg: Pombiliti 20 mg/kg IV + Opfolda 260 mg (or 4 capsules) PO every other week • Members weighing ≥ 40 kg to < 50 kg: Pombiliti 20 mg/kg IV + Opfolda 195 mg (or 3 capsules) PO every other week 	Pombiliti 20 mg/kg and Opfolda 260 mg every other week

VI. Product Availability

Drug Name	Availability
cipaglicosidase alfa-atga (Pombiliti)	Vial with lyophilized powder for reconstitution: 105 mg
miglustat (Opfolda)	Oral capsule: 65 mg

VII. References

1. Pombiliti Prescribing Information. Philadelphia, PA: Amicus Therapeutics US, LLC; September 2023. Available at: <https://amicusrx.com/pi/pombiliti.pdf>. Accessed October 3, 2023.
2. Opfolda Prescribing Information. Philadelphia, PA: Amicus Therapeutics US, LLC; September 2023. Available at: <https://amicusrx.com/pi/opfolda.pdf>. Accessed October 3, 2023.
3. Schoser B, Roberts M, Byrne BJ, et al. Safety and efficacy of cipaglicosidase alfa plus miglustat versus alglucosidase alfa plus placebo in late-onset Pompe disease (PROPEL): an international, randomised, double-blind, parallel-group, phase 3 trial. *Lancet Neurology* 2021;20:1027-37.

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- Cupler EJ, Berger KI, Leshner RT, et al. Consensus treatment recommendations for late-onset Pompe disease. Muscle Nerve 2012;45:319-33.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals
J3590	Unclassified biologics

Reviews, Revisions, and Approvals	Date
Policy created	01/2024