



Lumizyme[®]

(alglucosidase alfa)

Pocket Guide for Treatment

Please see Important Safety Information on page 2 and accompanying Full Prescribing Information, including boxed WARNING.

sanofi

Indication and Important Safety Information

INDICATION

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

IMPORTANT SAFETY INFORMATION

WARNING: HYPERSENSITIVITY REACTIONS INCLUDING ANAPHYLAXIS, IMMUNE-MEDIATED REACTIONS, AND RISK OF ACUTE CARDIORESPIRATORY FAILURE

Hypersensitivity Reactions Including Anaphylaxis

Patients treated with enzyme replacement therapies have experienced life-threatening hypersensitivity reactions, including anaphylaxis. Anaphylaxis has occurred during the early course of enzyme replacement therapy and after extended duration of therapy. Initiate LUMIZYME in a healthcare setting with appropriate medical monitoring and support measures, including cardiopulmonary resuscitation equipment. If a severe hypersensitivity reaction (e.g. anaphylaxis) occurs, discontinue LUMIZYME immediately and initiate appropriate medical treatment, including the use of epinephrine.

Consider risks and benefits of re-administering LUMIZYME following severe hypersensitivity reactions. If a mild or moderate hypersensitivity reaction occurs, the infusion rate may be slowed or temporarily stopped. Prior to LUMIZYME administration, consider pretreating with antihistamines, antipyretics, and/or corticosteroids.

Immune-Mediated Reactions

Immune-mediated reactions presenting as proteinuria, nephrotic syndrome, and necrotizing skin lesions have occurred in some patients following LUMIZYME treatment. Monitor patients for the development of systemic immune-mediated reactions involving skin and other organs while receiving LUMIZYME.

Risk of Acute Cardiorespiratory Failure

Infantile-onset Pompe disease (IOPD) patients with compromised cardiac or respiratory function may be at risk of serious acute exacerbation of their cardiac or respiratory compromise due to fluid overload and require additional monitoring.

WARNINGS AND PRECAUTIONS

Infusion Associated Reactions (IARs): Infusion Associated Reactions (IARs) have been observed in patients treated with Lumizyme. Discontinue immediately or adjust the infusion rate and provide medical treatment based on the severity of the reaction. Closely monitor patients who have experienced IARs when re-administering LUMIZYME.

Risk of Cardiac Arrhythmia and Sudden Cardiac Death during General Anesthesia for Central Venous Catheter Placement: Caution should be used when administering general anesthesia for the placement of a central venous catheter intended for LUMIZYME infusion.

Risk of Developing Anti-alglucosidase Alfa Antibodies (ADA): Patients with IOPD should have a cross-reactive immunologic material (CRIM) assessment early in their disease course and be managed by a specialist knowledgeable in immune tolerance induction in Pompe disease to optimize treatment. Evidence suggests that patients who develop high and sustained IgG ADA antibody titers may experience reduced clinical efficacy.

Patients should be monitored for IgG ADA antibody formation beginning at baseline, then regularly during the first year of treatment with subsequent monitoring as clinically warranted. Patients who experience hypersensitivity reactions, including anaphylaxis, may also be tested for IgE antibodies to LUMIZYME and other mediators of anaphylaxis.

ADVERSE REACTIONS

The most frequently reported adverse reactions ($\geq 5\%$) in clinical trials were hypersensitivity reactions and included: anaphylaxis, rash, pyrexia, flushing/feeling hot, urticaria, headache, hyperhidrosis, nausea, cough, decreased oxygen saturation, tachycardia, tachypnea, chest discomfort, dizziness, muscle twitching, agitation, cyanosis, erythema, hypertension/increased blood pressure, pallor, rigors, tremor, vomiting, fatigue, and myalgia.



In this reference guide, you'll find important information on Lumizyme® (alglucosidase alfa) treatment, including the following resources:

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Sample Physician Order

It is recommended that the following information, at a minimum, be included in the physician order to the pharmacy and infusion staff.

Sample Physician Order for Lumizyme® (alglucosidase alfa)

Patient Name: _____ Diagnosis: _____

Date of Birth: _____ Patient Weight (kg): _____

Today's Date: _____

Notify Dr. _____ at Pager _____ when patient arrives.

Obtain vital signs and pulse oximetry. If any vital signs are not within specified ranges, wait _____ minutes and repeat. If vital signs continue to be outside the range, page Dr. _____.

1. Obtain and record patient weight (kg) above.
2. Obtain vital signs immediately prior to infusion.
3. Prior to infusion, consider pretreating with antihistamines, antipyretics, and/or corticosteroids
4. Prepare 20 mg/kg alglucosidase alfa in 0.9% Sodium Chloride for Injection, USP to a total volume of _____ mL.

5. Using an infusion pump, administer intravenously in a stepwise manner. Use a 0.2 µm in-line, low protein-binding filter.

Begin the infusion at rate of 1 mg/kg/hr (_____ mL/hr) and administer for at least 30 minutes.

Obtain vital signs and if stable...

Increase the infusion rate to 3 mg/kg/hr (_____ mL/hr) and administer for at least 30 minutes.

Obtain vital signs and if stable...

Increase the infusion rate to 5 mg/kg/hr (_____ mL/hr) and administer for at least 30 minutes.

Obtain vital signs and if stable...

Increase the infusion rate to 7 mg/kg/hr (_____ mL/hr) and administer at this rate for the remainder of the infusion.

6. Flush infusion line per institution's protocol.

7. Obtain vital signs _____ hours after completion of the infusion.

Contact Dr. _____ in the event of a hypersensitivity reaction.

Physician's Signature: _____ MD

Pager Number: _____

Dosing and Infusion Rates

Alglucosidase alfa does not contain any preservatives. Vials are single-dose only. Discard any unused product.

The total volume of infusion is determined by the patient's body weight and should be administered over approximately 4 hours. Infusions should be administered in a stepwise manner using an infusion pump. The initial infusion rate should be no more than 1 mg/kg/hr. The infusion rate may be increased by 2 mg/kg/hr every 30 minutes, after patient tolerance to the infusion rate is established, until a maximum rate of 7 mg/kg/hr is reached. Vital signs should be obtained at the end of each step. If the patient is stable, alglucosidase alfa may be administered at the maximum rate of 7 mg/kg/hr until the infusion is completed. The infusion rate may be slowed or temporarily stopped in the event of mild to moderate hypersensitivity reactions. In the event of anaphylaxis or severe hypersensitivity reaction, immediately discontinue administration of alglucosidase alfa, and initiate appropriate medical treatment. See table below for the rate of infusion at each step, expressed as mL/hr based on the recommended infusion volume by patient weight.

If one or more doses are missed, restart LUMIZYME treatment as soon as possible, maintaining the 2-week interval between infusions thereafter.

See page 7 & 8, "Guidelines on the Management of Hypersensitivity Reactions," for information on managing hypersensitivity reactions.

Calculating the Dose

- Determine the number of vials to be reconstituted based on the individual patient's weight and the recommended dose of 20 mg/kg
- Patient weight (kg) x dose (mg/kg) = patient dose (in mg)
- Patient dose (in mg) divided by 50 mg/vial = number of vials to reconstitute. If the number of vials includes a fraction, round up to the next whole number

Example: Patient weight (68 kg) x dose (20 mg/kg) = patient dose (1,360 mg)
1,360 mg divided by 50 mg/vial = 27.2 vials; therefore, 28 vials should be reconstituted

- Remove the required number of vials from the refrigerator and allow them to reach room temperature prior to reconstitution (approximately 30 minutes)

RECOMMENDED INFUSION VOLUMES AND RATES					
Patient Weight Range (kg)	Total Infusion Volume (mL)	Step 1: 1 mg/kg/hr (mL/hr)	Step 2: 3 mg/kg/hr (mL/hr)	Step 3: 5 mg/kg/hr (mL/hr)	Step 4: 7 mg/kg/hr (mL/hr)
1.25–2.5	25	1.25	3.75	6.25	6.6
2.6–10	50	3	8	13	18
10.1–20	100	5	15	25	35
20.1–30	150	8	23	38	53
30.1–35	200	10	30	50	70
35.1–50	250	13	38	63	88
50.1–60	300	15	45	75	105
60.1–100	500	25	75	125	175
100.1–120	600	30	90	150	210
120.1–140	700	35	105	175	245
140.1–160	800	40	120	200	280
160.1–180	900	45	135	225	315
180.1–200	1,000	50	150	250	350

Administration Setting

Prior to LUMIZYME administration, consider pretreating with antihistamines, antipyretics, and/or corticosteroids. Because of the potential for severe hypersensitivity reactions, appropriate medical support measures, including cardiopulmonary resuscitation equipment, should be readily available when alglucosidase alfa is administered. Administration should be supervised by a healthcare provider knowledgeable in the management of hypersensitivity reactions including anaphylaxis.

Filter Recommendations

The reconstituted solution may occasionally contain some particles (typically less than 10 in a vial) in the form of thin white strands or translucent fibers. These particles have been shown to contain alglucosidase alfa and may appear after the initial reconstitution step and increase over time. Studies have shown that these particles are removed via in-line filtration without having a detectable effect on the purity or strength.



Okay to use



Clear and colorless.

Okay to use



Strands or fibers shown to contain alglucosidase alfa.

Do not use



Opaque particulate matter and discoloration.

Report any such vials to
 Sanofi Medical Information at
 1-800-745-4447, option 2 or
 1-617-768-9000, option 2.

Management of Hypersensitivity Reactions



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Immune-Mediated Reactions

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Risk of Acute Cardiorespiratory Failure

Infantile-onset Pompe disease (IOPD) patients with compromised cardiac or respiratory function may be at risk of serious acute exacerbation of their cardiac or respiratory compromise due to fluid overload and require additional monitoring.

Prior to LUMIZYME administration, consider pretreating with antihistamines, antipyretics, and/or corticosteroids. Appropriate medical support, including cardiopulmonary resuscitation equipment, should be readily available when LUMIZYME is administered.

If the patient experiences symptoms suggestive of a hypersensitivity reaction during the infusion of alglucosidase alfa, the patient should be managed according to general standards of care consistent with treatment of the reaction. This may include some or all of the following interventions, depending on the severity of the reaction:

- If anaphylaxis or severe hypersensitivity reactions occur, immediate discontinuation of the administration of alglucosidase alfa should be considered and appropriate medical treatment should be initiated
- Severe hypersensitivity reactions are generally managed with infusion interruption, administration of antihistamines, corticosteroids, intravenous fluids, and/or oxygen, when clinically indicated. In some cases of anaphylactic reactions, epinephrine was administered. Patients who have experienced hypersensitivity reactions should be treated with caution when they are re-administered alglucosidase alfa
- If a hypersensitivity reaction occurs, decreasing the infusion rate, temporarily stopping the infusion, and/or administration of antihistamines and/or antipyretics may ameliorate the symptoms

Continued on next page

Management of Hypersensitivity Reactions continued

The risks and benefits of re-administering alglucosidase alfa following an anaphylactic or severe hypersensitivity reaction should be considered. Some patients have been rechallenged and have continued to receive alglucosidase alfa under close clinical supervision. Extreme care should be exercised, with appropriate resuscitation measures available, if the decision is made to readminister the product.

Patients may be rechallenged using slower infusion rates at a dosage lower than the recommended dosage.

Patients who have experienced hypersensitivity reactions should be treated with caution when they are re-administered alglucosidase alfa.

In clinical trials, anaphylaxis and hypersensitivity reactions were managed with infusion interruption, decreased infusion rate, administration of antihistamines, corticosteroids, intravenous fluids, and/or oxygen, when clinically indicated. In some cases of anaphylactic reactions, epinephrine was administered. Patients who have experienced anaphylaxis or hypersensitivity reactions should be treated with caution when they are re-administered alglucosidase alfa.

Some patients who tested positive for alglucosidase alfa-specific IgE antibodies and experienced hypersensitivity reactions were able to be rechallenged with alglucosidase alfa using a slower infusion rate at lower starting doses and have continued to receive treatment under close clinical supervision. Since patients who develop IgE antibodies to alglucosidase alfa appear to be at a higher risk for developing anaphylaxis and hypersensitivity reactions, these patients should be monitored more closely during administration of alglucosidase alfa.

Risk of Developing Anti-alglucosidase Alfa Antibodies (ADA):

Patients with IOPD should have a cross-reactive immunologic material (CRIM) assessment early in their disease course. Immune tolerance induction administered prior to and in conjunction with initiation of alglucosidase alfa has been reported to aide tolerability of alglucosidase alfa in CRIM-negative patients. CRIM status has been shown to be associated with immunogenicity and patients' responses to enzyme replacement therapies.

In clinical studies, the majority of patients developed IgG antibodies to alglucosidase alfa, typically within 3 months of treatment. There is evidence to suggest that some patients who develop high and sustained IgG antibody titers, including CRIM-negative patients, may experience reduced clinical alglucosidase alfa treatment efficacy, such as loss of motor function, ventilator dependence, or death.

Antibody Testing

Patients should be monitored for IgG antibody formation every 3 months for 2 years and then annually thereafter. Testing for IgG titers may also be considered if patients develop hypersensitivity reactions, other immune-mediated reactions, or lose clinical response. Patients who experience reduced clinical response may also be tested for inhibitory antibody activity. Patients who experience anaphylactic or hypersensitivity reactions may also be tested for IgE antibodies to alglucosidase alfa and other mediators of anaphylaxis.

Testing services for antibodies against alglucosidase alfa are available through Sanofi. Contact Sanofi at 1-800-745-4447 for information on testing.

Notes

Spot Glue PI
2.125" x 2.875"

An Ongoing Commitment

For nearly 30 years, Sanofi has been committed to researching and developing treatments for people living with lysosomal storage disorders, such as Pompe disease. Providing comprehensive and confidential support services that address the unique needs of those living with Pompe disease is part of this ongoing commitment.

Sanofi
450 Water St.
Cambridge, MA 02142 USA

1-800-745-4447, option 2 or 1-617-768-9000, option 2

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MAT-US-2001800-v4.0-02/2025

The Sanofi logo, featuring the word "sanofi" in a bold, lowercase, sans-serif font. The letter "i" is stylized with a small dot above it.