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Lumizyme® (alglucosidase alfa)
1.16 Risk Evaluation and Mitigation Strategy (REMS)
Initial REMS Approval: 05/2010
Most Recent Modification: 07/2012

BLA 125291 LUMIZYME® (alglucosidase alfa)

Genzyme Corporation
500 Kendall Street, Cambridge MA 02142
1-800-745-4447

"LUMIZYME ACE Program®"

(Alglucosidase Alfa Control and Education)

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

1. GOALS

- To mitigate the potential risk of rapid disease progression in infantile-onset Pompe disease patients and patients with late (non-infantile) onset disease less than 8 years of age for whom the safety and effectiveness of Lumizyme have not been evaluated.

- To ensure that the known risks of anaphylaxis and severe allergic reactions associated with the use of Lumizyme are communicated to patients and prescribers, and to ensure that the potential risks of severe cutaneous and systemic immune mediated reactions to Lumizyme are communicated to patients and prescribers.

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2. REMS ELEMENTS

A. Communication Plan

Genzyme will implement a communication plan consisting of a Prescriber Introductory Letter and a Healthcare Professional Introductory Letter that will be distributed to neurologists, metabolic specialists, pulmonologists and geneticists, infusion nurses and pharmacists in hospitals and infusion.

The communication plan will provide for the dissemination of risk information about rapid disease in infantile-onset Pompe disease patients and patients with late (non-infantile) onset disease less than 8 years of age, anaphylaxis, severe allergic reactions and severe cutaneous and systemic immune mediated reactions to Lumizyme.

The introductory letters will be distributed by mail at launch.

Please see the appended introductory letters.

- Lumizyme Prescriber Introductory Letter
- Lumizyme Healthcare Professional Introductory Letter

B. Elements to Assure Safe Use

1. Healthcare providers who prescribe Lumizyme will be specially certified.

    a. Genzyme will ensure that healthcare professionals who prescribe Lumizyme are specially certified in the Lumizyme ACE Program. To become certified into the Lumizyme ACE Program, each healthcare professional must complete the training and enroll in the Lumizyme ACE Program by submitting a completed Prescriber Enrollment and Attestation Form attesting to the following:

        i. I have completed educational training about Lumizyme (alglucosidase alfa) and understand the risks and benefits of Lumizyme.

        ii. I understand that Lumizyme is indicated for patients 8 years and older with late (non-infantile) onset Pompe disease who do not have evidence of cardiac hypertrophy. The safety and efficacy of

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Lumizyme have not been evaluated in controlled clinical trials in infantile-onset patients or in late-onset disease patients less than 8 years of age.

iii. I understand that by completing the training program and signing this attestation form, I am now enrolled in the Lumizyme ACE Program and can prescribe and administer Lumizyme.

iv. I understand that I must enroll all patients being treated with Lumizyme into the Lumizyme ACE Program by completing a Patient Enrollment and Acknowledgement Form.

v. I understand that I am responsible for providing the Patient Enrollment and Acknowledgement Form to patients (or, as appropriate, their parents/guardians) and for obtaining their signature on the Patient Enrollment and Acknowledgement Form prior to initiating them on treatment with Lumizyme.

vi. I will advise patients and caregivers about the known (e.g., anaphylaxis and severe allergic reactions) and potential risks (e.g., severe cutaneous and systemic immune mediated reactions) associated with administration of Lumizyme and will review the risks and benefits of Lumizyme as per the product labeling.

vii. I understand that patients may experience anaphylaxis or severe allergic reactions to Lumizyme and I have access to appropriate medical support measures.

viii. I understand that I will be required to sign a Prescriber Enrollment and Attestation Form on an annual basis to maintain my enrollment in the Lumizyme ACE Program and to prescribe Lumizyme.

b. Genzyme will ensure healthcare professionals who intend to prescribe Lumizyme (alglucosidase alfa) receive training on the elements of the Lumizyme ACE Program via on-line training or on-site training (in-person). Upon completion of on-line training or on-site training, the healthcare professional will print a Prescriber Enrollment and

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Attestation Form, sign, and return it to Genzyme. This form is an acknowledgement that the prescriber received the training and that he/she attests to knowledge of the Lumizyme ACE Program and agrees to follow the procedures outlined in the program. Upon receipt of the signed form, Genzyme will maintain a validated and secure database of certified prescribers in the Lumizyme ACE Program.

c. Genzyme will ensure prescribers complete a Prescriber Enrollment and Attestation Form on an annual basis in order to remain enrolled in the Lumizyme ACE Program. Genzyme will send a letter to all enrolled prescribers when their enrollment is nearing expiration. Genzyme will require prescribers to re-enroll in the Lumizyme ACE Program by reviewing, signing and returning the Prescriber Enrollment and Attestation Form to Genzyme. Prescribers who do not complete the attestation form on an annual basis will be removed from the Lumizyme ACE Program. Educational materials listed below will be distributed by Genzyme to certified prescribers annually, as well as upon request of the prescribers.

The following materials are part of the REMS and are appended:

- Lumizyme ACE Program: Information for HCPs
- Lumizyme (alglucosidase alfa) and the Lumizyme ACE Program Training and Certification for HCPs
- Prescriber Enrollment and Attestation Form
- Patient Enrollment and Acknowledgement Form

2. Lumizyme will only be dispensed by healthcare facilities that are specially certified

   a. Genzyme will ensure that healthcare facilities that dispense Lumizyme are specially certified into the Lumizyme ACE program. To become certified into the Lumizyme ACE Program, healthcare facility representatives (director of pharmacy and/or infusion center

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representative [e.g., physician, head nurse, director of infusion center or director of education]) must enroll the healthcare facility in the Lumizyme ACE Program by submitting a completed Healthcare Facility Enrollment and Attestation Form attesting to the following:

i. The Lumizyme ACE Program educational materials have been received by the healthcare facility and provided to the healthcare facility staff who are responsible for the ordering, dispensing and administration of Lumizyme.

ii. Healthcare facility staff has completed training that includes:

- The procedure for ordering Lumizyme.
- Procedures for dispensing Lumizyme only after completing Section 1 of the Lumizyme Infusion Confirmation Form (Healthcare Professional Preparing Lumizyme Infusion).
    a. In rare events such as vial breakage, patient weight change impacting the current dose, or a rescheduled infusion where Lumizyme vials cannot be shipped to the facility in time, vials designated for a patient enrolled in the Lumizyme ACE Program can be used for another patient also enrolled in the Lumizyme ACE Program at the same healthcare facility. Prior to using these vials, the healthcare facility must contact Genzyme to review the details of the event and to order replacement vials.
- Procedures for administering Lumizyme only after verifying that the patient is enrolled in the Lumizyme ACE Program, completing Section 2 of the Lumizyme Infusion Confirmation Form (Healthcare Professional Administering Lumizyme Infusion Therapy), faxing the completed Lumizyme Infusion Confirmation Form to Genzyme and affixing the sticker

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section of the form to the patient's file or scanning the form and saving it in the patient's electronic medical record.

iii. The healthcare facility has system procedures and/or other measures in place for appropriate monitoring of patients for early recognition of anaphylaxis and severe allergic reactions.

iv. The healthcare facility has staff that is prepared to treat patients who experience anaphylaxis or severe allergic reactions to Lumizyme.

v. Healthcare facility staff understand that Lumizyme is indicated for patients 8 years and older with late (non-infantile) onset Pompe disease who do not have evidence of cardiac hypertrophy. The safety and efficacy of Lumizyme have not been evaluated in controlled clinical trials in infantile-onset patients or in late-onset disease patients less than 8 years of age.

vi. Healthcare facility staff will dispense and administer Lumizyme only after ensuring each patient receives his/her designated drug by completing the Lumizyme Infusion Confirmation Form.

vii. The healthcare facility understands that Genzyme may periodically perform audits at this healthcare facility to verify compliance with the procedures detailed in the Lumizyme ACE Program.

b. Healthcare facilities that intend to dispense or administer Lumizyme will receive training via on-line training or in-person. In an emergency situation where REMS training has not occurred, Genzyme will conduct training over the phone and will follow up with an in-person visit. The representative at each healthcare facility where Lumizyme is administered will be provided with educational materials and instructions on how to access the on-line training program.

c. The healthcare facility will be required to sign a Healthcare Facility Enrollment and Attestation Form on an annual basis to maintain enrollment in the Lumizyme ACE Program and to dispense and

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administer Lumizyme. Genzyme will send a letter to all enrolled healthcare facilities when their enrollment is nearing expiration. The healthcare facility will be required to re-enroll in the Lumizyme ACE Program by reviewing, signing and returning the Healthcare Facility Enrollment and Attestation Form to Genzyme. Healthcare facilities that do not complete the attestation form on an annual basis will be removed from the Lumizyme ACE Program. In addition, the educational materials listed below will be distributed by Genzyme to certified healthcare facilities annually and upon the request of the healthcare professional or healthcare facility.

The following materials are part of the REMS and are appended:

- Lumizyme ACE Program: Information for HCPs
- Lumizyme (alglucosidase alfa) and the Lumizyme ACE Program Training and Certification for HCPs
- Healthcare Facility Enrollment and Attestation Form
- Lumizyme Infusion Confirmation Form

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3. Lumizyme will be dispensed to patients with evidence or other documentation of safe-use conditions. Genzyme will ensure that each patient treated with Lumizyme is enrolled in the Lumizyme ACE Program.

    a. Prior to initiating treatment, each patient or patient guardian will sign a Patient Enrollment and Acknowledgment Form to enroll in the Lumizyme ACE Program and receive the product. Patient enrollment requires the patient to attest to the following:

        - My doctor/prescriber (or my child's doctor/prescriber) has provided me with information about the benefits and risks of Lumizyme (alglucosidase alfa) treatment and the Lumizyme ACE Program.
        - I have asked my doctor/prescriber (or my child's doctor/prescriber) any questions I may have about Lumizyme.
        - My doctor/prescriber (or my child's doctor/prescriber) has counseled me on the safety information in the product labeling for Lumizyme. I understand the risks of Lumizyme treatment including life-threatening or severe allergic reactions, and severe skin and systemic immune mediated reactions associated with the use of Lumizyme.

    b. Upon enrollment, patients will be given a signed copy of the Patient Enrollment and Acknowledgement Form by their prescriber. The prescriber will return the form to Genzyme. The prescriber will also place a copy of the form in the patient's file or scan the form and save it in the patient's electronic medical record. Genzyme will maintain a validated and secure database of patients enrolled in the Lumizyme ACE Program. Genzyme will ensure that certified healthcare facilities will dispense and administer Lumizyme only after verifying the patient is enrolled in the Lumizyme ACE Program.

    c. To ensure that each patient has received his/her designated drug, Genzyme will ensure that certified healthcare facilities complete the Lumizyme

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Infusion Confirmation Form after each patient has received his/her designated drug.

d. The healthcare facility will fax the completed Lumizyme Infusion Confirmation Form to Genzyme and affix the sticker section of the form to the patient's file or scan the form and save it in the patient's electronic medical record.

The following materials are part of the REMS and are appended:

- Patient Enrollment and Acknowledgement Form
- Lumizyme Infusion Confirmation Form

C. Implementation System

The Implementation System includes the following:

1. Genzyme will maintain a validated and secure database of certified prescribers and healthcare facilities and of patients enrolled in the Lumizyme ACE Program.
2. Genzyme will monitor re-enrollment of certified participants and take appropriate corrective actions if they do not re-enroll.
3. Genzyme will monitor certified healthcare facilities and certified HCPs to ensure that only enrolled patients are receiving Lumizyme.
4. Genzyme will monitor use of Lumizyme:
   - in patients with late (non-infantile) onset Pompe disease, ages 8 years and older, who do not have evidence of cardiac hypertrophy.
   - in infantile-onset patients of any age or late-onset disease patients less than 8 years of age.
5. Genzyme will monitor the distribution of Lumizyme by Genzyme directly or any certified distributor to determine whether the product is only distributed to certified healthcare facilities and certified HCPs that dispense or administer the product and whether a signed Prescriber Enrollment and Attestation Form, Patient Enrollment

and Acknowledgement Form, and Healthcare Facility Enrollment and Attestation Form are on file for the intended shipping location.

6. If a preferred distributor is used, Genzyme will certify preferred Lumizyme distributors by contractual arrangement to ensure they will distribute Lumizyme according to the ACE Program. To be certified distributors must agree to:

   - Confirm appropriate prescribing by referencing the list of enrolled patients and certified prescribers provided by Genzyme or by calling Genzyme.
   - Shipping Lumizyme on a named-patient basis to minimize the risk for confusion with Myozyme® (alglucosidase alfa). Each shipment will include a Lumizyme Infusion Confirmation Form which must be completed by healthcare facility staff who dispense and administer Lumizyme.

7. Genzyme will monitor to determine whether for each infusion, the Lumizyme Infusion Confirmation Form is received by Genzyme.

8. Genzyme will monitor to determine whether the sticker portion of the Lumizyme Infusion Confirmation Form is affixed to the patient's file or a copy of the form has been saved in the patient's electronic medical record.

9. Genzyme will monitor to determine whether there is confusion between Lumizyme and Myozyme.

10. Genzyme will monitor and evaluate the implementation of these elements to assure safe use and Genzyme will take reasonable steps to work to improve implementation of these elements.

D. Timetable for Submission of Assessments

Genzyme will submit REMS Assessments to FDA at 6 months and 1 year from the date of approval of the REMS (May 24, 2010), then annually thereafter. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Genzyme will submit each assessment so it will be received by the FDA on or before the due date.

[To be printed on Genzyme letterhead]
<<Date>>

<<Prescriber Name>>
<<Address>>
<<Address>>

Dear Dr. <<Name>>:

Genzyme is introducing Lumizyme® (alglucosidase alfa) and the Lumizyme ACE (Alglucosidase Alfa Control and Education) Program. Lumizyme was approved in the US on MM-DD-YYYY.

Lumizyme is a lysosomal glycogen-specific enzyme indicated for patients 8 years and older with late (non-infantile) onset Pompe disease [acid α-glucosidase (GAA) deficiency] who do not have evidence of cardiac hypertrophy. The safety and efficacy of Lumizyme have not been evaluated in controlled clinical trials in infantile-onset patients, or in late (non-infantile) onset patients less than 8 years of age.

The product labeling includes a **boxed warning** that includes the following information:

WARNING: ANAPHYLAXIS and RESTRICTED DISTRIBUTION PROGRAM

Life-threatening anaphylactic reactions, severe allergic reactions and immune mediated reactions have been observed in some patients during LUMIZYME infusions. Therefore, appropriate medical support should be readily available when LUMIZYME is administered.

Because of the potential risk of rapid disease progression in Pompe disease patients less than 8 years of age, LUMIZYME is available only through a restricted distribution program called the LUMIZYME ACE Program. Only prescribers and healthcare facilities enrolled in the program may prescribe, dispense, or administer LUMIZYME. LUMIZYME may be administered only to patients who are enrolled in and meet all the conditions of the LUMIZYME ACE Program. To enroll in the LUMIZYME ACE Program call 1-800-745-4447.

Anaphylaxis and severe allergic reactions have been observed in patients during and up to 3 hours after Lumizyme infusion. Some reactions were life-threatening and included anaphylactic shock, respiratory arrest, apnea, dyspnea, bradycardia, tachycardia, and hypotension. Other accompanying reactions included chest discomfort/pain, throat tightness, bronchospasm, wheezing, tachypnea, cyanosis, decreased oxygen saturation/hypoxia, convulsions, angioedema (including tongue or lip swelling, periorbital edema, and face edema), pruritus, rash, urticaria, hyperhidrosis, nausea, dizziness, hypertension, flushing/erythema, fever, pallor, peripheral coldness, feeling hot, restlessness, nervousness, headache, back pain, and paraesthesia. Some of these reactions were IgE-mediated.

If severe allergic or anaphylactic reactions occur, immediate discontinuation of the administration of Lumizyme should be considered and appropriate medical treatment should be initiated.

Severe cutaneous reactions have been reported with Lumizyme including necrotizing skin lesions. Systemic immune mediated reactions, including possible type III immune mediated reactions have been observed with alglucosidase alfa. These reactions occurred several weeks to 3 years after initiation of alglucosidase alfa infusions. Patients should be monitored for the development of systemic immune mediated reactions involving skin and other organs while receiving Lumizyme.

Adverse events should be reported promptly to Genzyme Medical Information at **1-800-745-4447, option 2**. Please see enclosed Full Prescribing Information, including Boxed Warning.

There are two available enzyme replacement therapies for Pompe disease in the US, Lumizyme and Myozyme® (alglucosidase alfa). Lumizyme and Myozyme are two different products. Lumizyme cannot be substituted for Myozyme. Lumizyme has only been studied and shown to be safe and effective in the late (non-infantile) onset population. Lumizyme should only be used in patients 8 years of age and older with late (non-infantile) onset Pompe disease who do not have evidence of cardiac hypertrophy. Lumizyme is not for use in patients with infantile-onset disease of any age or late-onset Pompe disease who are less than 8 years of age.

Lumizyme is available only under a restricted distribution program called the Lumizyme ACE Program. The Lumizyme ACE Program has been implemented to:

- Mitigate the potential risk of rapid disease progression in infantile-onset Pompe disease patients and patients with late (non-infantile) onset disease less than 8 years of age for whom the safety and effectiveness of Lumizyme have not been evaluated.
- Ensure that the known risks of anaphylaxis and severe allergic reactions associated with the use of Lumizyme are communicated to patients and prescribers and to ensure that the potential risks of severe cutaneous and systemic immune mediated reactions to Lumizyme are communicated to patients and prescribers.

The Lumizyme ACE Program is mandatory and requires your full participation if you intend to prescribe, dispense or administer Lumizyme.

Under the Lumizyme ACE Program, Lumizyme may be prescribed, dispensed and administered only by certified healthcare professionals and healthcare facilities. In order to become certified, healthcare professionals and healthcare facilities must enroll in the Lumizyme ACE Program following the completion of an online certification program. Patients must also be enrolled in the program by the treating prescriber. Lumizyme can only be prescribed and administered by healthcare professionals and healthcare facilities enrolled in the Lumizyme ACE Program and dispensed only to patients also enrolled in the program. To complete the certification process, please visit the link below.

www.lumizyme.com/ACE

As a prescriber, to enroll in the program, you must:

1) Complete the **online training program** available at www.lumizyme.com/ACE (on-site training is available – please call 1-800-745-4447, option 2, to make the request); and

2) **Enroll yourself.** Complete a **Prescriber Enrollment and Attestation Form** (available for download from the online training program) certifying that you have completed the required training and agree to follow the procedures outlined in the Lumizyme ACE Program, which are explained in the training; and

3) **Enroll your patients.** Review the risks and benefits of Lumizyme with all patients who will receive treatment, then return a completed and signed **Patient Enrollment and Acknowledgment Form** for each patient who will receive Lumizyme. Note that the Patient Enrollment and Acknowledgment Form contains information to be completed by both the physician and patient; and

4) Fax the completed and signed forms to Genzyme at **1-888-378-7667**.

Lumizyme is available directly through Genzyme or its distributors. Lumizyme will be shipped only upon verification that the healthcare professional and healthcare facility have completed the online training program, and that patients to whom Lumizyme will be prescribed have been enrolled. Genzyme's hours

of operation are Monday – Friday 8:00 am – 6:00 pm (EST). Call Genzyme Patient and Product Services at **1-800-745-4447, option 1 or 617-768-9000** for more information on ordering Lumizyme.

Genzyme Patient and Product Services offers comprehensive support services, including information and assistance on reimbursement issues. Call **1-800-745-4447, option 3 or 617-768-9000** for more information.

Please contact Genzyme Medical Information at **1-800-745-4447, option 2** with any additional questions you may have.

Sincerely,

John Yee, MD, MPH
Vice President, Global Medical Affairs

Enclosures

LZ-US-P005-06-12

[To be printed on Genzyme letterhead]
<<Date>>

<< Name>>
<<Address>>
<<Address>>

Dear Healthcare Professional:

Genzyme is introducing Lumizyme® (alglucosidase alfa) and the Lumizyme ACE (Alglucosidase Alfa Control and Education) Program. Lumizyme was approved in the US on MM-DD-YYYY.

Lumizyme is a lysosomal glycogen-specific enzyme indicated for patients 8 years and older with late (non-infantile) onset Pompe disease [acid α-glucosidase (GAA) deficiency] who do not have evidence of cardiac hypertrophy. The safety and efficacy of Lumizyme have not been evaluated in controlled clinical trials in infantile-onset patients, or in late (non-infantile) onset patients less than 8 years of age.

The product labeling includes a **boxed warning** that includes the following information:

WARNING: ANAPHYLAXIS and RESTRICTED DISTRIBUTION PROGRAM

Life-threatening anaphylactic reactions, severe allergic reactions and immune mediated reactions have been observed in some patients during LUMIZYME infusions. Therefore, appropriate medical support should be readily available when LUMIZYME is administered.

Because of the potential risk of rapid disease progression in Pompe disease patients less than 8 years of age, LUMIZYME is available only through a restricted distribution program called the LUMIZYME ACE Program. Only prescribers and healthcare facilities enrolled in the program may prescribe, dispense, or administer LUMIZYME. LUMIZYME may be administered only to patients who are enrolled in and meet all the conditions of the LUMIZYME ACE Program. To enroll in the LUMIZYME ACE Program call 1-800-745-4447.

Anaphylaxis and severe allergic reactions have been observed in patients during and up to 3 hours after Lumizyme infusion. Some reactions were life-threatening and included anaphylactic shock, respiratory arrest, apnea, dyspnea, bradycardia, tachycardia, and hypotension. Other accompanying reactions included chest discomfort/pain, throat tightness, bronchospasm, wheezing, tachypnea, cyanosis, decreased oxygen saturation/hypoxia, convulsions, angioedema (including tongue or lip swelling, periorbital edema, and face edema), pruritus, rash, urticaria, hyperhidrosis, nausea, dizziness, hypertension, flushing/erythema, fever, pallor, peripheral coldness, feeling hot, restlessness, nervousness, headache, back pain, and paraesthesia. Some of these reactions were IgE-mediated.

If severe allergic or anaphylactic reactions occur, immediate discontinuation of the administration of Lumizyme should be considered and appropriate medical treatment should be initiated.

Severe cutaneous reactions have been reported with Lumizyme including necrotizing skin lesions. Systemic immune mediated reactions, including possible type III immune mediated reactions have been observed with alglucosidase alfa. These reactions occurred several weeks to 3 years after initiation of alglucosidase alfa infusions. Patients should be monitored for the development of systemic immune mediated reactions involving skin and other organs while receiving Lumizyme.

Adverse events should be reported promptly to Genzyme Medical Information at **1-800-745-4447, option 2**. Please see enclosed Full Prescribing Information, including Boxed Warning.

There are two available enzyme replacement therapies for Pompe disease in the US, Lumizyme and Myozyme® (alglucosidase alfa). Lumizyme and Myozyme are two different products. Lumizyme cannot be substituted for Myozyme. Lumizyme has only been studied and shown to be safe and effective in the late (non-infantile) onset population. Lumizyme should only be used in patients 8 years of age and older with late (non-infantile) onset Pompe disease who do not have evidence of cardiac hypertrophy. Lumizyme is not for use in patients with infantile-onset disease of any age or late-onset Pompe disease who are less than 8 years of age.

Lumizyme is available only under a restricted distribution program called the Lumizyme ACE Program. The Lumizyme ACE Program has been implemented to:

- Mitigate the potential risk of rapid disease progression in infantile-onset Pompe disease patients and patients with late (non-infantile) onset disease less than 8 years of age for whom the safety and effectiveness of Lumizyme have not been evaluated.
- Ensure that the known risks of anaphylaxis and severe allergic reactions associated with the use of Lumizyme are communicated to patients and prescribers and to ensure that the potential risks of severe cutaneous and systemic immune mediated reactions to Lumizyme are communicated to patients and prescribers.

The Lumizyme ACE Program is mandatory and requires your full participation if you intend to dispense or administer Lumizyme.

Under the Lumizyme ACE Program, Lumizyme may be prescribed, dispensed and administered only by certified healthcare professionals and healthcare facilities. In order to become certified, healthcare professionals and healthcare facilities must enroll in the Lumizyme ACE Program following the completion of an online certification program. Patients must also be enrolled in the program by the treating prescriber. Lumizyme can only be prescribed and administered by healthcare professionals and healthcare facilities enrolled in the Lumizyme ACE Program and dispensed only to patients also enrolled in the program. To complete the certification process, please visit the link below.

www.lumizyme.com/ACE

As a healthcare facility, to enroll in the program, you must:

1) Have an authorized representative (e.g. director of pharmacy and/or infusion center representative such as physician, head nurse, director of infusion center or director of education) complete the **online training program** available at www.lumizyme.com/ACE (on-site training is available – please call 1-800-745-4447, option 2, to make the request); and

2) Complete a **Healthcare Facility Enrollment and Attestation Form** (available for download from the online training program) certifying that you have completed the required training and agree to follow the procedures outlined in the Lumizyme ACE Program, which are explained in the training; and

3) Fax the completed and signed form to Genzyme at **1-888-378-7667.**

Lumizyme is available directly through Genzyme or its distributors. Lumizyme will be shipped only upon verification that the healthcare professional and healthcare facility have completed the online training program, and that patients to whom Lumizyme will be prescribed have been enrolled. Genzyme's hours of operation are Monday – Friday 8:00 am – 6:00 pm (EST). Call Genzyme Patient and Product Services at **1-800-745-4447, option 1 or 617-768-9000** for more information on ordering Lumizyme.

Genzyme Patient and Product Services offers comprehensive support services, including information and assistance on reimbursement issues. Call **1-800-745-4447, option 3 or 617-768-9000** for more information.

Please contact Genzyme Medical Information at **1-800-745-4447, option 2** with any additional questions you may have.

Sincerely,

John Yee, MD, MPH
Vice President, Global Medical Affairs

Enclosures

LZ-US-P008-06-12

Lumizyme ACE Program

(Alglucosidase Alfa Control and Education)

Lumizyme ACE Program:
Information for healthcare professionals

What is the Lumizyme ACE Program?

The Lumizyme ACE Program is a risk evaluation and mitigation strategy designed to:

- Mitigate the potential risk of rapid disease progression in infantile-onset Pompe disease patients and patients with late (non-infantile) onset disease less than 8 years of age for whom the safety and effectiveness of Lumizyme® (alglucosidase alfa) have not been evaluated.

- Ensure that the known risks of anaphylaxis and severe allergic reactions associated with the use of Lumizyme are communicated to patients and prescribers and to ensure that the potential risks of severe cutaneous and systemic immune mediated reactions to Lumizyme are communicated to patients and prescribers.

Lumizyme® (alglucosidase alfa)

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A SANOFI COMPANY

Reference ID: 3159304

Why is the Lumizyme ACE Program necessary?

Lumizyme is only for use in patients 8 years and older, with late (non-infantile) onset Pompe disease who do not have evidence of cardiac hypertrophy.

There are two available enzyme replacement therapies for Pompe disease, Lumizyme and Myozyme® (alglucosidase alfa). Lumizyme and Myozyme are two different products. Lumizyme cannot be substituted for Myozyme.

Enrollment in the Lumizyme ACE Program is required to ensure that Lumizyme is administered to the intended patient population.

What are the requirements of the Lumizyme ACE Program?

All prescribers of Lumizyme, healthcare professionals and healthcare facilities where Lumizyme will be dispensed and administered, and patients who will receive treatment with Lumizyme are required to enroll in the Lumizyme ACE Program.

- For prescribers, healthcare professionals and healthcare facilities, enrolling in the Lumizyme ACE Program involves completing an online training and certification program and returning a completed and signed attestation form to Genzyme.
- Prescribers must also return a completed and signed Patient Enrollment and Acknowledgement Form for each patient who will receive treatment with Lumizyme. This form contains information to be completed by both the patient and prescriber.
- A completed Lumizyme Infusion Confirmation Form is required for each patient after each infusion to confirm that Lumizyme was administered to the intended patient. The completed form must be returned to Genzyme via fax.
  - The Lumizyme Infusion Confirmation Form is included with the product shipment.
  - The form includes sections to be completed by both the person responsible for preparing the infusion and the person who administers the Lumizyme infusion.
  - Request additional copies of the Lumizyme Infusion Confirmation Form by contacting Genzyme at 800-745-4447, option 1.

To complete the enrollment process for the Lumizyme ACE Program and authorize product for shipment, the following forms must be signed and returned to Genzyme:

- Prescriber Enrollment and Attestation Form
- Patient Enrollment and Acknowledgement Form
- Healthcare Facility Enrollment and Attestation Form

Please see the tables on page 3 for Instructions for Enrollment.

The Lumizyme ACE Program is mandatory and requires your full participation if you intend to prescribe and administer Lumizyme.

How do I receive training?

- Prescribers and representatives of the healthcare facilities can access the online training program at www.lumizyme.com/ACE.
- On-site training is available upon request by contacting Genzyme Medical Information at 800-745-4447, option 2.

Instructions for Enrollment: Prescribers

If you are a prescriber:

1) Complete the **online training program** available at **www.lumizyme.com/ACE** (on-site training is available – please call 800-745-4447, option 2, to make the request).
2) **Enroll yourself.** Complete a **Prescriber Enrollment and Attestation Form** (available for download from the online training program) certifying that you have completed the required training and agree to follow the procedures outlined in the Lumizyme ACE Program, which are explained in the training.
3) **Enroll your patients.** Review the risks and benefits of Lumizyme with all patients who will receive treatment, then return a completed and signed **Patient Enrollment and Acknowledgement Form** for each patient who will receive Lumizyme.
   - Note that the Patient Enrollment and Acknowledgement Form contains information to be completed by both the physician and patient.
   - Provide the patient a copy of the Patient Enrollment and Acknowledgement Form and maintain a copy in the patient's file.
   - Note that once the patient is enrolled, a healthcare professional at the infusion site should verify that the patient enrollment form is on file and check the patient's identification prior to each infusion of Lumizyme.
4) Complete the Prescriber Enrollment and Attestation Form online or fax the completed and signed form to Genzyme at 888-378-7667.
5) Fax the completed and signed Patient Enrollment and Acknowledgement Form to Genzyme at 888-378-7667. Note that patient enrollment is not available online.
6) You will receive a confirmation notice when the forms are received.
7) You are required to re-enroll in the Lumizyme ACE Program annually. A reminder will be sent 60 days prior to the re-enrollment deadline.

Instructions for Enrollment: Healthcare Facilities

If you are a healthcare facility:

1) An authorized representative (e.g. director of pharmacy and/or infusion center representative such as physician, head nurse, director of infusion center or director of education) must complete the **online training program** available at **www.lumizyme.com/ACE** (on-site training is available – please call 800-745-4447, option 2, to make the request).
   - The healthcare facility representative is responsible for training all staff at the site who will be involved with ordering, dispensing and administering Lumizyme.
2) Complete the **Healthcare Facility Enrollment and Attestation Form** (available for download from the online training program) certifying that you have completed the required training and agree to follow the procedures outlined in the Lumizyme ACE Program, which are explained in the training.
3) Complete the Healthcare Facility Enrollment and Attestation Form online or fax the completed and signed form to Genzyme at 888-378-7667.
4) You will receive a confirmation notice when the attestation form is received.
5) You are required to re-enroll in the Lumizyme ACE Program annually. A reminder will be sent 60 days prior to the re-enrollment deadline.

Indication

Lumizyme (alglucosidase alfa) is a lysosomal glycogen-specific enzyme indicated for patients 8 years and older with late (non-infantile) onset Pompe disease [acid α-glucosidase (GAA) deficiency] who do not have evidence of cardiac hypertrophy. The safety and efficacy of Lumizyme have not been evaluated in controlled clinical trials in infantile-onset patients, or in late (non-infantile) onset patients less than 8 years of age.

WARNING: ANAPHYLAXIS and RESTRICTED DISTRIBUTION PROGRAM

Life-threatening anaphylactic reactions, severe allergic reactions and immune mediated reactions have been observed in some patients during LUMIZYME infusions. Therefore, appropriate medical support should be readily available when LUMIZYME is administered.

Because of the potential risk of rapid disease progression in Pompe disease patients less than 8 years of age, LUMIZYME is available only through a restricted distribution program called the LUMIZYME ACE Program. Only prescribers and healthcare facilities enrolled in the program may prescribe, dispense, or administer LUMIZYME. LUMIZYME may be administered only to patients who are enrolled in and meet all the conditions of the LUMIZYME ACE Program. To enroll in the LUMIZYME ACE Program call 1-800-745-4447.

For complete safety information, see accompanying Full Prescribing Information, including Boxed Warning, below.

To enroll in the Lumizyme ACE Program, visit www.lumizyme.com/ACE

Genzyme Corporation
500 Kendall Street
Cambridge, MA 02142
800-745-4447 (option 2)
or 617-768-9000 (option 2)
Monday – Friday 8:00 am – 6:00 pm EST
medinfo@genzyme.com

Affix PI here

genzyme
A SANOFI COMPANY

Lumizyme®
(alglucosidase alfa)

Prescriber Enrollment and Attestation Form

☐ Initial Enrollment ☐ Re-Enrollment

Prescriber Contact Information			
	Name/Degree (first, middle, last)		NPI#
	Street Address		
	City	State	Zip Code
	Phone	Fax	E-mail address
	Name of Institution or Healthcare Facility		
	Street Address (if different than above)		
	City	State	Zip Code
	Phone	Fax	E-mail address

The Lumizyme ACE (alglucosidase alfa control and education) Program® is designed to:

- Mitigate the potential risk of rapid disease progression in infantile-onset Pompe disease patients and patients with late (non-infantile) disease less than 8 years of age for whom the safety and effectiveness of Lumizyme® (alglucosidase alfa) have not been evaluated.
- Ensure that the known risks of anaphylaxis and severe allergic reactions associated with the use of Lumizyme are communicated to patients and prescribers and to ensure that the potential risks of severe cutaneous and systemic immune mediated reactions to Lumizyme are communicated to patients and prescribers.

Prescriber Attestation

- I have completed educational training about Lumizyme (alglucosidase alfa) and understand the risks and benefits of Lumizyme.
- I understand that Lumizyme is indicated for patients 8 years and older with late (non-infantile) onset Pompe disease who do not have evidence of cardiac hypertrophy. The safety and efficacy of Lumizyme have not been evaluated in controlled clinical trials in infantile-onset patients, or in late-onset patients less than 8 years of age.
- I understand that by completing the training program and signing this attestation form, I am now enrolled in the Lumizyme ACE Program and can prescribe and administer Lumizyme.
- I understand that I must enroll all patients being treated with Lumizyme into the Lumizyme ACE Program by completing a Patient Enrollment and Acknowledgement Form.
- I understand that I am responsible for providing the Patient Enrollment and Acknowledgement Form to patients (or, as appropriate, their parents/guardians) and for obtaining their signature on the Patient Enrollment and Acknowledgement Form prior to initiating them on treatment with Lumizyme.
- I will advise patients and caregivers about the known (e.g., anaphylaxis and severe allergic reactions) and potential risks (e.g., severe cutaneous and systemic immune mediated reactions) associated with administration of Lumizyme and will review the risks and benefits of Lumizyme as per the product labeling.
- I understand that patients may experience anaphylaxis or severe allergic reactions to Lumizyme and I have access to appropriate medical support measures.
- I understand that I will be required to sign a Prescriber Enrollment and Attestation Form on an annual basis to maintain my enrollment in the Lumizyme ACE Program and to prescribe Lumizyme.

Prescriber's Signature: _____ Date: _____

Printed Name: _____

Adverse events should be reported promptly to Genzyme Medical Information at 800-745-4447, option 2.

Complete the Prescriber Enrollment and Attestation Form online or fax the completed and signed form to Genzyme at 888-378-7667.

Healthcare Facility Enrollment and Attestation Form

Enrollment in the Lumizyme ACE Program® permits healthcare facilities to order and dispense Lumizyme®.

❒ Initial Enrollment ❒ Re-Enrollment

Healthcare Facility Contact Information			
	Name of Institution or Healthcare Facility		NPI#
	Institution or Healthcare Facility Address		
	City	State	Zip Code
	Phone	Fax	E-mail address
	Name of Healthcare Facility Representative		Job Title*

** For example: director of pharmacy and/or infusion center representative such as physician, head nurse, director of infusion center or director of education.*

The Lumizyme ACE (alglucosidase alfa control and education) Program is designed to:

- Mitigate the potential risk of rapid disease progression in infantile-onset Pompe disease patients and patients with late (non-infantile) disease less than 8 years of age for whom the safety and effectiveness of Lumizyme have not been evaluated.
- Ensure that the known risks of anaphylaxis and severe allergic reactions associated with the use of Lumizyme are communicated to patients and prescribers and to ensure that the potential risks of severe cutaneous and systemic immune mediated reactions to Lumizyme are communicated to patients and prescribers.

The healthcare facility representative acknowledges that:

- The Lumizyme ACE Program educational materials have been received by the healthcare facility and provided to the healthcare facility staff who are responsible for the ordering, dispensing and administration of Lumizyme.
- Healthcare facility staff has completed training that includes:
  - The procedure for ordering Lumizyme;
  - Procedures for dispensing Lumizyme only after completing Section 1 of the Lumizyme Infusion Confirmation Form (Healthcare Professional Preparing Lumizyme Infusion)
  - Procedures for administering Lumizyme only after verifying that the patient is enrolled in the Lumizyme ACE Program, completing Section 2 of the Lumizyme Infusion Confirmation Form (Healthcare Professional Administering Lumizyme Infusion Therapy), faxing the completed Lumizyme Infusion Confirmation Form to Genzyme and affixing the sticker section of the form to the patient's file or scanning the form and saving it in the patient's electronic medical record.
- The healthcare facility has system procedures and/or other measures in place for appropriate monitoring of patients for early recognition of anaphylaxis and severe allergic reactions.
- The healthcare facility has staff that is prepared to treat patients who experience anaphylaxis or severe allergic reactions to Lumizyme.
- Healthcare facility staff understand that Lumizyme is indicated for patients 8 years and older with late (non-infantile) onset Pompe disease who do not have evidence of cardiac hypertrophy.
- The safety and efficacy of Lumizyme have not been evaluated in controlled clinical trials in infantile-onset patients or in late-onset disease patients less than 8 years of age.
- Healthcare facility staff will dispense and administer Lumizyme only after ensuring each patient receives his/her designated drug by completing the Lumizyme Infusion Confirmation Form.
- The Healthcare facility understands that Genzyme may periodically perform audits at this healthcare facility to verify compliance with the procedures detailed in the Lumizyme ACE Program.

The healthcare facility representative confirms that:

- He/she understands that this information will be used to enable Genzyme to verify that the healthcare facility is certified in the Lumizyme ACE Program and may be shared with others working with Genzyme, and may be shared with government agencies.
- He/she understands that their signature will be required on the Healthcare Facility Enrollment and Attestation Form on an annual basis to maintain enrollment of the healthcare facility in the Lumizyme ACE Program and to dispense and administer Lumizyme.

Healthcare Facility Representative's Signature: _____ Date: _____

Printed Name: _____

Adverse events should be reported promptly to Genzyme Medical Information at 800-745-4447, option 2.

Complete the Healthcare Facility Enrollment and Attestation Form online or fax the completed and signed form to Genzyme at 888-378-7667.

Patient Enrollment and Acknowledgement Form

Complete one (1) form for each patient. All information must be completed on the form below prior to sending to Genzyme Corporation. Upon completion, print name, sign, and date the form at the bottom of the page then fax the form to 888-378-7667.

Patient Information *(to be completed by the prescriber)*			
Name			Date of Birth (MM/DD/YYYY)
Street Address	City	State	Zip Code
Parent/Guardian Name	Relationship	Phone Number	
Patient Gender (check below) ☐ Male ☐ Female	Date of Pompe Diagnosis (MM/DD/YYYY)		

Is the patient diagnosed with infantile-onset or late-onset Pompe disease (check below)?

☐ Infantile-onset Pompe disease

☐ Late-onset (non-infantile) Pompe disease

Lumizyme (alglucosidase alfa) is a lysosomal glycogen-specific enzyme indicated for patients 8 years and older with late (non-infantile) onset Pompe disease [acid α-glucosidase (GAA) deficiency] who do not have evidence of cardiac hypertrophy. The safety and efficacy of Lumizyme have not been evaluated in controlled clinical trials in infantile-onset patients, or in late (non-infantile) onset patients less than 8 years of age.

Patients 8 years and older with late-onset disease may still receive Lumizyme if they have cardiac hypertrophy unrelated to their Pompe disease.

The Lumizyme ACE (Alglucosidase Alfa Control and Education) Program® will ensure that you receive Lumizyme® (alglucosidase alfa) as prescribed by your doctor/prescriber for treatment of your Pompe disease.

Your doctor/prescriber should have talked to you about the risks associated with use of Lumizyme:

- The risks of Lumizyme treatment include life-threatening or severe allergic reactions (hives [bumpy and itchy skin rash], problems breathing, low blood pressure, throat and lip swelling), and that severe skin reactions (e.g., deep skin tissue reaction with open sore) and systemic immune mediated reactions (e.g., kidney problems, and skin rashes) may occur with treatment.
- And other important safety information for Lumizyme.

Your doctor/prescriber should have talked to you about certain situations that may affect your treatment with Lumizyme, including the following:

- Previous infusion reactions that you may have experienced in the past.
- Other illnesses (e.g., cold or flu symptoms) you may have that may place you at higher risk for infusion reactions with Lumizyme.
- If you may be pregnant or are breast-feeding, your doctor needs to know as soon as possible.
- Any medical problems or allergies even if they are not related to your Pompe disease.
- Any medications, including over-the-counter medicines and dietary supplements you are taking.

Your doctor/prescriber should have talked to you about certain conditions that may arise during your infusion of Lumizyme, including the following:

- If you currently have trouble breathing or have heart problems, you may be at risk for worsening of your breathing problems or heart problems during the infusion, and you should be checked for this during the infusion by a trained infusion center staff member and/or doctor/prescriber.
- If you develop signs of a serious allergic reaction such as itching, rash, trouble breathing, or lip or throat swelling, you should be checked immediately by a trained infusion center staff member and/or doctor/prescriber.

By signing below, I acknowledge that:

- My doctor/prescriber (or my child's doctor/prescriber) has provided me with information about the benefits and risks of Lumizyme treatment and the Lumizyme ACE Program.
- I have asked my doctor/prescriber (or my child's doctor/prescriber) any questions I may have about Lumizyme .
- My doctor/prescriber (or my child's doctor/prescriber) has counseled me on the safety information in the product labeling for Lumizyme. I understand the risks of Lumizyme treatment including life-threatening or severe allergic reactions, and severe skin and systemic immune mediated reactions (as described above) associated with the use of Lumizyme.

Doctor/Prescriber Information *(to be completed by the prescriber)*			
Name			
Name of Institution or Facility			
Secondary Contact Name	Phone Number	E-Mail Address	
Street Address	City	State	Zip Code
Site Where Infusion Will Be Administered	Infusion Site Contact	Phone Number	
Street Address	City	State	Zip Code

Doctor/Prescriber Signature: _____ Date: _____

Printed Name: _____

HIPAA/Release of Patient Information

(to be completed by patient/caregiver)

By signing below, you also allow Genzyme and its agents to:

- use your personal health information to help you to receive Lumizyme based on information provided by your doctor/prescriber;
- to release your personal health information to the doctor/prescriber, distributor/wholesaler, pharmacy, or health agency that sends out your medication, in order to help you to receive your Lumizyme based on information provided by your doctor/prescriber; and
- to release your personal health information to the United States Food and Drug Administration ("FDA") and other governmental regulatory agents, as required by the FDA as a condition of participating in the Lumizyme ACE Program.

Signature of Patient or Patient's Legal Representative: _____ Date: _____

Printed Name: _____

Complete the following only if the person signing this Authorization is not the Patient:

Person Authorizing Release: _____ Date: _____

Relationship to Patient (check one):

☐ Custodial Parent ☐ Legal Guardian or Representative ☐ Other (please explain) _____

To complete your registration in the Lumizyme ACE Program, sign and fax the completed form to Genzyme at 888-378-7667.

Genzyme Corporation, 500 Kendall St., Cambridge, MA 02142 Phone: 800-745-4447

LZ-US-P018-06-12

Reference ID: 3159304

Lumizyme Infusion Confirmation Form

Do not remove sticker until completed and faxed to Genzyme

Peel-Off Section

Please fax this completed form to Genzyme at (888) 378-7667.

SECTION 1: Healthcare Professional Preparing Lumizyme Infusion

Patient Name (Print Name)			Date of Birth (MM/DD/YYYY)
Name of Institution or Healthcare Facility			
Address			
City	State	Zip Code	Phone
Total Dose _____ mg Lumizyme® (alglucosidase alfa)	Dose_____mg/kg Frequency_____		
Vial Lot Number(s)* Number of Vials Prepared_____	Prepared By (Print Name) **Prepared By (Signature)**		
Genzyme Case Number (see below)*	Date Prepared		

SECTION 2: Healthcare Professional Administering Lumizyme Infusion Therapy

Patient Name (Print Name)	Date of Birth (MM/DD/YYYY)
☐ I have verified that the above named patient is enrolled in the Lumizyme ACE Program® *(To verify patient enrollment, check the patient's medical record for a copy of the patient's enrollment form or contact the Lumizyme ACE Program at 877-868-7152.)*	
☐ I have verified that the above named patient was administered Lumizyme on (date) _____	
Infusion Administered By (Print Name)	
Administered By (Signature)	Date Administered

Instructions:

1. The healthcare professional preparing the medication for infusion completes Section 1 above.
2. Enclose this form with the delivery of the prepared medication to the infusion site.
3. The healthcare professional administering the Lumizyme infusion completes Section 2 above.
4. Please fax this completed form to Genzyme at **(888) 378-7667**.
5. File the form in the patient's record either by affixing the sticker to the patient's file or scanning the form and saving it in the patient's electronic medical record.

THIS FORM MUST BE COMPLETED AND FAXED TO GENZYME AFTER EVERY LUMIZYME INFUSION.

Report all adverse events to Genzyme Medical Information at (800) 745-4447, option 2.

*__Genzyme Case Number:__ In rare events such as vial breakage, patient weight change impacting the current dose, or a rescheduled infusion where Lumizyme vials cannot be shipped to the facility in time, vials designated for a patient enrolled in the Lumizyme ACE Program can be used for another patient also enrolled in the Lumizyme ACE Program at the same healthcare facility. Prior to using these vials, you must contact Genzyme to review the details of the event and to order replacement vials. Genzyme will provide a Case Number to be entered on the Lumizyme Infusion Confirmation Form (field labeled "Genzyme Case Number") to document the incident. (i.e. 123456-01Jan2011)

Request additional copies of the Lumizyme Infusion Confirmation Form by contacting Genzyme at 800-745-4447, option 1.

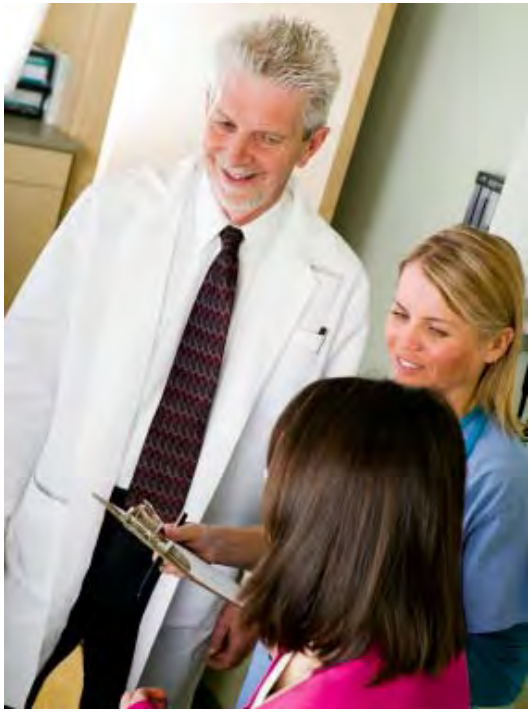
LUMIZYME® (alglucosidase alfa) and the LUMIZYME ACE PROGRAM® (*Alglucosidase Alfa Control and Education)*

Training and Certification for Healthcare Professionals

LZ-US-P023-06-12

Reference ID: 3159304

CONTENTS



This training module contains important information about how to prescribe, dispense and administer Lumizyme.

INTRODUCTION

Lumizyme (alglucosidase alfa) is available **only through a restricted distribution program** called the Lumizyme ACE (Alglucosidase Alfa Control and Education) Program and must be administered **only to patients enrolled in the program**.

- Prescribers and representatives of healthcare facilities are required to complete this online training and enroll in the Lumizyme ACE Program prior to prescribing, dispensing and administering Lumizyme.
- Prescribers or healthcare professionals that prefer on-site training should contact Genzyme Medical Information at 800-745-4447, option 2 to request the contact name for their local representative.

This training module contains important information about how to prescribe, dispense and administer Lumizyme.

LUMIZYME PRODUCT INFORMATION

INDICATION

Lumizyme (alglucosidase alfa) is a lysosomal glycogen-specific enzyme indicated for patients:

... **8 years and older**

... with **late (non-infantile) onset** Pompe disease [acid α-glucosidase (GAA) deficiency]

... who ***do not*** have evidence of cardiac hypertrophy.

- The safety and efficacy of Lumizyme *have not* been evaluated in controlled clinical trials in infantile-onset patients, or in late (non-infantile) onset patients less than 8 years of age.
- Lumizyme *is not for use* in patients with infantile-onset Pompe disease or late (non-infantile) onset Pompe disease who are less than 8 years of age.
- Patients 8 years and older may still receive Lumizyme if they have cardiac hypertrophy resulting from conditions unrelated to their Pompe disease.

IMPORTANT CONSIDERATIONS

There are 2 enzyme replacement therapies available for the treatment of Pompe disease - Lumizyme and Myozyme® (alglucosidase alfa)

- Lumizyme and Myozyme are **two different products**.
- ***Lumizyme cannot be substituted for Myozyme.***
- Lumizyme should be prescribed **according to the approved indication**.

BOXED WARNING

The prescribing information for Lumizyme (alglucosidase alfa) includes the following boxed warning:

WARNING: ANAPHYLAXIS and RESTRICTED DISTRIBUTION PROGRAM

Life-threatening anaphylactic reactions, severe allergic reactions and immune mediated reactions have been observed in some patients during LUMIZYME infusions. Therefore, appropriate medical support should be readily available when LUMIZYME is administered.

Because of the potential risk of rapid disease progression in Pompe disease patients less than 8 years of age, LUMIZYME is available only through a restricted distribution program called the LUMIZYME ACE Program. Only prescribers and healthcare facilities enrolled in the program may prescribe, dispense or administer LUMIZYME. LUMIZYME may be administered only to patients who are enrolled in and meet all the conditions of the LUMIZYME ACE Program. To enroll in the LUMIZYME ACE Program call 1-800-745-4447.

LEARNING CHECK

- Every provider should be able to answer these questions about the approved indication for Lumizyme.
- If you have problems answering these questions, please review the previous slides before moving ahead with this training.

Learning Check 1

Question 1 of 3

The safety and efficacy of Lumizyme have not been evaluated in controlled clinical trials in infantile-onset patients, or in late (non-infantile) onset patients less than 8 years of age.

- ○ True
- ○ False

SUBMIT

Learning Check 1

Question 2 of 3

Lumizyme may be substituted for Myozyme® (alglucosidase alfa) enzyme replacement therapy in the treatment of Pompe disease.

- ○ True
- ○ False

SUBMIT

Learning Check 1

Question 3 of 3

Lumizyme is indicated for patients 10 years and older with late (non-infantile) onset Pompe disease [acid α-glucosidase (GAA) deficiency] who have evidence of cardiac hypertrophy.

- ○ True
- ○ False

SUBMIT

Learning Check 1

If you had problems answering these important questions about the indication and safety/efficacy of Lumizyme, please review the previous slides before you proceed with this training.

Retry Quiz Finish

ANAPHYLAXIS AND ALLERGIC REACTIONS

Anaphylaxis and severe allergic reactions have been observed in patients during and up to 3 hours after Lumizyme infusion. Some reactions were life-threatening and included:

- Anaphylactic shock
- Respiratory arrest
- Apnea
- Dyspnea
- Bradycardia
- Tachycardia
- Hypotension

Some of these reactions were IgE-mediated.

ANAPHYLAXIS AND ALLERGIC REACTIONS

Other accompanying reactions included:

- Chest discomfort/pain
- Throat tightness
- Bronchospasm
- Wheezing
- Tachypnea
- Cyanosis
- Decreased oxygen saturation/ hypoxia
- Convulsions
- Angiodema (including tongue or lip swelling, periorbital edema, and face edema)
- Pruritis
- Rash
- Urticaria
- Hyperhidrosis
- Nausea
- Abdominal pain
- Vomiting
- Dizziness
- Hypertension
- Flushing/erythema
- Fever
- Pallor
- Peripheral coldness
- Feeling hot
- Restlessness
- Nervousness
- Headache
- Back pain
- Paraesthesia

Some of these reactions were IgE-mediated.

ANAPHYLAXIS AND ALLERGIC REACTIONS

Important Reminder

Because of the potential for severe allergic reactions, **appropriate medical support, including cardiopulmonary resuscitation equipment**, should be readily available when Lumizyme is administered.

If anaphylaxis or other severe allergic reactions occur, **immediate discontinuation of the administration of Lumizyme should be considered**, and appropriate medical treatment should be initiated.

IMMUNE MEDIATED REACTIONS

Systemic immune mediated reactions:

- **Severe cutaneous reactions** have been reported with alglucosidase alfa including necrotizing skin lesions. **Systemic immune mediated reactions**, including possible type III immune mediated reactions have been observed with alglucosidase alfa. These reactions occurred several weeks to 3 years after initiation of alglucosidase alfa infusions.
- Skin biopsy in one patient demonstrated **deposition of anti-rhGAA antibodies** in the lesion. Another patient developed **severe inflammatory arthropathy** in association with fever and elevated erythrocyte sedimentation rate.

(continues)

IMMUNE MEDIATED REACTIONS

Systemic immune mediated reactions *(continued)*

- **Nephrotic syndrome** secondary to membranous glomerulonephritis was observed in a few Pompe patients treated with alglucosidase alfa who had persistently positive anti-rhGAA IgG antibody titers. In these patients renal biopsy was consistent with immune complex deposition. Patients improved following treatment interruption. It is therefore recommended to perform periodic urinalysis.

Important Reminder

Patients should be monitored for the development of systemic immune mediated reactions involving skin and other organs while receiving Lumizyme.

RISK OF ACUTE CARDIORESPIRATORY FAILURE

Patients with acute underlying respiratory illness or compromised cardiac and/or respiratory function may be at risk of serious exacerbation of their cardiac or respiratory compromise during infusions.

Important Reminder

Appropriate medical support and monitoring measures should be readily available during Lumizyme infusions, and some patients may require prolonged observation times.

INFUSION REACTIONS

The **most common adverse reactions** observed in clinical studies were **infusion reactions**. Infusion reactions reported in ≥ 5% of Lumizyme-treated patients compared to placebo included:

- Anaphylaxis, urticaria, diarrhea, vomiting, dyspnea, pruritus, rash/erythema, pharyngolaryngeal pain, neck pain, hypoacusis, flushing/feeling hot, pain in extremity, fall, and chest discomfort.
- Additional infusion reactions observed in other clinical trials and expanded access programs with Lumizyme included:
  - Respiratory distress, cough, livedo reticularis, agitation, irritability, retching, rigors, tremor and increased lacrimation.

LEARNING CHECK

- Every provider should be able to answer these questions about adverse reactions.
- If you have problems, please review the previous slides before moving ahead with this training.

Learning Check 2

Question 1 of 2

Which of the following are symptoms of serious allergic reactions that can occur in patients treated with Lumizyme?

Click all that apply.

- ☐ Swelling of the face, throat or lips
- ☐ Recurring nose bleeds
- ☐ Skin rash or hives
- ☐ Bronchospasm and/or dyspnea

SUBMIT

Learning Check 2

Question 2 of 2

Which of the following are symptoms of severe cutaneous and systemic immune-mediated reactions that can occur in patients treated with Lumizyme?

Click all that apply.

- ☐ Inflammatory arthropathy
- ☐ Heartburn
- ☐ Kidney problems
- ☐ Skin lesions

SUBMIT

Learning Check 2

If you had trouble answering these important questions about adverse reactions, please go back and review this section before you go on to the rest of this training.

Retry Quiz Finish

MONITORING: DURING AND POST-INFUSION

Monitor patients for adverse reactions:

- **Patients should be observed during and after** the completion of each infusion by appropriate medical personnel familiar with Pompe disease and potential reactions.
- Infusions should be administered in a **step-wise manner** (*refer to Table 1 in the full Prescribing Information*) and vital signs obtained at the end of each step.
- The appropriate **length of post-infusion monitoring** is to be determined by the treating physician based on the individual patient's clinical status and infusion history.
- **Delayed onset reactions** (within 48 hours of infusion) may include urticaria, dizziness, procedural pain, pharyngolaryngeal pain, malaise, muscle spasms, musculoskeletal pain, weakness or stiffness, neck pain, insomnia and epistaxis.

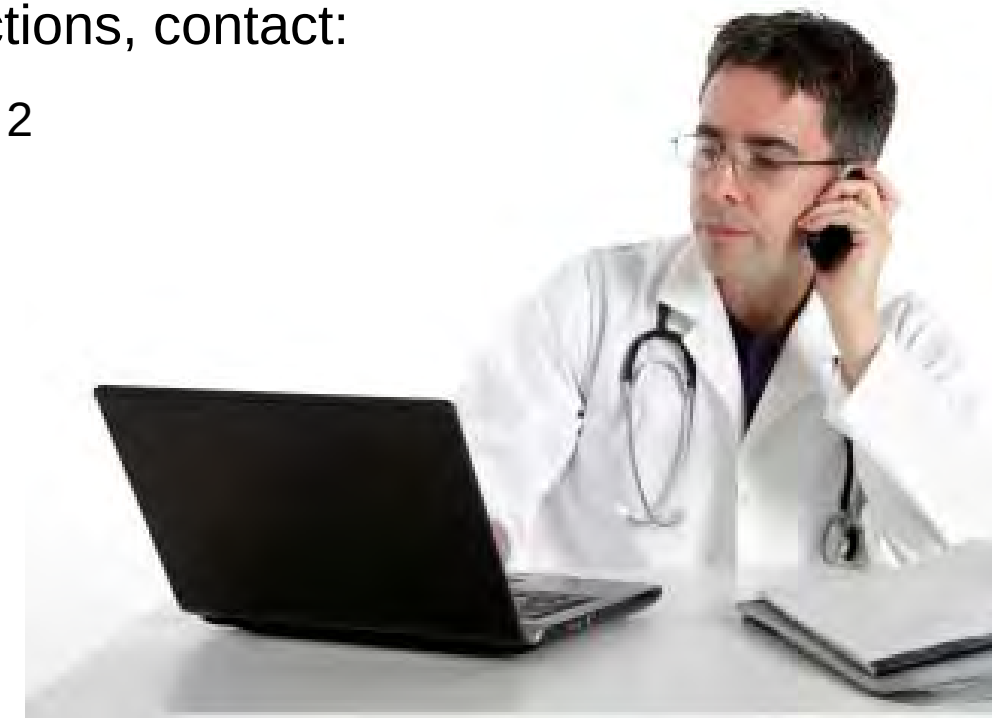
REPORT SUSPECTED ADVERSE REACTIONS

To report suspected adverse reactions, contact:

- Genzyme at 800-745-4447, option 2

or

- FDA at 800-FDA-1088 or www.fda.gov/safety/medwatch.



Genzyme also accepts reports via fax or e-mail:

- Fax: 617-761-8506 with a detailed description of the event
- E-mail: Pharmacovigilancesafety@genzyme.com

MANAGING ADVERSE REACTIONS

- If an **infusion reaction** occurs:
  - Decrease infusion rate or temporarily stop the infusion and/or;
  - Administer antihistamines and/or antipyretics
- If **severe allergic or anaphylactic reactions** occur:
  - Consider immediate discontinuation of the infusion
  - Initiate appropriate medical treatment which may include administration of antihistamines, corticosteroids, intravenous fluids, and/or oxygen.
  - The risks and benefits of re-administering Lumizyme following an anaphylactic or severe allergic reaction should be considered. Some patients have been rechallenged and have continued to receive Lumizyme under close clinical supervision.
  - Extreme care should be exercised, with appropriate resuscitation measures available, if product is re-administered.
- **Delayed onset reactions** (within 48 hours after infusion)
  - Counsel patients about possibility of delayed onset reactions and provide proper follow up instructions

MONITORING: ANAPHYLACTIC REACTIONS/IMMUNE MEDIATED REACTIONS

Important Reminder

Patients should be **monitored for IgG antibody formation** every three months for 2 years and then annually thereafter.

Test for IgE antibodies to alglucosidase alfa and other mediators (complement activation and tryptase) of anaphylaxis if patients experience allergic or anaphylactic reactions

DOSING AND ADMINISTRATION

Recommended dosage/administration:

- The recommended dosage of Lumizyme is **20 mg/kg body weight** administered **every 2 weeks** as an intravenous infusion over approximately **4 hours**.
- Infusions should be administered in a **step-wise 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.

DOSING AND ADMINISTRATION

Important Reminder

Vital signs should be obtained at the end of each step. If the patient is stable, Lumizyme may be administered at the maximum rate of 7 mg/kg/hr until the infusion is completed.

Appropriate medical support should be readily available when Lumizyme is administered.

LEARNING CHECK

- Every provider should be able to answer these questions about Lumizyme dosing and administration.
- If you have problems answering these questions, please review the previous slides before moving ahead with this training.

Learning Check 3

Question 1 of 3

The recommended dosage of Lumizyme is 30 mg/kg body weight administered every week as an intravenous infusion over approximately 2 hours.

- ○ True
- ○ False

SUBMIT

Learning Check 3

Question 2 of 3

If an infusion reaction occurs, you should reduce the infusion rate or temporarily stop the infusion and/or administer antihistamines and/or antipyretics.

- ○ True
- ○ False

SUBMIT

Learning Check 3

Question 3 of 3

Patients should be monitored for IgG antibody formation:

- monthly for 1 year, and then every three months thereafter.
- weekly for 1 year, and then monthly thereafter.
- every three months for 2 years, and then annually thereafter.

SUBMIT

Learning Check 3

If you had trouble answering these important questions about dosing and administration, please review the previous slides before you go on with this training.

Retry Quiz

Finish

ORDERING

Lumizyme is available **only through a restricted distribution program** called the Lumizyme ACE Program. To order Lumizyme, contact Genzyme at 800-745-4447, option 1.

- Prescribers, healthcare facilities, and patients **must be enrolled** in the Lumizyme ACE Program before Lumizyme will be authorized for shipment.
- Lumizyme is **only available** to patients 8 years and older with late (non-infantile) onset Pompe disease (GAA deficiency) who do not have evidence of cardiac hypertrophy.
- Lumizyme is **individually bagged and shipped on a named-patient basis**. Vials should be used only for the intended patient .

LUMIZYME ACE PROGRAM

OVERVIEW

The Lumizyme ACE (Alglucosidase Alfa Control and Education) Program is a **restricted distribution program for Lumizyme**.

- Before ordering, dispensing and administering Lumizyme, prescribers and representatives of healthcare facilities **must complete the training and certification program and sign and return the appropriate attestation forms** to enroll in the Lumizyme ACE Program.
- Lumizyme **must be administered only to patients enrolled** in the Lumizyme ACE Program.

PROGRAM GOALS

The Lumizyme ACE Program is designed to:

- Mitigate the potential risk of rapid disease progression in infantile-onset Pompe disease patients and patients with late (non-infantile) onset disease less than 8 years of age for whom the safety and effectiveness of Lumizyme have not been evaluated.
- Ensure that the known risks of anaphylaxis and severe allergic reactions associated with the use of Lumizyme are communicated to patients and prescribers and to ensure that the potential risks of severe cutaneous and systemic immune mediated reactions to Lumizyme are communicated to patients and prescribers.

LEARNING CHECK

- Every provider should be able to answer these questions about ordering Lumizyme.
- If you have problems, please review the previous slides before moving ahead with this training.

Learning Check 4

Question 1 of 2

Lumizyme is *only* available to patients 8 years and older with late-onset Pompe who *do not* have evidence of cardiac hypertrophy.

- ○ True
- ○ False

SUBMIT

Learning Check 4

Question 2 of 2

Who of the following must be enrolled in the Lumizyme ACE Program before Lumizyme will be authorized for shipment?

Click all that apply.

- ☐ Prescribers
- ☐ Patients
- ☐ Healthcare facilities

SUBMIT

Learning Check 4

If you had trouble answering these important questions about ordering Lumizyme, please review the previous slides before you go on with this training.

Retry Quiz Finish

INSTRUCTIONS FOR ENROLLMENT - PRESCRIBERS

Prescribers must complete the online training and certification program and return a completed and signed attestation form in order to enroll in the Lumizyme ACE Program.

Prescribers must attest to the following in order to complete enrollment in the Lumizyme ACE Program:

Prescriber Attestation

- I have completed educational training about Lumizyme® (alglucosidase alfa) and understand the risks and benefits of Lumizyme.
- I understand that Lumizyme is indicated for patients 8 years and older with late (non-infantile) onset Pompe disease who do not have evidence of cardiac hypertrophy. The safety and efficacy of Lumizyme have not been evaluated in controlled clinical trials in infantile-onset patients, or in late-onset patients less than 8 years of age.
- I understand that by completing the training program and signing this attestation form, I am now enrolled in the Lumizyme ACE Program and can prescribe and administer Lumizyme.
- I understand that I must enroll all patients being treated with Lumizyme into the Lumizyme ACE Program by completing a Patient Enrollment and Acknowledgement Form.
- I understand that I am responsible for providing the Patient Enrollment and Acknowledgement Form to patients (or, as appropriate, their parents/guardians) and for obtaining their signature on the Patient Enrollment and Acknowledgement Form prior to initiating them on treatment with Lumizyme
- I will advise patients and caregivers about the known (e.g. anaphylaxis and severe allergic reactions) and potential risks (e.g. severe cutaneous and systemic immune mediated reactions) associated with administration of Lumizyme and will review the risks and benefits of Lumizyme as per the product labeling.
- I understand that patients may experience anaphylaxis or severe allergic reactions to Lumizyme and I have access to appropriate medical support measures.
- I understand that I will be required to sign a Prescriber Enrollment and Attestation Form on an annual basis to maintain my enrollment in the Lumizyme ACE Program and to prescribe Lumizyme.

INSTRUCTIONS FOR ENROLLMENT - PRESCRIBERS

Prescribers must:

- Complete this online training and certification program
  - On-site training is available upon request but is not required if the prescriber completes the online training.
- Complete the Prescriber Enrollment and Attestation Form
  - Enrollment forms and instructions on how to submit are available at the end of this training program
- Remember to file a copy of the signed attestation form with the Lumizyme ACE Program materials maintained at the healthcare facility

IMPORTANT REMINDER

Annual re-enrollment in the Lumizyme ACE Program is required. A reminder will be sent to enrolled prescribers 60 days prior to the re-enrollment deadline.

INSTRUCTIONS FOR ENROLLMENT – HEALTHCARE FACILITY

A representative of the healthcare facility must complete the online training and certification program and return a completed and signed attestation form in order to enroll in the Lumizyme ACE Program.

- The healthcare facility representative may include director of pharmacy and/or infusion center representative such as physician, head nurse, director of infusion center or director of education

The healthcare facility representative is responsible for training all staff at the site who will be involved with ordering, dispensing and administering Lumizyme.

- For materials to facilitate training at your site, click here.

HEALTHCARE FACILITY ATTESTATION

The representative from the healthcare facility **must attest to the following** in order to complete enrollment in the Lumizyme ACE Program:

Healthcare Facility Attestation

- The Lumizyme ACE Program educational materials have been received by the healthcare facility and provided to the healthcare facility staff who are responsible for the ordering, dispensing and administration of Lumizyme.
- Healthcare facility staff has systems, procedures and/or other measures in place for:
  - The procedure for ordering Lumizyme;
  - Procedures for dispensing Lumizyme only after completing Section 1 of the Lumizyme Infusion Confirmation Form (Healthcare Professional Preparing Lumizyme Infusion); and,
  - Procedures for administering Lumizyme only after verifying that the patient is enrolled in the Lumizyme ACE Program, completing Section 2 of the Lumizyme Infusion Confirmation Form (Healthcare Professional Administering Lumizyme Infusion Therapy), faxing the completed Lumizyme Infusion Confirmation Form to Genzyme and affixing the sticker section of the form to the patient's file or scanning the form and saving it in the patient's electronic medical record.

Attestation continues, next page…

HEALTHCARE FACILITY ATTESTATION

Healthcare Facility Attestation

…Attestation (continued)

- The healthcare facility has system procedures and/or other measures in place for appropriate monitoring of patients for early recognition of anaphylaxis, severe allergic reactions, and immune mediated reactions.
- The healthcare facility has staff that is prepared to treat patients who experience anaphylaxis or severe allergic reactions to Lumizyme.
- Healthcare facility staff understand that Lumizyme is indicated for patients 8 years and older with late (non-infantile) onset Pompe disease who do not have evidence of cardiac hypertrophy.
- The safety and efficacy of Lumizyme have not been evaluated in controlled clinical trials in infantile-onset patients or in late-onset disease patients less than 8 years of age.
- Healthcare facility staff will dispense and administer Lumizyme only after ensuring each patient receives his/her designated drug by completing the Lumizyme Infusion Confirmation Form.
- The healthcare facility understands that Genzyme may periodically perform audits at this healthcare facility to verify compliance with the procedures detailed in the Lumizyme ACE Program.

INSTRUCTIONS FOR ENROLLMENT – HEALTHCARE FACILITY

- Complete this online training and certification program
  - On-site training is available upon request but is not required if the healthcare facility representative completes the online training.
- Complete the Healthcare Facility Enrollment and Attestation Form
  - Enrollment forms and instructions on how to submit are available at the end of this training program
- Remember to file a copy of the signed attestation form with the Lumizyme ACE Program materials maintained at the healthcare facility
- Additional site staff may access the training program for educational purposes, but only one attestation form per facility is required.

IMPORTANT REMINDER

Annual re-enrollment in the Lumizyme ACE Program is required. A reminder will be sent to the healthcare facility 60 days prior to the re-enrollment deadline.

INSTRUCTIONS FOR ENROLLMENT – PATIENTS

- Prescribers **must review the safety and efficacy** of Lumizyme and the requirements of the Lumizyme ACE Program with patients who will receive treatment.
- Patients must attest to the following in order to complete enrollment in the program:

Patient Attestation

- My doctor/prescriber (or my child's doctor/prescriber) has provided me with information about the benefits and risks of Lumizyme treatment and the Lumizyme ACE Program.
- I have asked my doctor/prescriber (or my child's doctor/prescriber) any questions I may have about Lumizyme.
- My doctor/prescriber (or my child's doctor/prescriber) has counseled me on the safety information in the product labeling for Lumizyme. I understand the risks of Lumizyme treatment including life-threatening or severe allergic reactions, and severe skin and systemic immune mediated reactions associated with the use of Lumizyme.

INSTRUCTIONS FOR ENROLLMENT – PATIENTS

- After reviewing the safety and efficacy of Lumizyme and the requirement of the Lumizyme ACE Program with patients:
  - Print the *Patient Enrollment and Acknowledgement Form* and complete the required information and sign the form.
    - Enrollment forms and instructions on how to submit are available at the end of this training program
    - Note that the Patient Enrollment and Acknowledgement Form contains information to be completed by both the prescriber and patient.
  - The treating prescriber should fax the signed and completed form to Genzyme. This will complete the patient's enrollment in the Lumizyme ACE Program.
  - Confirmation will be sent to prescriber upon receipt of the enrollment form.
  - A copy of the enrollment form should be maintained in the patient's file and a signed copy provided to the patient.
- Annual re-enrollment in the Lumizyme ACE Program *is not* required for patients.
- A copy of the patient's enrollment form should be maintained at the infusion site or patient enrollment in the Lumizyme ACE Program documented in the patient's file (paper or electronic).
- A healthcare professional at the infusion site should verify that the patient enrollment form is on file and check the patient's identification prior to each infusion of Lumizyme.

LUMIZYME INFUSION CONFIRMATION FORM

A completed *Lumizyme Infusion Confirmation Form* is **required for each patient after each infusion** to confirm that Lumizyme was administered to the intended patient.

- The completed Form must be returned to Genzyme via fax at 888-378-7667.
  - The Lumizyme Infusion Confirmation Form is included with the product shipment.
  - The Form includes sections to be completed by both the person responsible for preparing the infusion (Section 1) and the person who administers the Lumizyme infusion (Section 2).
  - Request additional copies of the Lumizyme Infusion Confirmation Form by contacting Genzyme at 800-745-4447, option 1.

IMPORTANT NOTE

The healthcare facility is responsible for returning these forms in a timely manner. If at any time, 2 of these forms are outstanding for the patient, Lumizyme cannot be shipped for that patient.

LUMIZYME INFUSION CONFIRMATION FORM

Steps to complete the form:

- The healthcare professional preparing the Lumizyme infusion will:
  - Complete Section 1 of the Lumizyme Infusion Confirmation Form including:
    - Patient name and date of birth
    - Dose Information
    - Vial lot number(s)
    - Number of vials prepared
    - Preparer name and signature
  - Include the Lumizyme Infusion Confirmation Form with the final preparation to be delivered to site of infusion.
- The healthcare professional that administers the Lumizyme must:
  - Confirm that the patient is enrolled in the Lumizyme ACE Program
  - Confirm that Lumizyme is the appropriate product and is intended for the named patient; and,
  - Complete Section 2 of the Lumizyme Infusion Confirmation Form
- Fax the completed form to Genzyme at 888-378-7667.

LUMIZYME INFUSION CONFIRMATION FORM

Lumizyme Infusion Confirmation Form

Do not remove sticker until completed and faxed to Genzyme

Peel-Off Section

Please fax this completed form to Genzyme at (888) 378-7667.

SECTION 1: Healthcare Professional Preparing Lumizyme Infusion

Patient Name (Print Name)	Date of Birth (MM/DD/YYYY)
Name of Institution or Healthcare Facility	
Address	
City	
Total Dose _____ mg Lumizyme® (alglucos	
Vial Lot Number(s)*	
Number of Vials Prepared_____	
Genzyme Case Number (see below)*	Date Prepared

SECTION 2: Healthcare Professional Administering Lumizyme Infusion Therapy

Patient Name (Print Name)	Date of Birth (MM/DD/YYYY)
☐ I have verified that the above named patient is enrolled in the Lumizyme ACE Program® *(To verify patient enrollment, check the patient's medical record for a copy of the patient's enrollment form or contact the Lumizyme ACE Program at 877-868-7152.)*	
☐ I have verified that the above named patient was administered Lumizyme on (date) _____	
Infusion Administered By (Print Name)	
Administered By (Signature)	Date Administered

After the form has been faxed to Genzyme...

Remember to remove and affix the peel-off sticker from the form to the patient's file or scan the form and save it in the patient's electronic medical record

LEARNING CHECK

- Every provider should be able to answer these questions about enrollment in the Lumizyme ACE Program and the Lumizyme Infusion Confirmation Form.
- If you have problems, please review the previous slides before moving ahead with this training.

Learning Check 5

Question 1 of 2

The Lumizyme Infusion Confirmation Form:

- Must be completed for each patient after each infusion.
- Must be returned to Genzyme via fax.
- Must be returned to Genzyme in a timely manner.
- All of the above are required.

SUBMIT

Learning Check 5

Question 2 of 2

Which of the following statements are *true*?

Click all that apply.

- ☐ Prescribers and healthcare facilities need to re-enroll in the program annually.
- ☐ Prescribers must enroll their patients in the Lumizyme ACE Program if they intend to treat them with Lumizyme.
- ☐ Genzyme is responsible for training all staff at the site who will be involved with ordering, dispensing and administering Lumizyme.
- ☐ Prescribers must complete training either online or in-person and return a completed and signed attestation form in order to enroll in the Lumizyme ACE Program.

SUBMIT

Learning Check 5

If you had trouble answering these important questions about the Lumizyme ACE Program requirements, please review the previous slides before you go on with this training.

Retry Quiz Finish

SUMMARY

On completion of this training, you should know and understand:

- There are 2 enzyme replacement therapies available for the treatment of Pompe disease. Lumizyme and Myozyme® (alglucosidase alfa) are two different products. **Lumizyme cannot be substituted for Myozyme.** Lumizyme should be prescribed according to the approved indication.
- Lumizyme is indicated for use only in patients **8 years and older** with **late (non-infantile) onset Pompe disease** who **do not have evidence of cardiac hypertrophy**.
- **Life-threatening anaphylactic reactions, severe allergic reactions and immune mediated reactions** have been observed in some patients during Lumizyme infusions.

Summary continues, next page

SUMMARY (CONTINUED)

On completion of this training, you should know and understand:

(continued from previous page)

- Prescribers will **advise patients and caregivers** about the known (e.g. anaphylaxis and severe allergic reactions) and potential (e.g. severe cutaneous and systemic immune mediated reactions) risks associated with administration of Lumizyme and will review the risks and benefits of Lumizyme as per the product labeling.
- Lumizyme is available **only through a restricted distribution program** called the Lumizyme ACE (Alglucosidase Alfa Control and Education) Program and must be administered only to patients enrolled in the program.
- Prescribers, representatives of healthcare facilities, and patients **must complete training and enroll** in the Lumizyme ACE Program before product will be authorized for shipment.

Summary continues, next page

SUMMARY (CONTINUED)

On completion of this training, you should know and understand:

(continued from previous pages)

- Prescribers and healthcare facilities will be required to **re-enroll** in the Lumizyme ACE Program on an annual basis.
- Prescribers and patients may be asked to periodically c**omplete surveys** to assess their understanding of the serious risks of Lumizyme.
- To complete the enrollment process for the Lumizyme ACE Program, the following **forms must be signed and returned t**o Genzyme:
  - Prescriber Enrollment and Attestation Form
  - Healthcare Facility Enrollment and Attestation Form
  - Patient Enrollment and Acknowledgement Form

Summary continues, next page

SUMMARY (CONTINUED)

On completion of this training, you should know and understand:

(continued from previous pages)

- A **Lumizyme Infusion Confirmation Form must be completed and returned** to Genzyme for **each patient after every infusion** to confirm that Lumizyme was administered to the intended patient
- Genzyme will maintain a **validated database** containing all prescriber, healthcare facility, and patient enrollment information.

If you are not sure that you understand all these critical points, please go back and review this training before moving ahead.

Training Acknowledgement

Question 1 of 1

Please click here to acknowledge that you have completed the Lumizyme ACE Program training and certification

- ○ Yes, I have read and completed the Lumizyme ACE Program training
- ○ No, I haven't completed the Lumizyme ACE Program training

SUBMIT

Reference ID: 3159304

Training Acknowledgement

You have completed the Lumizyme ACE Program training and certification.

Finish

YOU HAVE COMPLETED THE LUMIZYME ACE PROGRAM TRAINING AND CERTIFICATION.

If you are the prescriber or healthcare facility representative, the following forms must also be signed and returned to Genzyme:

- Prescriber Enrollment and Attestation Form
- Healthcare Facility Enrollment and Attestation Form
- Patient Enrollment and Acknowledgement Form

Click here to enroll

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JOYCE A KORVICK
07/16/2012