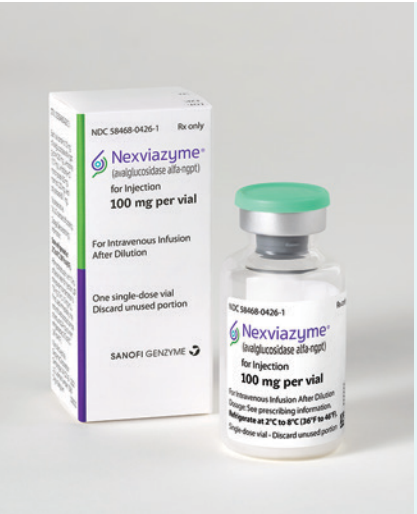
Nexviazyme®
(avalglucosidase alfa-ngpt)

PREPARATION FOR WHAT'S NEX

# DOSING & ADMINISTRATION GUIDE

## Supplies and equipment




- ☐ **NEXVIAZYME single-use vials** (see next page for dose calculation)
- ☐ **Intravenous (IV) administration set** with 0.2 micrometer, low-protein-binding (in-line) filter
- ☐ **Sterile water for injection**, for reconstitution—10 mL for each vial
- ☐ **5% dextrose injection (D5W)**, for dilution
- ☐ **Syringes and needles** for reconstitution and dilution
- ☐ Additional supplies per institution protocol

**NOTE:** Filter needles should NOT be used during preparation of NEXVIAZYME.

### INDICATION

NEXVIAZYME (avalglucosidase alfa-ngpt) is indicated for the treatment of patients 1 year of age and older with late-onset Pompe disease [lysosomal acid alpha-glucosidase (GAA) deficiency].

### IMPORTANT SAFETY INFORMATION

**WARNING: SEVERE HYPERSENSITIVITY REACTIONS, INFUSION-ASSOCIATED REACTIONS, and RISK OF ACUTE CARDIORESPIRATORY FAILURE IN SUSCEPTIBLE PATIENTS**

**Hypersensitivity Reactions Including Anaphylaxis**

**Patients treated with NEXVIAZYME have experienced life-threatening hypersensitivity reactions, including anaphylaxis. Appropriate medical support measures, including cardiopulmonary resuscitation equipment, should be readily available during NEXVIAZYME administration. If a severe hypersensitivity reaction (e.g., anaphylaxis) occurs, NEXVIAZYME should be discontinued immediately and appropriate medical treatment should be initiated. In patients with severe hypersensitivity reaction, a desensitization procedure to NEXVIAZYME may be considered.**

**Infusion-Associated Reactions (IARs)**

**Patients treated with NEXVIAZYME have experienced severe IARs. If severe IARs occur, consider immediate discontinuation of NEXVIAZYME, initiation of appropriate medical treatment, and the benefits and risks of readministering NEXVIAZYME following severe IARs. Patients with an acute underlying illness at the time of NEXVIAZYME infusion may be at greater risk for IARs. Patients with advanced Pompe disease may have compromised cardiac and respiratory function, which may predispose them to a higher risk of severe complications from IARs.**

**Risk of Acute Cardiorespiratory Failure in Susceptible Patients**

**Patients susceptible to fluid volume overload, or those with acute underlying respiratory illness or compromised cardiac or respiratory function for whom fluid restriction is indicated may be at risk of serious exacerbation of their cardiac or respiratory status during NEXVIAZYME infusion. More frequent monitoring of vitals should be performed during NEXVIAZYME infusion.**

**Please see Important Safety Information on back cover and accompanying full Prescribing Information, including Boxed WARNING.**

# NEXVIAZYME OVERVIEW

## The #1 prescribed ERT for LOPD[1,2,*]

**Questions about NEXVIAZYME?** Connect with a local representative.

## NEXVIAZYME IS A MONOTHERAPY[†] INDICATED FOR LOPD PATIENTS 1 YEAR AND OLDER WHO ARE ERT-NAIVE AND EXPERIENCED[1]

**Switching to NEXVIAZYME can be a seamless process.**[1,2]

- Patients who are switching to NEXVIAZYME can begin receiving treatment immediately, with **no washout period** between the final alglucosidase alfa dose and the first NEXVIAZYME dose. Patients may also be able to keep their same dosing schedule and infusion center

**NEXVIAZYME does not require fasting or stabilizers.**[1,2]

- Prior to administration, HCP to **consider pretreating** with antihistamines, antipyretics, and/or corticosteroids

**Recommended biweekly dose[1]:**

- Patients weighing ≥30 kg: 20 mg/kg[‡]
- Patients weighing <30 kg: 40 mg/kg[‡]

**The initial recommended infusion rate is 1 mg/kg/hour.**

- Gradually increase the infusion rate every 30 minutes if there are no signs of infusion-associated reactions (IARs) (see page 6)

**NEXVIAZYME must be reconstituted and diluted prior to use** (see pages 4 and 5).

## ADMINISTRATION MODIFICATIONS DUE TO HYPERSENSITIVITY REACTIONS AND/OR IARs

**In the event of a severe hypersensitivity reaction (including anaphylaxis) or a severe IAR**, immediately discontinue NEXVIAZYME administration and initiate appropriate medical treatment[1]

**In the event of a mild or moderate hypersensitivity reaction or a mild or moderate IAR**, consider temporarily holding the infusion for 30 minutes or slowing the infusion rate by 50% and initiating appropriate medical treatment[1]

- If symptoms persist for longer than 30 minutes despite holding or slowing the infusion, stop the infusion and monitor the patient. Consider re-initiating the infusion on the same day when symptoms subside at 50% of the rate at which the reaction occurred with appropriate pretreatment[1]
- If symptoms subside after holding the infusion, resume infusion at 50% of the rate at which the reaction occurred, and subsequently increase the infusion rate every 15 to 30 minutes by 50% as tolerated. Alternatively, if symptoms subside after slowing the infusion, complete the infusion at the reduced rate as tolerated[1]
- Starting with the next infusion, increase the infusion rate until the infusion rate at which the reaction occurred is reached. Consider continuing to increase the infusion rate in a stepwise manner until reaching the recommended infusion rate. Closely monitor the patient[1]

*Prescription data as of June 5, 2023.
[†]Not including premedication or pretreatment.
[‡]Of actual body weight.

# RECOMMENDED DOSE & INFUSION RATE

## STEP 1

Determine the number of vials to be reconstituted based on the individual patient's weight and the **recommended dose (see dose calculation below).**[1]

**Calculating dose and vials example:**

Total patient weight (kg) **x** Dosage selection (weight based) 20 mg/kg or 40 mg/kg = **Total patient dose** (mg)

Total patient dose (mg) / Vial concentration (100 mg/vial) = **Total vial count** (round up to the nearest whole vial)

**Example:**

42 kg **x** 20 mg/kg = **840 mg**

840 mg / 100 mg/vial = **8.4 vials**

**9 vials total of NEXVIAZYME are needed**

## STEP 2

Determine the projected intravenous infusion volume and rate for NEXVIAZYME administration according to patient weight.[1] Administer the infusion incrementally, as determined by the patient's comfort and response.[1]

**4-STEP PROCESS**

| PATIENT WEIGHT RANGE (kg) | TOTAL INFUSION VOLUME (mL) | RECOMMENDED DOSE (mg/kg) | Step 1 1 mg/kg/hour | Step 2 3 mg/kg/hour | Step 3 5 mg/kg/hour | Step 4 7 mg/kg/hour | APPROXIMATE TOTAL INFUSION DURATION |
|---|---|---|---|---|---|---|---|
| | | | INFUSION RATE (mL/hour) | | | | |
| 5 to 9.9 | 100 | 40 | 3 | 8 | 13 | 18 | 7 hours |
| 10 to 19.9 | 200 | | 5 | 15 | 25 | 35 | |
| 20 to 29.9 | 300 | | 8 | 23 | 38 | 53 | |
| 30 to 34.9 | 200 | 20 | 10 | 30 | 50 | 70 | 4-5 hours |
| 35 to 49.9 | 250 | | 13 | 38 | 63 | 88 | |
| 50 to 59.9 | 300 | | 15 | 45 | 75 | 105 | |
| 60 to 99.9 | 500 | | 25 | 75 | 125 | 175 | |
| 100 to 119.9 | 600 | | 30 | 90 | 150 | 210 | |
| 120 to 140 | 700 | | 35 | 105 | 175 | 245 | |

**5-STEP PROCESS***

| PATIENT WEIGHT RANGE (kg) | TOTAL INFUSION VOLUME (mL) | RECOMMENDED DOSE (mg/kg) | Step 1 1 mg/kg/hour | Step 2 3 mg/kg/hour | Step 3 6 mg/kg/hour | Step 4 8 mg/kg/hour | Step 5 10 mg/kg/hour | APPROXIMATE TOTAL INFUSION DURATION |
|---|---|---|---|---|---|---|---|---|
| | | | INFUSION RATE (mL/hour) | | | | | |
| 5 to 9.9 | 100 | 40 | 3 | 8 | 15 | 20 | 25 | 5 hours |
| 10 to 19.9 | 200 | | 5 | 15 | 30 | 40 | 50 | |
| 20 to 29.9 | 300 | | 8 | 23 | 45 | 60 | 75 | |

40 mg/kg

20 mg/kg

Step 1 indicates the starting infusion rate. If there are no signs of IARs, gradually increase the infusion rate every 30 minutes to the subsequent step.

*The 5-step process should be used only for subsequent infusions.

# RECONSTITUTION

## Use aseptic technique during preparation[1]

## STEP 3

**A**

Remove the required number of NEXVIAZYME vials from the refrigerator and allow the vials to sit for 30 minutes at room temperature 20°C to 25°C (68°F to 77°F) before use.[1]
(See page 2 to determine the number of vials.)

**B**

Reconstitute each vial by injecting 10 mL of sterile water for injection (SWFI), down the inside wall of each vial.[1]

- Avoid adding the SWFI to the vial forcefully or directly onto the lyophilized powder to minimize foaming[1]

**C**

- Gently tilt and roll each vial to enhance the dissolution process[1]
- Do not invert, swirl, or shake the vial[1]
- Allow the solution to become dissolved[1]
- Each vial will yield a concentration of 100 mg/10 mL (10 mg/mL) of avalglucosidase alfa-ngpt[1]

## STEP 4

Perform an immediate visual inspection of the reconstituted solution in vials for particulate matter and discoloration.[1]

- Reconstituted solution should be clear, colorless to pale yellow[1]
- Do not use if solution is discolored or if opaque particles are observed[1]

**Acceptable**
Clear, colorless to pale yellow

**Not acceptable**
Discolored, opaque particles, or foreign matter

### Storage of the reconstituted solution[1]

Dilute the reconstituted solution without delay.

- If the reconstituted solution is not diluted immediately, refrigerate at 36°F to 46°F (2°C to 8°C) for up to 24 hours
- Do not freeze

# DILUTION

## STEP 5

Reconstituted NEXVIAZYME solution should be diluted in D5W to a final concentration of 0.5 mg/mL to 4 mg/mL (see page 3 for infusion rates and volumes).[1]

**A**

Check the volume for dilution from step 1 (eg, 84 mL). Select an appropriate size 5% dextrose injection infusion bag. Prepare by removing a volume equal to the required NEXVIAZYME volume and any overfill to achieve a fixed total volume based on actual body weight.[1]

**B**

Slowly withdraw the required volume of reconstituted solution from the NEXVIAZYME vial(s). Discard any unused reconstituted solution remaining in the vial.[1]

**C**

Gently inject the NEXVIAZYME reconstituted solution into the port of the 5% dextrose injection bag.[1]

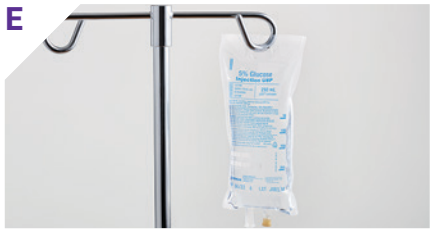
- Avoid foaming or agitation of the infusion bag[1]
- Avoid introducing air into the infusion bag[1]

**D**

Gently invert the infusion bag to mix the solution.[1]

- Do not shake[1]
- After dilution, the solution will have a final concentration of 0.5 to 4 mg/mL of NEXVIAZYME[1]

**E**



Administer the diluted solution without delay.[1]

- The recommended infusion duration is between 4 to 7 hours depending on the dose[1]
- Discard any unused diluted solution after 9 hours[1]

All images shown are for illustrative purposes. The actual images of product and supplies may vary.

### Storage of the diluted solution[1]

If the diluted solution is not used immediately, refrigerate the diluted solution at 36°F to 46°F (2°C to 8°C) for up to 24 hours.

- The diluted solution must be infused within 9 hours after removal from the refrigerator, inclusive of infusion time, or discarded
- If the diluted solution was refrigerated, allow solution to equilibrate to room temperature for 30 minutes prior to infusion
- Once the diluted solution is removed from the refrigerator, it must not be restored back into the refrigerator
- Do not freeze

# ADMINISTRATION

## Infusion rate overview

NEXVIAZYME should be administered incrementally as determined by patient response and comfort.[1]

## WHEN THE RECOMMENDED DOSE IS 20 MG/KG

### Initial and subsequent infusions[2]

The recommended starting infusion rate is 1 mg/kg/hour. If there are no signs of IARs, gradually increase the infusion rate every 30 minutes in each of the following 4 steps:

| 1 mg/kg/hour | 3 mg/kg/hour | 5 mg/kg/hour | 7 mg/kg/hour |
|---|---|---|---|

Then maintain the infusion rate at 7 mg/kg/hour until the infusion is complete. The approximate total infusion duration is 4 to 5 hours.

## WHEN THE RECOMMENDED DOSE IS 40 MG/KG

### Initial infusion[2]

The recommended starting infusion rate is 1 mg/kg/hour. If there are no signs of IARs, gradually increase the infusion rate every 30 minutes in each of the following 4 steps:

| 1 mg/kg/hour | 3 mg/kg/hour | 5 mg/kg/hour | 7 mg/kg/hour |
|---|---|---|---|

Then maintain the infusion rate at 7 mg/kg/hour until the infusion is complete (4-step process). The approximate total infusion duration is 7 hours.

### Subsequent infusions[2]

The recommended starting infusion rate is 1 mg/kg/hour, with gradual increase in infusion rate every 30 minutes if there are no signs of IARs. The process may use either the above 4-step process or the following 5-step process:

| 1 mg/kg/hour | 3 mg/kg/hour | 6 mg/kg/hour | 8 mg/kg/hour | 10 mg/kg/hour |
|---|---|---|---|---|

Then maintain the infusion rate at 10 mg/kg/hour until the infusion is complete. The approximate total 5-step infusion duration is 5 hours.

## Infusion process

1 Explain the administration procedure to the patient.

2 Obtain vital signs prior to and during the infusion.

3 Prior to NEXVIAZYME administration, HCP to consider pretreating with antihistamines, antipyretics, and/or corticosteroids.[1]

4 Obtain IV access.
**NOTE:** Do not infuse NEXVIAZYME in the same IV line with other products.[1]

5 Complete any required blood work.

6 Prime the line with D5W.

7 Set up and prime the administration set with the NEXVIAZYME infusion solution. Use care to prevent the appearance of air bubbles in the tubing.

8 Connect the NEXVIAZYME solution administration set to the 0.2 micrometer, **low-protein-binding filter** and prime the line to minimize air bubbles.[1]

9 Administer infusions in a stepwise manner using an infusion pump.*

10 When the infusion is complete, flush with D5W to ensure that entire dose of NEXVIAZYME is administered. **Flush should not be pushed (IVP) and should be continued at the last tolerated dose.** Discard any unused diluted product after 9 hours.[1]

11 Appropriate length of post-infusion monitoring is to be determined by the treating physician and/or infusion center's protocol.

*It is recommended that the infusion be performed with the use of a programmable IV infusion pump.

# SAMPLE PHYSICIAN ORDER

*Scan the QR code to receive a copy of this form*

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

Patient Name: _____ Diagnosis: _____

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

Today's Date: _____

Notify Dr. _____ at pager _____ when patient arrives.

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**1.** Obtain and record patient weight (kg) above.

**2.** Obtain vital signs prior to infusion.

**3.** Prepare:

☐ 20 mg/kg (for patients weighing ≥30 kg) avalglucosidase alfa-ngpt in 5% dextrose injection, to a total volume of _____ mL.

☐ 40 mg/kg (for patients weighing <30 kg) avalglucosidase alfa-ngpt in 5% dextrose injection, to a total volume of _____ mL.

**Monitor vital signs during NEXVIAZYME infusion as prescribed by the healthcare provider. It is recommended that patients susceptible to fluid volume overload, or those with acute underlying respiratory illness or compromised cardiac or respiratory function for whom fluid restriction is indicated, have more frequent monitoring of vitals.**

**4.** Pre-treatment medication: _____

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

a. Begin the infusion at rate of 1 mg/kg/hr ( _____ mL/hr) and administer for at least 30 minutes.
If no signs of IARs...

b. Increase the infusion rate to _____ mg/kg/hr ( _____ mL/hr) and administer for at least 30 minutes.
If no signs of IARs...

c. Increase the infusion rate to _____ mg/kg/hr ( _____ mL/hr) and administer for at least 30 minutes.
If no signs of IARs...

d. Increase the infusion rate to _____ mg/kg/hr ( _____ mL/hr) and administer at this rate for the remainder of the infusion if 4-step process. If 5-step process, this rate should be administered for at least 30 minutes.
If no signs of IARs...

e. If 5-step process, increase the infusion rate to _____ mg/kg/hr ( _____ mL/hr) and administer at this rate for the remainder of the infusion.

**6.** Flush infusion line with 5% dextrose per institution's protocol.

**7.** Obtain vital signs _____ hours after completion of the infusion. Some patients may require prolonged observation times.

Contact Dr. _____ immediately in the event of a hypersensitivity reaction or infusion-associated reaction.

To report **suspected adverse reactions**, contact Sanofi at 1-800-745-4447, option 2 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Physician's Signature: _____ MD Date: _____

Pager Number:

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This sample order is a template and is intended to serve as an informational resource only. It does not include all of the information that may be necessary. The provider is responsible for ensuring the accuracy, adequacy, and supportability of all information provided. Sanofi is not a healthcare provider and does not provide medical diagnoses or treatment. Determining the information to include in an order is solely the responsibility of the provider.

## IMPORTANT REMINDERS

- Follow your institution's policy for IV insertion and medication infusion[1]
- Infusion reactions can occur.[1] In this event, the infusion rate may be slowed and/or temporarily stopped. In the event of a severe hypersensitivity reaction (including anaphylaxis) or a severe infusion-associated reaction, immediately discontinue NEXVIAZYME administration and administer appropriate medical treatment[1]

**To report adverse event(s) and/or pregnancy complications occurring in association with the use of NEXVIAZYME, please contact Sanofi Medical Information.**

**1-800-745-4447, option 2**

## INDICATION AND IMPORTANT SAFETY INFORMATION

### INDICATION

NEXVIAZYME (avalglucosidase alfa-ngpt) is indicated for the treatment of patients 1 year of age and older with late-onset Pompe disease [lysosomal acid alpha-glucosidase (GAA) deficiency].

### IMPORTANT SAFETY INFORMATION

**WARNING: SEVERE HYPERSENSITIVITY REACTIONS, INFUSION-ASSOCIATED REACTIONS, and RISK OF ACUTE CARDIORESPIRATORY FAILURE IN SUSCEPTIBLE PATIENTS**

**Hypersensitivity Reactions Including Anaphylaxis**

**Patients treated with NEXVIAZYME have experienced life-threatening hypersensitivity reactions, including anaphylaxis. Appropriate medical support measures, including cardiopulmonary resuscitation equipment, should be readily available during NEXVIAZYME administration. If a severe hypersensitivity reaction (e.g., anaphylaxis) occurs, NEXVIAZYME should be discontinued immediately and appropriate medical treatment should be initiated. In patients with severe hypersensitivity reaction, a desensitization procedure to NEXVIAZYME may be considered.**

**Infusion-Associated Reactions (IARs)**

**Patients treated with NEXVIAZYME have experienced severe IARs. If severe IARs occur, consider immediate discontinuation of NEXVIAZYME, initiation of appropriate medical treatment, and the benefits and risks of readministering NEXVIAZYME following severe IARs. Patients with an acute underlying illness at the time of NEXVIAZYME infusion may be at greater risk for IARs. Patients with advanced Pompe disease may have compromised cardiac and respiratory function, which may predispose them to a higher risk of severe complications from IARs.**

**Risk of Acute Cardiorespiratory Failure in Susceptible Patients**

**Patients susceptible to fluid volume overload, or those with acute underlying respiratory illness or compromised cardiac or respiratory function for whom fluid restriction is indicated may be at risk of serious exacerbation of their cardiac or respiratory status during NEXVIAZYME infusion. More frequent monitoring of vitals should be performed during NEXVIAZYME infusion.**

### WARNINGS AND PRECAUTIONS

**Hypersensitivity Reactions Including Anaphylaxis:** See Boxed WARNING. Prior to NEXVIAZYME administration, consider pretreating with antihistamines, antipyretics, and/or corticosteroids. The risks and benefits of readministering NEXVIAZYME following severe hypersensitivity reaction (including anaphylaxis) should be considered. If a mild or moderate hypersensitivity reaction occurs, the infusion rate may be slowed or temporarily stopped.

**Infusion-Associated Reactions:** See Boxed WARNING. IARs may still occur in patients after receiving pretreatment. If mild or moderate IARs occur regardless of pretreatment, decreasing the infusion rate or temporarily stopping the infusion may ameliorate the symptoms.

**Risk of Acute Cardiorespiratory Failure in Susceptible Patients:** See Boxed WARNING.

### ADVERSE REACTIONS

The most common adverse reactions (>5%) were headache, fatigue, diarrhea, nausea, arthralgia, dizziness, myalgia, pruritus, vomiting, dyspnea, erythema, paresthesia and urticaria.

**Please see accompanying full Prescribing Information, including Boxed WARNING.**

**References: 1.** NEXVIAZYME (avalglucosidase alfa-ngpt) [prescribing information]. Genzyme Corporation, Cambridge, MA.
**2.** Data on file. Genzyme Corporation.

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**Please see Important Safety Information on back cover and accompanying full Prescribing Information, including Boxed WARNING.**

Nexviazyme® (avalglucosidase alfa-ngpt)