MEDICAL MUTUAL®

Drug Policy

Policy:	Opfolda® (miglustat capsules – Amicus)	Annual Review Date: 12/19/2024 Last Revised Date: 12/19/2024

OVERVIEW

Opfolda, an enzyme stabilizer, is indicated in combination with Pombiliti® (cipaglucosidase alfa intravenous infusion), a hydrolytic lysosomal glycogen-specific recombinant human α-glucosidase enzyme, for **late-onset Pompe disease** (lysosomal acid α-glucosidase deficiency) in adults weighing ≥ 40 kg who are not improving on their current enzyme replacement therapy.[1] Opfolda binds with, stabilizes, and reduces inactivation of Pombiliti after infusion. Bound Opfolda dissociates from Pombiliti after it is internalized and transported into lysosomes. Opfolda as monotherapy has no pharmacological activity in Pompe disease.

Disease Overview

Pompe disease (glycogen storage disease type II, or acid maltase deficiency), is a rare lysosomal storage disorder characterized by a deficiency in acid α-glucosidase activity leading to the accumulation of glycogen, particularly in muscle.[2,3] The onset, progression, and severity of Pompe disease is variable. Infantile-onset Pompe disease usually manifests in the first few months of life and death often occurs in the first year of life, if left untreated.[2] Clinical manifestations of infantile-onset Pompe disease includes hypotonia, difficulty feeding, and cardiopulmonary failure.[4] Late-onset Pompe disease has a more variable clinical course and can manifest any time after 12 months of age.[3,4] Patients typically present with progressive muscle weakness which can progress to respiratory insufficiency. The diagnosis of Pompe disease is established by demonstrating decreased acid α-glucosidase activity in blood, fibroblasts, or muscle tissue, or by genetic testing.

POLICY STATEMENT

This policy involves the use of Opfolda. Prior authorization is recommended for pharmacy and medical benefit coverage of Opfolda. Approval is recommended for those who meet the conditions of coverage in the **Criteria, Dosing, Initial/Extended Approval, Duration of Therapy**, and **Labs/Diagnostics** for the diagnosis provided. **Waste Management** applies for all covered conditions that are administered by a healthcare professional. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria and Waste Management section. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Opfolda as well as the monitoring required for AEs and long-term efficacy, initial approval requires Opfolda be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Opfolda is recommended in those who meet the following criteria:
FDA-Approved Indication

1. **Acid Alpha-Glucosidase Deficiency (Pompe Disease). Initial approval criteria.** Approve for 1 year if the patient meets the following (A, B, C, D, E, and F):
   - **A)** Patient is ≥ 18 year of age; AND
   - **B)** Patient weighs ≥ 40 kg; AND
   - **C)** The medication will be used in combination with Pombiliti; **AND**
   - **D)** Patient has not demonstrated an improvement in objective measures after receiving one of the following for at least one year (i or ii):
     Note: Examples of objective measures include forced vital capacity (FVC) and six-minute walk test (6MWT).
     - **i.** Lumizyme (alglucosidase alfa) intravenous infusion; **OR**
     - **ii.** Nexviazyme (avalglucosidase alfa-ngpt) intravenous infusion; **AND**
   - **E)** Patient has late-onset acid alpha-glucosidase deficiency (late-onset Pompe disease) with diagnosis established by one of the following (i or ii):
     - **i.** Patient has a laboratory test demonstrating deficient acid alpha-glucosidase activity in blood, fibroblasts, or muscle tissue; OR
     - **ii.** Patient has a molecular genetic test demonstrating acid alpha-glucosidase gene mutation; **AND**
   - **F)** The medication is prescribed by or in consultation with a geneticist, neurologist, a metabolic disorder sub-specialist, or a physician who specializes in the treatment of lysosomal storage disorders.

   Renewal Criteria. Approve for 1 year if the patient meets the following (A, B, AND C):
   - **A)** 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**
   - **B)** 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/or 6-MWT; **AND**
   - **C)** Patient is being monitored for antibody formation (including neutralizing antibodies).

Initial Approval/ Extended Approval.
A) *Initial Approval:* 1 year (365 days)
B) *Extended Approval:* 1 year (365 days)

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Coverage of Opfolda is not recommended in the following situations:

1. **Gaucher Disease.** An alternate dosage of miglustat is available for the treatment of Gaucher disease.[5]

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:
The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Opfolda ® capsules [prescribing information]. Philadelphia, PA: Amicus; September 2023.
2. Chien YH, Hwu WL, Lee NC. Pompe disease: Early diagnosis and early treatment make a difference. *Pediatr Neonatol*. 2013;54:219-227.
3. Llerena Junior JC, Nascimento OJM, Oliveira ASB, et al. Guidelines for the diagnosis, treatment and clinical monitoring of patients with juvenile and adult Pompe disease. *Arq Neuropsiquiatr*. 2016;74:166-176.
4. Cupler EJ, Berger KI, Leshner RT, et al. Consensus treatment recommendations for late-onset Pompe disease. *Muscle Nerve*. 2012;45:319-333.
5. Zavesca® capsules [prescribing information]. South San Francisco, CA: Actelion; August 2022.