Pharmacy Policy Bulletin: J-1338 Opfolda (miglustat) – Commercial and Healthcare Reform	
Number: J-1338	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-1338-002	**Original Date:** 12/06/2023
Effective Date: 12/20/2024	**Review Date:** 12/04/2024

Drugs Product(s):	• Opfolda (miglustat)
FDA-Approved Indication(s):	• In combination with Pombiliti (cipaglucosidase alfa-atga) 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)

Background:	• GAA deficiency results in intra-lysosomal accumulation of glycogen in various tissues. ○ Pombiliti provides an exogenous source of GAA. After binding to M6P receptors, it is internalized and transported into lysosomes where it undergoes proteolytic cleavage and N-glycans trimming which are both required to yield the most mature and active form of GAA. Pombiliti then exerts enzymatic activity in cleaving glycogen. Opfolda binds, stabilizes, and reduces the inactivation of Pombiliti in the blood after infusion. The bound Opfolda is dissociated from Pombiliti after it is internalized and transported into lysosomes. Opfolda alone has no pharmacological activity in cleaving glycogen. • Pompe disease (also known as glycogen storage disease type II, acid maltase deficiency, and glycogenosis type II) is a rare, multisystem, autosomal recessive disorder characterized by a mutation of the GAA gene, causing glycogen accumulation in muscle tissues, leading to muscle weakness, respiratory damage, decreased quality of life, and shortened lifespan. Pompe disease can develop at any age and is classified as infantile onset Pompe disease (IOPD) (i.e., 1 year of age and younger) or late-onset Pompe disease (LOPD) (i.e., over 1 year of age). The prevalence of Pompe disease is estimated at approximately 3,500 patients in the United States (US). • Signs ERT is improving the patient's LOPD include decreased heart size, normal heart function, improvement of muscle function/tone/strength, and reduced glycogen accumulation. Depending on the severity of LOPD, additional nonpharmacologic treatments include physical or occupational therapy, a feeding

	tube, and/or mechanical ventilation. The effectiveness of ERT may decline over time requiring a different ERT to improve response. • Pombiliti plus Opfolda did not achieve statistical superiority to alglucosidase alfa plus placebo for improving 6-min walk distance in the overall population of patients with LOPD. • Prescribing Considerations: ○ Other ERTs available include Lumizyme (alglucosidase alfa) and Nexviazyme (avalglucosidase alfa-ngpt). Pombiliti, Lumizyme, and Nexviazyme are healthcare-administered by intravenous infusion. ○ Administer Pombiliti in combination with Opfolda. Start Pombiliti in combination with Opfolda 2 weeks after the last ERT dose. If the Opfolda dosage is missed, Pombiliti should not be administered and treatment should be rescheduled at least 24 hours after Opfolda was last taken. If Opfolda in combination with Pombiliti are both missed, re-start treatment as soon as possible. ○ Opfolda is taken with an unsweetened beverage approximately 1 hour before the start of Pombiliti infusion. Other beverages or food should not be consumed for at least 2 hours prior to and 2 hours after taking Opfolda. ○ Consider administering antihistamines, antipyretics, and/or corticosteroids prior to Pombiliti administration. ○ Pombiliti has a BBW for severe hypersensitivity reactions, IARs, and risk of acute cardiorespiratory failure in susceptible patients.

Approval Criteria

I. Initial Authorization

When a benefit, coverage of Opfolda may be approved when all of the following criteria are met **(A. through F.)**:

A. The member is 18 years of age or older.
B. The member weighs ≥40 kg.
C. The member has a diagnosis of late-onset Pompe disease (LOPD).
D. The member is not improving on their current ERT.
E. The member is using Opfolda in combination with Pombiliti.
F. There is confirmation that the member meets one (1) of the following criteria **(1. or 2.)**:
  1. The member has coverage of Pombiliti through their medical insurance.
  2. The member has coverage of Pombiliti through another form of coverage (e.g., out-of-pocket expense).

II. Reauthorization

When a benefit, reauthorization of Opfolda may be approved when all of the following criteria is met **(A., B., and C.)**:

A. The member meets one (1) of the following criteria **(1. or 2.)**:
  1. The member has experienced improvement in signs or symptoms for Pompe disease from baseline (e.g., decreased heart size, normal heart function, improvement of muscle strength, improvement in walking distance, improvement in respiratory function).
  2. The member has reduced glycogen accumulation from baseline.
B. The member continues to use Opfolda in combination with Pombiliti.
C. There is confirmation that the member has coverage of Pombiliti through their medical insurance or another form of coverage.

II. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Pombiliti [package insert]. Philadelphia, PA: Amicus Therapeutics US, LLC; July 2024.
2. Opfolda [package insert]. Philadelphia, PA: Amicus Therapeutics US, LLC; July 2024.
3. Toscano A, Rodolico C, Musumeci O. Multisystem late onset Pompe disease (LOPD): an update on clinical aspects. *Ann Transl Med*. 2019;7:284.
4. National Organization for Rare Disorders. Pompe Disease. Available at: https://rarediseases.org/rare-diseases/pompe-disease/. Accessed October 4, 2023.
5. Cleveland Clinic. Pompe Disease. Available at: https://my.clevelandclinic.org/health/diseases/15808-pompe-disease. Accessed October 4, 2023.
6. Stevens D, Milani-Nejad S, Mozaffar T. Pompe Disease: A Clinical, Diagnostic, and Therapeutic Overview. *Curr Treat Options Neurol*. 2022;24(11):573-588.
7. DRUGDEX System (Micromedex 2.0). Greenwood Village, CO: Truven Health Analytics; 2023.
8. Cupler EJ, Berger KI, Leshner RT, et al. Consensus treatment recommendations for late-onset Pompe disease. *Muscle Nerve*. 2012;45:319-33.