Protocol for Pompe Disease Products

Approved January 2024

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Lumizyme (alglucosidase alfa)
Nexviazyme (avalglucosidase alfa)
Pombiliti + Opfolda (cipaglucosidase alfa-atga + miglustat)

Background:
Pompe disease is a rare, autosomal recessive disorder caused by deficiency of the glycogen-degrading lysosomal enzyme, acid alpha-glucosidase (GAA). Late-onset Pompe disease is a multisystem condition, with a heterogeneous clinical presentation that mimics other neuromuscular disorders.

Lumizyme *(alglucosidase alfa) is a hydrolytic lysosomal glycogen-specific enzyme indicated for patients with Pompe disease or GAA deficiency.*

*P**ombiliti** (cipaglucosidase alfa-atga) is a hydrolytic lysosomal glycogen-specific enzyme indicated, in combination with Opfolda, an enzyme stabilizer, 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**),** for example: improvement in % predicted forced vital capacity (FVC) in the sitting position or change in 6-minute walk test (6MWT).*

Opfolda *(miglustat) 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, for example: improvement in % predicted forced vital capacity (FVC) in the sitting position or change in 6-minute walk test (6MWT).*

Nexviazyme *(avalglucosidase alfa) is a hydrolytic lysosomal glycogen-specific enzyme indicated for the treatment of patients with late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency).*

Criteria for Approval:

A. For Nexviazyme or Pombiliti + Opfolda

1. Patient meets the minimum age per drug labeling:
   a. Nexviazyme: Patient is 1 year old or older
   b. Pombiliti + Opfolda: Patient is 18 years old or older

2. Patient has the diagnosis of late-onset Pompe disease as confirmed by ONE of the following:

a. Absence or deficiency (< 40% of the lab specific normal mean) acid alpha-glucosidase deficiency activity in fibroblasts, lymphocytes, or muscle; **OR**
b. Increased lysosomal glycogen; **OR**
c. Molecular genetic testing for deletion or mutation in the GAA gene; **OR**
d. Confirmation of positive GAA activity assay in dry blood spots

3. For Pombiliti + Opfolda:
   a. Pombiliti is given in combination with Opfolda
   b. Patient is not pregnant

B. Lumizyme

1. Patient has the diagnosis of infantile-onset Pompe disease as confirmed by ONE of the following:
   a. Absence or deficiency (< 1% of the lab specific normal mean) acid alpha-glucosidase deficiency activity in fibroblasts, lymphocytes, or muscle; **OR**
   b. Increased lysosomal glycogen; **OR**
   c. Molecular genetic testing for deletion or mutation in the GAA gene; **OR**
   d. Confirmation of positive GAA activity assay in dry blood spots
2. Patient has the diagnosis of late-onset (non-infantile) Pompe disease as confirmed by ONE of the following:
   a. Absence or deficiency (< 40% of the lab specific normal mean) GAA activity in lymphocytes, fibroblasts, or muscle; **OR**
   b. Increased lysosomal glycogen; **OR**
   c. Molecular genetic testing for deletion or mutation in the GAA gene; **OR**
   d. Confirmation of positive GAA activity assay in dry blood spots; **AND**
3. Patient will not receive Lumizyme with either Nexviazyme or Pombiliti + Opfolda
4. Patient has no evidence of cardiac hypertrophy

C. Medication is prescribed by or in consultation with a geneticist, metabolic disorders specialist, or an expert in the disease state

D. Patient's weight must be provided and have been taken within the last four weeks to ensure accurate dosing

E. Patient does not have any contraindication(s) to the requested medication

F. Medication is prescribed in accordance with Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with medically appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs (Lexicomp), national guidelines, or other peer- reviewed evidence

Continuation of therapy:

1. Patient has experienced a positive clinical response to therapy such as improved cardiac or respiratory function.
2. For Pombiliti + Opfolda: Pombiliti continues to be prescribed in combination with Opfolda
3. For dose increase requests, weight must be received

4. Medication is prescribed in accordance with Food and Drug Administration (FDA) established indications and dosing regimens or in accordance with medically appropriate off-label indications and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs (Lexicomp), national guidelines, or other peer reviewed evidence.

Note: Lumizyme, Pombiliti and Nexviazyme have Black Box warnings for risk of anaphylaxis, hypersensitivity, and cardiorespiratory failure.

Initial and Renewal Approval Duration: 12 months

Quantity Level Limit: Opfolda (miglustat) 65mg capsules - 8 capsules per 28 days

References:

1. Lumizyme [Product information]. Genzyme Corporation . Cambridge MA 02142. 2/2020
2. Nexviazyme [packet insert]. Genzyme Corporation. Cambridge, MA 02142. August 2021
3. Opfolda [packet insert]. Amicus Therapeutics US, LLC. Philadelphia, PA 19104. September 2023
4. Pombiliti [packet insert]. Amicus Therapeutics US, LLC. Philadelphia, PA 19104. September 2023
5. Tarnopolsky M et al. Pompe Disease: Diagnosis and Management. Evidence-Based Guidelines from a Canadian Expert Panel. Can J Neurol Sci. 2016; 43: 472-485. Volume 43, No. 4 – July 2016
6. Clinical Pharmacology (online database). Tampa FL: Gold Standard Inc.: 2019. Updated periodically
7. Cupler EJ, Berger KI et al. Consensus Treatment Recommendations for Late-Onset Pompe Disease. AANEM Muscle Nerve 45: 319–333, 2012
8. Bali D et al. Pompe disease diagnosis and management guideline. Genet Med. 2006 May; 8(5): 267–288
9. Musumeci O, Toscano A. Diagnostic tools in late onset Pompe disease (LOPD). Ann Transl Med. 2019 Jul;7(13):286. doi: 10.21037/atm.2019.06.60
10. Di Iorio G, Cipullo F, Stromillo L, Sodano L, Capone E, Farina O. S1.3 Adult-onset Pompe disease. Acta Myol. 2011 Dec;30(3):200–2
11. Hahn A, Schänzer A. Long-term outcome and unmet needs in infantile-onset Pompe disease. Ann Transl Med. 2019 Jul;7(13):283