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

Reference Number: CP.PHAR.567
Effective Date: 09.28.23
Last Review Date: 02.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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 ≥ 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 ≥ 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 health plans affiliated with Centene Corporation® that Pombiliti + Opfolda are **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, b, or c):
   a. Enzyme assay confirming low GAA activity;
   b. DNA testing;
   c. Increased lysosomal glycogen;
2. Age ≥ 18 years;
3. Member weighs ≥ 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 ≥ 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:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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: 6 months

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Pompe Disease (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*

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:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Niemann-Pick Disease Type C (off-label) (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line

of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

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	• 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
cipaglucosidase 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. October 21, 2024.
2. Opfolda Prescribing Information. Philadelphia, PA: Amicus Therapeutics US, LLC; July 2024. Available at: https://amicusrx.com/pi/opfolda.pdf. Accessed October 21, 2024.
3. 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. 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 Riol 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	P&T Approval Date
Policy created pre-emptively	11.16.21	02.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.06.22	
1Q 2023 annual review: no significant changes as the drug is not yet FDA-approved; references reviewed and updated.	11.15.22	02.23
1Q 2024 annual review: drug is now FDA-approved – description section updated per FDA labeling; criteria updated per FDA labeling: added requirement that Pombiliti and Opfolda be prescribed together in both initial approval and continued therapy sections, added exclusion against concurrent use with Lumizyme and Nexviazyme for Continued Therapy; updated HCPCS codes: [C9399] and [J3590]; references reviewed and updated.	10.03.23	02.24
Added HCPCS codes [G0138, J1202, J1203] and removed HCPCS codes [C9399, J3590].	02.22.24	
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; references reviewed and updated.	12.02.24	02.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering

benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members, and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.