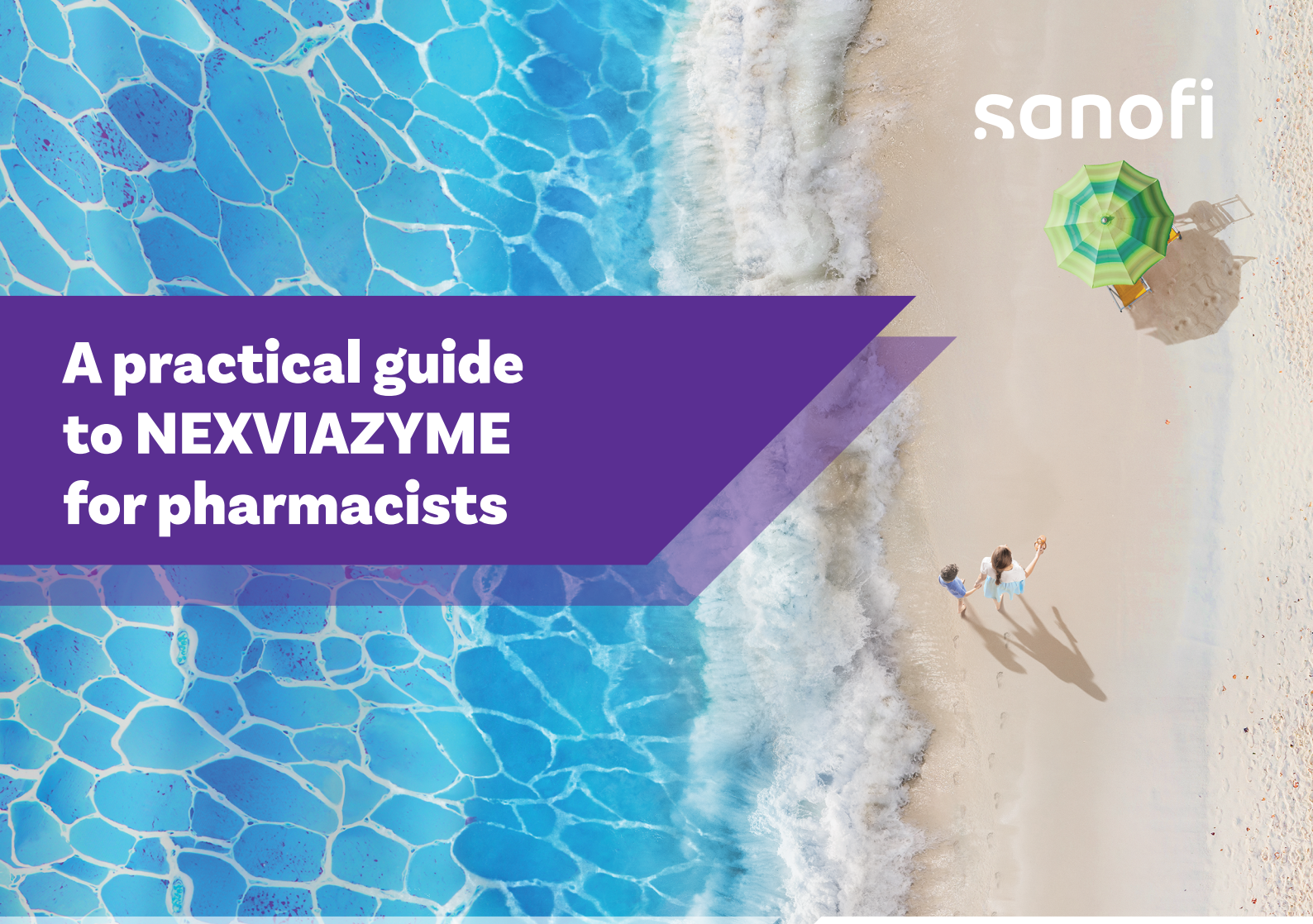
A practical guide to NEXVIAZYME for pharmacists



NEXVIAZYME is indicated for long-term enzyme replacement therapy for the treatment of patients one year of age and older with Pompe disease (acid α-glucosidase deficiency).[1]

Nexviazyme® (avalglucosidase alfa)

▼ This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

What is NEXVIAZYME?[1]

NEXVIAZYME replaces the GAA enzyme, which is lacking or dysfunctional in people living with Pompe disease. It has the same mechanism of action as MYOZYME®. Upon uptake, the GAA enzyme can degrade and clear lysosomal glycogen to help prevent irreversible muscle damage.

Myozyme® (alglucosidase alfa-rch)

For patients <1 year of age[2]

Infants (Infantile-onset)

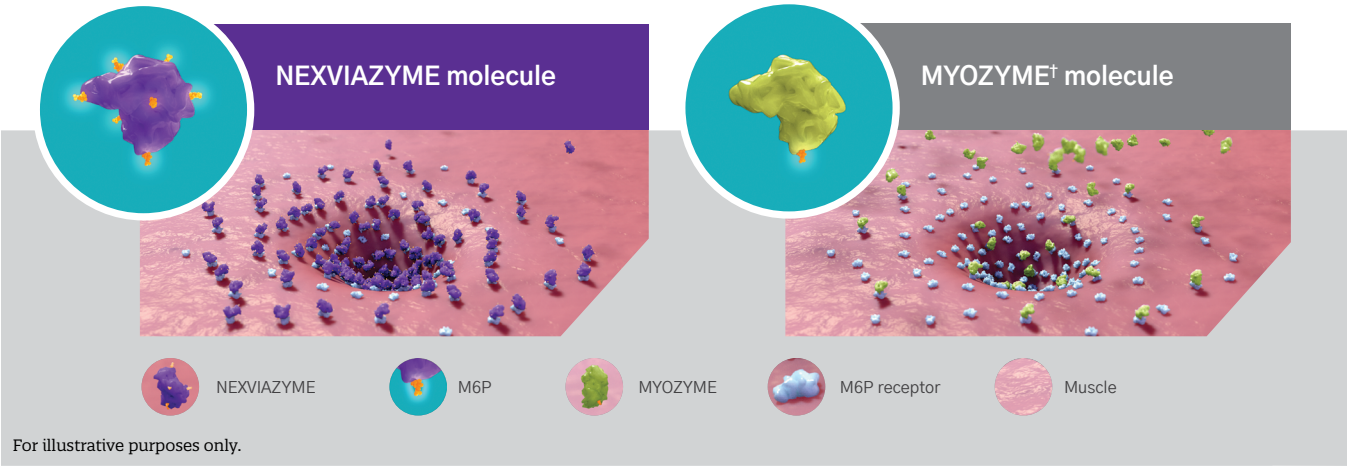
Children and adults (Late-onset)

Nexviazyme® (avalglucosidase alfa)

An ERT for patients ≥1 year of age[1]

NEXVIAZYME is an innovative ERT enhanced with 15x more mannose-6-phosphate (M6P) moieties vs MYOZYME, for increased uptake into muscle cells[1,3,4*]

*NEXVIAZYME displayed increased uptake into murine cells versus MYOZYME (P-value not assessed). Animal data does not necessarily predict clinical effects.



†MYOZYME was the first ERT approved for the treatment of Pompe disease.[5]

NEXVIAZYME compared with MYOZYME

EFFICACY OUTCOMES

Favourable improvements in their motor and respiratory function at Week 97 as compared to MYOZYME:[1]

- 2.43% improvement in predicted FVC (primary endpoint) (*P*=0.06, not significant)[‡§]
- 30-metre gain in 6MWT (secondary endpoint) (nominal *P*=0.04)[§¶]

SAFETY MEASURES

Fewer patients with LOPD experienced IARs and SARs with NEXVIAZYME as compared to MYOZYME (P-value not assessed)[1§]

SIMPLE TO START OR SWITCH

Simplified preparation with 100 mg of medication per vial with NEXVIAZYME vs 50 mg per vial for MYOZYME:[1,2]

‡LS mean; 95% CI, -0.13, 4.99. Mean (SD) pre-treatment baseline FVC % predicted values were 62.5 (14.4) and 61.6 (12.4) for the NEXVIAZYME and MYOZYME treatment groups, respectively. The difference in respiratory function improvements exceeded the predefined noninferiority margin of -1.1 and achieved statistical noninferiority (*P*=0.0074).[1]

§Phase 3, randomised, double-blind study in patients with LOPD (N=100). Patients were naïve to treatment, aged 3 years or older at baseline, and were randomised 1:1 to receive 20 mg/kg of NEXVIAZYME or MYOZYME every 2 weeks for 49 weeks.[1,6]

¶LS mean; 95% CI, 1.33, 58.69. Mean (SD) pre-treatment baseline 6MWT distances were 399.3 m (110.9 m) and 378.1 m (116.2 m) for the NEXVIAZYME and MYOZYME treatment groups, respectively.[1]

NEXVIAZYME safety profile[1]

The safety of NEXVIAZYME has been evaluated across four clinical trials. The most common adverse drug reactions (>5%) associated with NEXVIAZYME were headache, nausea, pruritus, rash, urticaria, fatigue and chills.

Undesirable effects

- In clinical studies, IARs were reported to occur in patients at any time during and/or within a few hours after the infusion of NEXVIAZYME and were more likely with higher infusion rates
- 3 (2.2%) patients reported severe IARs including symptoms of chest discomfort, nausea, and increased blood pressure

Immunogenicity

- Treatment-emergent ADAs were reported in both treatment-naïve (95%) and treatment-experienced patients (49%). In the COMET trial, ADAs did not impact measures of efficacy while limited impacts on pharmacokinetics and pharmacodynamics were observed primarily with high-titre patients
- In adult patients with LOPD, 1 treatment-naive patient and 1 treatment-experienced patient developed anaphylaxis
- In paediatric patients with IOPD or LOPD, no patients developed anaphylactic reactions

NEXVIAZYME dosing and administration[1]

NEXVIAZYME is a monotherapy administered every other week via intravenous infusion, supervised by an experienced physician in the management of Pompe disease[1]

Calculating the correct dose of NEXVIAZYME

✓ **SELECT** dosage for intravenous infusion based on patient phenotype

20 mg/kg — **IOPD/LOPD:** Intravenous infusion every other week

40 mg/kg — **IOPD:*** Intravenous infusion every other week

*With insufficient control or declining response at the lower dose.

✓ **CALCULATE** the number of required vials based on individual patient weight and dosage:

- Total patient dose (mg) = Total patient weight (kg) × dose by phenotype (mg/kg)
- Total vial count (round up to the nearest whole vial) = $\frac{\text{total patient dose (mg)}}{\text{vial concentration (100 mg/vial)}}$

EXAMPLES:

	Patient weight (kg)		Dose (mg/kg)		Patient dose (mg)	Patient dose (mg) 100 (mg/vial)	Vials to reconstitute
Example 1	16	x	20	=	320	3.2 vials	4
Example 2	16	x	40	=	640	6.4 vials	7

Ensure recorded weight is up to date for accurate dosage

Supplies and equipment needed for infusion

- ☐ **NEXVIAZYME single-use vials** (see previous page for dose calculation)
- ☐ **Intravenous (IV) administration set** with 0.2 µm, low-protein-binding, in-line filter
- ☐ **Sterile water for injection,** for reconstitution—10 mL for each vial
- ☐ **5% dextrose in water** for dilution
- ☐ **Syringes and needles**—diameter not larger than 20-gauge-calibre for reconstitution and dilution
- ☐ Additional supplies per institution protocol

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

Reconstitution and dilution in 10 steps[1]

Reconstitution

NOTE: Use aseptic technique during preparation.

STEP 1

Remove the required number of vials needed for the infusion from the refrigerator and set aside for approximately 30 minutes to allow them to reach room temperature.

STEP 2

Reconstitute each vial by slowly injecting 10 mL of sterile water for injection (SWFI) into each vial.

- Inject SWFI by a slow drop-wise addition of the diluent down the inside of the vial and not directly onto the lyophilised powder
- Avoid forceful impact of the diluent on the lyophilised powder and avoid foaming

STEP 3

Tilt and roll each vial gently.

- Do not invert, swirl, or shake
- Allow the solution to become dissolved
- After reconstitution, each vial will yield 100 mg/10 mL (10 mg/mL) of NEXVIAZYME

Acceptable
Clear, colourless to pale yellow

Not acceptable
Discoloured, opaque particles, or foreign matter

STEP 4

Perform an immediate visual inspection of the reconstituted solution in vials for particulate matter and discolouration.

- Reconstituted solution should be clear, colourless to pale yellow
- Do not use if solution is discoloured or if opaque particles are observed

Dilution - Dilute in 5% dextrose in water immediately after reconstitution to a final concentration of 0.5 to 4 mg/mL NEXVIAZYME

STEP 5

Calculate the total volume of reconstituted NEXVIAZYME solution required (calculated according to patient's weight).

STEP 6

Check the volume for dilution.

- Remove and discard excess 5% dextrose in water solution (equivalent to the volume of reconstituted NEXVIAZYME solution).
- Remove air from inside the infusion bag to reduce the risk of foam or protein particle formation.

STEP 7

Slowly withdraw the volume of reconstituted solution from each vial (calculated according to patient's weight).

STEP 8

The reconstituted solution should be diluted slowly and directly into 5% dextrose in water.

- Make up the recommended total infusion volume based on the patient's weight
- Avoid foaming or agitation of the infusion bag, and avoid air introduction into the infusion bag
- Discard any unused reconstituted solution remaining in the vial

STEP 9

Mix the contents of the infusion bag by gently inverting or massaging the infusion bag. Do not shake.

Infusion volumes and rates

Table 1 Projected intravenous infusion volumes for Nexviazyme administration by patient weight at 20 and 40 mg/kg dose

PATIENT WEIGHT RANGE (kg)	TOTAL INFUSION VOLUME FOR 20 MG/KG (mL)	TOTAL INFUSION VOLUME FOR 40 MG/KG (mL)
5.1 to 10	50	100
10.1 to 20	100	200
20.1 to 30	150	300
30.1 to 35	200	400
35.1 to 50	250	500
50.1 to 60	300	600
60.1 to 100	500	1000
100.1 to 120	600	1200
120.1 to 140	700	1400
140.1 to 160	800	1600
160.1 to 180	900	1800
180.1 to 200	1000	2000

Table 2 Infusion rate schedule*

PATIENT		INFUSION RATE (mg/kg/hour)					APPROXIMATE DURATION (h)
		Step 1	Step 2	Step 3	Step 4	Step 5	
LOPD		1	3	5	7	n/a	4 to 5
IOPD	4-step process	1	3	5	7	n/a	7
	5-step process	1	3	6	8	10	5

*Optimal infusion rate should be determined for each patient as per the clinical site protocol.

Important reminders

- Follow your institution's policy for IV insertion and medication infusion.
- Infusion reactions can occur. In this event the infusion rate may be slowed and/or temporarily stopped. Administration of additional antipyretics, antihistamines, and/or corticosteroids may help prevent or reduce allergic reactions.

To report adverse event(s) and/or pregnancy complications occurring in association with the use of NEXVIAZYME, please call 1800 818 806 within Australia

Storage[1]

Can be stored **up to 24 hours** in a refrigerator (2°C to 8°C) and **up to 9 hours** (including infusion time) when stored at room temperature (up to 25 °C)

Once the diluted solution is removed from the refrigerator, **it cannot be re-stored in the refrigerator**

Completely infuse the diluted solution within **9 hours** after removal from the refrigerator

Discard the diluted solution if refrigerated for **more than 24 hours** or if the diluted solution is not able to be completely infused **within 9 hours** after removal from the refrigerator

Do not freeze

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ADAs, antidrug antibodies; ERT, enzyme replacement therapy; GAA, acid alpha-glucosidase; IAR, infusion associated reaction; IOPD, infantile-onset Pompe disease; LOPD, late-onset Pompe disease; M6P, mannose-6-phosphate.

PBS Information: NEXVIAZYME and MYOZYME are not listed on the PBS. These products are funded under the Life Saving Drugs Program.

Please review full Product Information before prescribing.
Full NEXVIAZYME Product Information is available from sanofi-aventis australia pty ltd at https://bit.ly/nexviazyme-pi or by contacting 1800 818 806. Full MYOZYME Product Information is available from sanofi-aventis australia pty ltd at https://bit.ly/myozyme-pi or by contacting 1800 818 806.

MINIMUM PRODUCT INFORMATION: Nexviazyme (avalglucosidase alfa) INDICATIONS: Nexviazyme is indicated for long-term enzyme replacement therapy for the treatment of patients one year of age and older with Pompe disease (acid α-glucosidase deficiency). **DOSAGE AND ADMINISTRATION:** The recommended dose of Nexviazyme is 20 mg/kg of body weight administered every other week as an intravenous infusion. Dose escalation to 40 mg/kg every other week may be considered for patients with infantile onset Pompe disease (IOPD) who experience insufficient control or declining response at the lower dose. Home administration by a trained health care professional may be considered for individual patients after safety and tolerability has been established in the clinical setting. **CONTRAINDICATIONS:** Life-threatening hypersensitivity to the active substance or to any of the excipients when re-challenge was unsuccessful. **PRECAUTIONS:** Hypersensitivity, infusion associated reactions (IARs), anaphylaxis, immunogenicity, monitor for IgG and IgE antibodies, cardiac hypertrophy, compromised cardiac and respiratory function. Refer to full PI. **INTERACTIONS:** No interaction studies have been performed. **ADVERSE EFFECTS:** Serious adverse reactions include headache, dyspnoea, respiratory distress, nausea, skin discoloration, chills, erythema, chest discomfort, pyrexia, blood pressure increase, body temperature increase, heart rate increase, and oxygen saturation decrease. Common IARs include chills, cough, diarrhoea, erythema, fatigue, headache, influenza-like illness, nausea, ocular hyperaemia, pain in extremity, pruritus, rash, rash erythematous, tachycardia, urticaria, vomiting, chest discomfort, dizziness, hyperhidrosis, lip swelling, pain, palmar erythema, swollen tongue and tremor. Refer to full PI. **NAME OF SPONSOR:** sanofi-aventis australia pty ltd, 12-24 Talavera Road, Macquarie Park, NSW 2113. Based on Full Product Information with TGA date of approval of 22 June 2023. Date of Preparation: 22 June 2023.

Minimum Product Information MYOZYME (Alglucosidase alfa 52.5 mg per 50 mg vial) INDICATION: Long-term treatment of patients with a confirmed diagnosis of Pompe disease (acid alfa-glucosidase deficiency). **DOSAGE AND ADMINISTRATION:** 20 mg/kg administered once every 2 weeks as an intravenous infusion, initial infusion rate 1mg/kg/hr, infusion rate may be increased by 2 mg/kg/hr every 30 minutes, after patient tolerance to the infusion rate is established, until the maximum rate of 7 mg/kg/hr – see full PI. Dilute prior to use – see full PI. Does not contain preservatives. Use within 24 hours of infusion preparation. **CONTRAINDICATIONS:** Hypersensitivity to the active or any of the excipients. **PRECAUTIONS:** Hypersensitivity, anaphylaxis, infusion reaction history, underlying cardiac hypertrophy, compromised cardiac and respiratory function, monitor for IgG antibodies, monitor following infusion, pregnancy (category B1), lactation, prior history of anaphylactoid reactions. No clinical experience in patients under 1 month or patients older than 65 years. Renal and hepatic impairment. See full PI. **INTERACTIONS:** No drug interaction data. **ADVERSE EFFECTS:** Hypersensitivity; anaphylactoid reactions, infusion and post-infusion reactions, flushing, fever, headache, rash, bronchospasm, wheezing, acute cardiorespiratory failure, cardiac arrest, decreased oxygen saturation, hypotension, oedema, nephrotic syndrome - see full PI. **NAME OF SPONSOR:** sanofi-aventis australia pty ltd, 12-24 Talavera Road, Macquarie Park, NSW 2113.

References: 1. NEXVIAZYME Australian Approved Product Information. **2.** MYOZYME Australian Approved Product Information. **3.** Zhu Y et al. Mol Ther 2009; 17(6): 954–63. **4.** Zhu Y et al. Biochem J 2005; 389(3): 619–28. **5.** van der Ploeg A et al. N Engl J Med 2010; 362(15): 1396–406. **6.** Diaz-Manera J et al. Lancet Neurol 2021;20:1012-26.

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Nexviazyme®
(avalglucosidase alfa)