Effective Date **3/15/2024**
Next Review Date… **3/15/2025**
Coverage Policy Number **IP0598**

Opfolda (miglustat) capsule

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for miglustat (**Opfolda**®).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Miglustat (Opfolda) is considered medically necessary when the following are met:

Acid Alpha-Glucosidase Deficiency (Pompe Disease). Individual meets **ALL** the following criteria:

A. Age 18 years or older
B. Weighs 40 kg or more
C. Medication will be used in combination with Pombiliti
D. Has not demonstrated an improvement in objective measures (for example, forced vital capacity [FVC] and six-minute walk test [6MWT]) after receiving ONE of the following for at least one year:

i. Lumizyme (alglucosidase alfa) intravenous infusion
ii. Nexviazyme (avalglucosidase alfa-ngpt) intravenous infusion

E. Documented diagnosis of late-onset acid alpha-glucosidase deficiency (late-onset Pompe disease) with diagnosis established by **ONE** of the following:
   i. Laboratory test demonstrating deficient acid alpha-glucosidase activity in blood, fibroblasts, or muscle tissue
   ii. Molecular genetic test demonstrating biallelic acid alpha-glucosidase (GAA) pathogenic variants

F. 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

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When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of miglustat (Opfolda) is considered medically necessary for Acid Alpha-Glucosidase Deficiency (Pompe Disease) when the above medical necessity criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration: up to 12 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational or unproven, including the following (this list may not be all inclusive):

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

2. **Concomitant Use with Other Medications Used to Treat Pompe Disease.** Opfolda is not recommended in combination with other pharmacologic treatments for Pompe disease (for example, Lumizyme and Nexviazyme). The Opfolda / Pombiliti pivotal trial excluded patients currently receiving any investigational therapy or pharmacologic treatment for Pompe disease.

Background

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.

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.