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Policy Number: C27241-A

Opfolda (miglustat)

PRODUCTS AFFECTED

Opfolda (miglustat)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. LATE ONSET POMPE DISEASE (LOPD):
   1. Documented diagnosis of late-onset Pompe disease (LOPD)
      AND

2. Documentation diagnosis was confirmed by ONE of the following: enzyme assay showing a deficiency of acid alpha-glucosidase (GAA) activity in the blood, skin, or muscle OR genetic testing showing a mutation in the GAA gene [DOCUMENTATION REQUIRED]
   AND
3. Documentation of member's baseline percent-predicted forced vital capacity (FVC), baseline walking distance or 6-minute walk test (6MWT), or gastrointestinal symptoms [DOCUMENTATION REQUIRED]
   AND
4. Documentation member is not improving on their current enzyme replacement therapy (ERT) (i.e., member is NOT ERT-naïve)
   AND
5. Prescriber attests or clinical reviewer has found that Pombiliti (cipaglucosidase alfa-atga) has been authorized for use concurrently
   AND
6. Prescriber attests females of childbearing potential and males have been counseled to use contraception while taking Pombiliti with Opfolda and for at least 60 days after discontinuing
   AND
7. Prescriber attests member is able to take Opfolda 1 to 3 hours before each Pombiliti infusion
   NOTE: If the Pombiliti infusion cannot be started within 3 hours of oral administration of Opfolda, reschedule Pombiliti in combination with Opfolda at least 24 hours after Opfolda was last taken.
   AND
8. Prescriber attests attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Opfolda (miglustat) include: pregnancy.]

CONTINUATION OF THERAPY:

A. LATE ONSET POMPE DISEASE (LOPD):

1. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity (e.g., severe infusion related reactions)
   AND
2. Documentation that member has demonstrated a beneficial response to therapy compared to pretreatment baseline as demonstrated by stabilization or improvement in FVC and/or 6MWT and signs/symptoms of the condition (e.g., gastrointestinal symptoms) [DOCUMENTATION REQUIRED]
   AND
3. Prescriber attests member is able to take Opfolda 1 to 3 hours before each Pombiliti infusion
   NOTE: If the Pombiliti infusion cannot be started within 3 hours of oral administration of Opfolda, reschedule Pombiliti in combination with Opfolda at least 24 hours after Opfolda was last taken.

DURATION OF APPROVAL:

Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a metabolic specialist, endocrinologist, biochemical geneticist, or physician experienced in the management of Pompe disease [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

18 years of age and older

QUANTITY:

≥40kgs-<50kgs: 195 mg every 2 weeks
≥50kgs: 260 mg every 2 weeks

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
GAA Deficiency Treatment – Agents

FDA-APPROVED USES:
Opfolda is an enzyme stabilizer indicated, in combination with Pombiliti, a hydrolytic lysosomal glycogen-specific enzyme, 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).

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Lysosomal acid alpha-glucosidase (GAA, also called acid maltase) deficiency (Pompe disease, formerly classified as glycogen storage disease type II [GSD II]) is an autosomal recessive disorder with considerable allelic heterogeneity. It is caused by mutations in the gene for lysosomal acid alpha-1,4-glucosidase. Deficiency of lysosomal GAA leads to accumulation of glycogen in lysosomes and cytoplasm, which results in tissue destruction.
The juvenile and adult form (late onset) is characterized by skeletal myopathy (usually in a limb-girdle distribution) and a protracted course leading to respiratory failure.
Juvenile or adult-onset GAA deficiency should be considered in patients with progressive weakness in a limb-girdle distribution. Supportive findings may include:

-Electromyogram demonstrating myopathic discharges, sometimes associated with abundant myotonic and complex repetitive discharges, most prominent in the paraspinal muscles
-Elevated serum creatine kinase
-Demonstration of reduced GAA activity in a dried blood spot or leukocytes, followed by sequencing of the GAA gene, confirms the disease. Enzyme activity assays using skin fibroblasts or muscle tissue are alternatives to genetic testing to confirm the diagnosis.

GAA deficiency is treated with enzyme replacement therapy (ERT), physical and occupational therapy, and supportive care (e.g., mechanical ventilation for respiratory failure).

Pombiliti is the third ERT to be approved for Pompe Disease and is the first to be used in combination with an enzyme stabilizer, which is the Opfolda component. Pombiliti and Opfolda became FDA-approved to be used in combination because of the results from the PROPEL trial. The PROPEL trial was a phase 3, randomized, double blind, parallel design, multicentered trial that compared Pombiliti with Opfolda to alglucosidase alfa (Lumizyme) with placebo in adult patients with LOPD who were either ERT naïve or had received alglucosidase alfa for two or more years at the recommended dose and intervals. The primary outcome of the study was improvement on the 6 Minute Walk Test (6MWT) in which greater distance travel indicated improved ambulatory function. Key secondary outcomes for efficacy included evaluating pulmonary function tests, lower muscular strength, and motor function. Treatments were assigned in a 2:1 ration, with 85 in the Pombiliti with Opfolda group and 38 in the alglucosidase alfa with placebo group. Participant characteristics were similar between groups. The Pombiliti with Opfolda group participants were an average of 47.6 years old, walked an average distance of 357.9 meters on the 6MT, and had an average FVC of 70.7%. Seventy-six percent of them were ERT-experienced. The alglucosidase-alfa with placebo group participants were an average of 45.1 years old, walked an average distance of 351.5 meters on the 6MWT, and had an average FVC of 69.7%. Seventy-nine percent of them were ERT-experienced.

Regarding the primary outcome of improvement on the 6MWT, the Pombiliti with Opfolda group averaged a mean change in 20.8 meters walked after 1 year versus 7.2 meters in the alglucosidase alfa with placebo group. However, the P value was 0.071 for the change in distance on the 6MWT, so the results did not show statistical significance and therefore could not claim superiority. For the secondary outcome of improvement on pulmonary function tests, the Pombiliti with Opfolda group had a mean change in sitting FVC of only -0.9%, while the alglucosidase alfa with placebo group had a mean change of -4%. The participants who were ERT-experienced but were assigned to the Pombiliti with Opfolda group had an improvement on their 6MWT by 16.9m and maintained their FVC throughout the study duration. The ERT-experienced participants who were assigned to the alglucosidase alfa with placebo group had no change on their 6MWD test and showed a 4% decline in their FVC. The potential clinically significant effects, particularly in the patients who were ERT-experienced and switched to Pombiliti with Opfolda, prompted their approval from the FDA.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Pombiliti (cipaglucosidase alfa-atga) with Opfolda (miglustat) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Opfolda (miglustat) include: pregnancy.

OTHER SPECIAL CONSIDERATIONS:
Opfolda should be taken about 1 hour before the Pombiliti infusion. If the Pombiliti infusion is not given within 3 hours of taking Opfolda, both doses will have to be rescheduled >24 hours after the last Opfolda dose was taken. The member should not consume food or beverages (other than water, tea, or coffee without sugar, cream, or sweeteners) 2 hours before and 2 hours after Opfolda administration.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Opfolda CAPS 65MG

REFERENCES

1. Opfolda (miglustat) [prescribing information]. Philadelphia, PA: Amicus Therapeutics; September 2023.
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3. Dasouki, M., Jawdat, O., Almadhoun, O., Pasnoor, M., McVey, A. L., Abuzinadah, A., Herbelin, L., Barohn, R. J., & Dimachkie, M. M. (2014, August). *Pompe disease: Literature review and case series*. Neurologic clinics. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4311397/#:~:text=Pompe%20disease%20is%20still%20considered,origin%20and%20South%20East%20Asians.
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5. Cupler EJ, et al. Consensus treatment recommendations for late-onset Pompe disease. Muscle Nerve. 2012;45(3):319-333. doi:10.1002/mus.22329
6. Kishnani PS, Steiner RD, Bali D, et al. Pompe disease diagnosis and management guidelines. Genet Med 2006; 8:267-88.

SUMMARY OF REVIEW/REVISIONS	DATE
NEW CRITERIA CREATION	Q1 2024