MEDICAL COVERAGE POLICY	
SERVICE:	**Alglucosidase alfa (Lumizyme®)**
Policy Number:	**316**
Effective Date:	**06/01/2025**
Last Review:	**05/12/2025**
Next Review:	**05/12/2026**

Important note: *Unless otherwise indicated, medical policies will apply to all lines of business. Medical necessity as defined by this policy does not ensure the benefit is covered. This medical policy does not replace existing federal or state rules and regulations for the applicable service or supply. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan documents. See the member plan specific benefit plan document for a complete description of plan benefits, exclusions, limitations, and conditions of coverage. In the event of a discrepancy, the plan document always supersedes the information in this policy.*

SERVICE: Alglucosidase alfa (Lumizyme®)

PRIOR AUTHORIZATION: Required

POLICY: Please review the plan's EOC (Evidence of Coverage) or Summary Plan Description (SPD) for details.

For Medicare plans, please refer to appropriate Medicare NCD (National Coverage Determination) or LCD (Local Coverage Determination). Medicare NCD or LCD specific InterQual criteria may be used when available. If there are no applicable NCD or LCD criteria, use the criteria set forth below.

For Medicaid plans, please confirm coverage as outlined in the Texas Medicaid Provider Procedures Manual | TMHP (TMPPM). Texas Mandate HB154 is applicable for Medicaid plans.

Baylor Scott & White Health Plan (BSWHP) may consider alglucosidase alfa (Lumizyme®) medically necessary for the treatment of Pompe disease when ALL of the following criteria are met:

Initial requests:

1. Member has a diagnosis of Pompe disease (alpha-glucosidase enzyme (GAA) deficiency) supported by documentation from medical records through at least 1 of the following:
    a. Enzyme assay confirming GAA deficiency
    b. Genetic testing

    AND
2. Prescribed by or in consultation with a metabolic specialist, geneticist, or any physician experienced with the management of Pompe disease **AND**
3. Dose will not exceed 20 mg/kg once every 2 weeks **AND**
4. For late-onset Pompe disease (LOPD), request is accompanied with baseline documentation of at least 1 of the following:
    a. % predicted forced vital capacity (FVC) if respiratory involvement
    b. Motor function via 6-minute walk test (6MWT)
5. Must not be used in combination with any other enzyme replacement therapy for Pompe disease (ex. avalglucosidase alfa [Nexviazyme], cipaglucosidase alfa with miglustat [Pombliti with Opfolda])

Renewal requests:
1. Member meets all initial criteria **AND**
2. Member has positive response to therapy as defined by improvement or slowed disease progression in any one of the following areas: motor function (ex: 6MWT), cardiac function, pulmonary function (ex: % predicted FVC), or delayed death.

Authorization duration – 6 months

BSWHP considers alglucosidase alfa (Lumizyme®) for the treatment of all other indications to be experimental and investigational because the effectiveness of this strategy has not been established.

All requests will be reviewed by a clinical pharmacist and medical director.

BACKGROUND:

Pompe disease, also known as acid maltase deficiency, is an autosomal recessive disease, which involves a deficiency in lysosomal acid alpha-glucosidase enzyme. This enzyme is responsible for glycogen breakdown. Without enough enzyme, glycogen will build up in muscles and other tissues throughout the body leading to tissue and muscle damage, especially in the heart, lung, and skeletal muscle. This inherited disorder can be caused by either a relative or absolute absence of acid alpha-glucosidase. Pompe disease can either manifest as infantile-onset or late-onset, with late-onset typically being more progressive in muscle weakness and lower in severity.

Infantile-onset Pompe disease (IOPD) typically presents in the earlier stages of life (birth to months) and has a worse prognosis compared to late-onset Pompe disease (LOPD). Clinical presentation may include hypotonia, macroglossia, failure to thrive, cardiac failure, and hepatomegaly, all of which can contribute to a poor prognosis or death at an early age. Death within the first year of life can be attributed to cardiorespiratory failure. In comparison, LOPD has a much more favorable prognosis. Disease progression is typically slower in this type and is commonly associated with progressive muscle weakness. Cardiac involvement is not as common in this subtype, but respiratory failure is still a concern.

Currently, Pompe disease affects approximately 1 in 40,000 people in the United States. Standard of care for Pompe disease involves enzyme replacement therapy (ERT).

Recombinant human alglucosidase alfa (rhGAA; Lumizyme®) is a hydrolytic lysosomal glycogen-specific enzyme that provides exogenous human lysosomal acid alpha glucosidase. This drug is indicated for both infantile-onset and late-onset Pompe disease.

Safety and efficacy of alglucosidase alfa in IOPD was evaluated in 3 trials. Trial 1 (NCT00059280) was an international open-label trial that involved 18 patients who were 7 months of age or younger. Each

patient was randomized 1:1 to receive either 20 mg/kg or 40 mg/kg of IV alglucosidase alfa every 2 weeks for at least 1 year. Efficacy was assessed through ventilator-free survival, where 15 out of 18 patients survived without the need for a ventilator. The other 3 patients required a ventilator, but were able to survive. Changes in left ventricular mass index (LVMI) were assessed, but decreases in LVMI did not correlate with ventilator-free survival.

Trial 2 (NCT00053573) was an international, multicenter, non-randomized, open-label trial that enrolled 21 patients with IOPD who were within the ages of 3 months to 3.5 years. At the time of infusion, 5 patients were already receiving ventilator support. That aside, all patients received 20 mg/kg of IV alglucosidase alfa every 2 weeks for up to 104 weeks. The primary outcome assessed was survival and at the end of the study, 16 of 21 patients were alive. Of the 16 patients who were not initially on a ventilator, by the end of the study, 4 patients died from this group and 2 patients required ventilatory support.

Trial 3 was an open-label single-center trial that enrolled 18 patients with confirmed IOPD via a newborn screening program. Patients were treated with IV alglucosidase alfa prior to 6 months of age. By 18 months of age, 16 patients were able to be evaluated, and those patients were able to survive without the use of a ventilator.

Trial 4 (NCT00158600)was a randomized, double-blind, placebo-controlled trial that assessed 90 patients within the ages of 10-70 years with LOPD. Patients were given either 20 mg/kg of IV alglucosidase alfa or placebo in a 2:1 ratio (60 to 30 patients) every 2 weeks for 78 weeks. Of the 90 patients enrolled in the study, 81 patients were able to complete the study. After 78 weeks, for efficacy compared to baseline, the mean upright % forced vital capacity (FVC) increased from 55 to 56.2% in the treatment group, whereas the placebo group decreased in mean upright % FVC from 55 to 52.8%. The 6-minute walk test (6MWT) for all patients at the beginning of the study was approximately 330 meters. By the end of the study, patients in the treatment group were able to increase their 6MWT by 25 meters, whereas the placebo group experienced a decrease in distance by 3 meters. 9 patients discontinued the study, with only 3 patients discontinuing due to an adverse event (2 in treatment group and 1 in placebo group) and 6 patients discontinuing for other reasons (switch to other therapy, clinical deterioration, and patient decision).

Other enzyme replacement therapies have been approved for late-onset Pompe disease, including avalglucosidase alfa-ngpt (Nexviazyme®) and cipaglucosidase alfa-atga (Pombliti™) in combination with miglustat (Opfolda™). These newer therapies have not been approved for use in early onset or infantile-onset Pompe disease (IOPD). More data will be needed from ongoing trials to support their use in the IOPD subtype (Mini-Comet).

The phase 3 COMET trial was a randomized double-blind head-to-head study that compared avalglucosidase alfa-ngpt to alglucosidase alfa. The study found that avalglucosidase alfa-ngpt was able to improve both breathing and walking distance compared to alglucosidase alfa and baseline.

These results demonstrated non-inferiority and could not establish statistical superiority over alglucosidase alfa.

The phase 3 PROPEL study was a randomized double-blind trial that compared cipaglucosidase alfa-atga and miglustat combination (AT-GAA) to either alglucosidase alfa or placebo. With a hierarchical fixed sequential testing strategy, the study first tested for non-inferiority and then for superiority if non-inferiority was met. The results from this study demonstrated a statistically significant difference in % predicted forced vital capacity (FVC), but not 6-minute walk distance (6MWD) in both patient groups combined. For patients who were ERT-naive, the study was not able to show a statistically significant difference in either outcome. However, for patients who had a history of ERT, the study was able to show a statistically significant difference in both FVC and 6MWD. Therefore, from these results, AT-GAA is non-inferior compared to alglucosidase alfa, but was not able to establish superiority.

CODES:

Important note: *Due to the wide range of applicable diagnosis codes and potential changes to codes, an inclusive list may not be presented, but the following codes may apply. Inclusion of a code in this section does not guarantee that it will be reimbursed, and patient must meet the criteria set forth in the policy language.*

CPT Codes:	96365 – Intravenous infusion therapy prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour 96366 – Each additional hour. (List separately in addition to primary procedure code, 96365)
HCPCS Codes:	J0221 Injection, alglucosidase alfa, (lumizyme), 10 MG
ICD10 codes:	E74.02 Pompe Disease
ICD10 Not covered:	

POLICY HISTORY:

Status	Date	Action
New	05/14/25	New policy

REFERENCES:

The following scientific references were utilized in the formulation of this medical policy. BSWHP will continue to review clinical evidence related to this policy and may modify it at a later date based upon the evolution of the published clinical evidence. Should additional scientific studies become available, and they are not included in the list, please forward the reference(s) to BSWHP so the information can be reviewed by the Medical Coverage Policy Committee (MCPC) and the Quality Improvement Committee (QIC) to determine if a modification of the policy is in order.

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11. Schoser B, Roberts M, Byrne BJ, et al. Safety and efficacy of cipaglucosidase alfa plus miglustat versus alglucosidase alfa plus placebo in late-onset Pompe disease (PROPEL): an international, randomised, double-blind, parallel-group, phase 3 trial [published correction appears in Lancet Neurol. 2023 Oct;22(10):e11. doi: 10.1016/S1474-4422(23)00311-3.]. Lancet Neurol. 2021;20(12):1027-1037. doi:10.1016/S1474-4422(21)00331-8
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***Note**:*
Health Maintenance Organization (HMO) products are offered through Scott and White Health Plan dba Baylor Scott & White Health Plan, and Scott & White Care Plans dba Baylor Scott & White Care Plan. Insured PPO and EPO products are offered through Baylor Scott & White Insurance Company. Scott and White Health Plan dba Baylor Scott & White Health Plan serves as a third-party administrator for self-funded employer-sponsored plans. Baylor Scott & White Care Plan and Baylor Scott & White Insurance Company are wholly owned subsidiaries of Scott and White Health Plan. These companies are referred to collectively in this document as Baylor Scott & White Health Plan.

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RightCare STAR Medicaid is offered through Scott and White Health Plan in the Central Texas Medicaid Rural Service Area (MRSA); FirstCare STAR is offered through SHA LLC dba FirstCare Health Plans (FirstCare) in the Lubbock and West MRSAs; and FirstCare CHIP is offered through FirstCare in the Lubbock Service Area.