

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

Reference Number: PA.CP.PHAR.567

Effective Date: 02/2024

Last Review Date: 01/2026

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;
 - c. Increased lysosomal glycogen;
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: 12 months

B. Niemann-Pick Disease Type C (off-label) (must meet all):

1. Diagnosis of NPC confirmed by one of the following (a or b):
 - a. Genetic analysis indicating mutation in both alleles of *NPC1* or *NPC2*;
 - b. Genetic analysis indicating mutation in one allele of *NPC1* or *NPC2* along with one of the following (i or ii):
 - i. Positive filipin staining test result;
 - ii. Positive biomarker result (e.g., oxysterol, lyso-sphingolipid, bile acid);
2. Request is for Opfolda without Pombiliti;
3. Prescribed by or in consultation with a geneticist, neurologist, endocrinologist, or metabolic disease specialist;
4. Member presents with at least one neurological sign or symptom of the disease (*see Appendix D*);
5. Dose does not exceed 585 mg (9 capsules) per day.

Approval duration: 12 months

C. 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.PHARM.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. Niemann-Pick Disease Type C (off-label) (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.PHARM.01) applies;
2. Request is for Opfolda without Pombiliti;

3. Member is responding positively to therapy as evidenced by an improvement or stabilization in a domain affected by NPC (e.g., ambulation, fine motor skills, swallowing, sitting, or speech);
4. If request is for a dose increase, new dose does not exceed 585 mg (9 capsules) per day.

Approval duration: 12 months

C. 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.PHARM.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

NPC: Niemann-Pick disease type C

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 for Pompe disease, 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.

- Examples of neurological signs or symptoms of NPC include hearing loss, vertical supranuclear gaze palsy, dysarthria, ataxia, dystonia, impaired ambulation, dysarthria, dysphagia, seizures, dementia.

**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; July 2024. Available at: <https://amicusrx.com/pi/pombiliti.pdf>. Accessed December 6, 2025.
2. Opfolda Prescribing Information. Philadelphia, PA: Amicus Therapeutics US, LLC; July 2024. Available at: <https://amicusrx.com/pi/opfolda.pdf>. Accessed December 6, 2025.
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.
4. Cupler EJ, Berger KI, Leshner RT, et al. Consensus treatment recommendations for late-onset Pompe disease. *Muscle Nerve* 2012;45:319-33.
5. Stevens D, Milani-Nejad S, Mozaffar T. Pompe disease: a clinical, diagnostic, and therapeutic overview. *Curr Treat Options Neurol*. 2022 November;24(11):573-88. doi:10.1007/s11940-022-00736-1.
6. Mengel E, Patterson MC, Da Riolo RM, et al. Efficacy and safety of arimoclomol in Niemann-Pick disease type C: Results from a double-blind, randomised, placebo-controlled, multinational phase 2/3 trial of a novel treatment. *J Inherit Metab Dis*. 2021;44(6):1463-1480. doi:10.1002/jimd.12428
7. Geberhiwot T, Moro Alessandro, Dardis A, et al. Consensus clinical management guidelines for Niemann-Pick disease type C. *Orphanet Journal of Rare Diseases* 2018 April 6;13(1):50.
8. Patterson MC, Clayton P, Gissen P, et al. Recommendations for the detection and diagnosis of Niemann-Pick disease type C: An update. *Neurol Clin Pract*. 2017;7(6):499-511.

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
G0138	Intravenous infusion of cipaglucosidase alfa-atga, including provider/supplier acquisition and clinical supervision of oral administration of miglustat in preparation of receipt of cipaglucosidase alfa-atga
J1202	Miglustat, oral, 65 mg
J1203	Injection, cipaglucosidase alfa-atga, 5 mg

Reviews, Revisions, and Approvals	Date
Policy created	01/2024
1Q 2025 annual review: added criteria for off-label use of Opfolda for NPC to align with coverage guidelines in the Zavesca (miglustat) and Miplyffa criteria; added increased lysosomal glycogen as an additional option for confirming a Pompe disease diagnosis; added HCPCS codes [G0138, J1202, J1203] and removed HCPCS codes [C9399, J3590]; references reviewed and updated.	01/2025
1Q 2026 annual review: no significant changes; updated initial auth duration from 6 months to 12 months; references reviewed and updated.	01/2026