Nexviadyme®
(avalglucosidase alfa)

PREPARATION AND ADMINISTRATION GUIDE

Nexviadyme is indicated for long-term enzyme replacement therapy for the treatment of patients with Pompe disease (acid α-glucosidase deficiency).

Supplies and equipment

- ☐ **Nexviadyme single-use vials** (see next 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% glucose[a] in water** for injection, for dilution
- ☐ **Syringes and needles**—diameter not larger than 20-gauge–caliber—for reconstitution and dilution
- ☐ Additional supplies per institution protocol

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

[a]5% dextrose and 5% glucose are interchangeable in some countries. Refer to your full local prescribing information before prescribing.

PREPARATION
Use aseptic technique during preparation

STEP 1

Determine the number of vials to be reconstituted based on the individual patient's weight and the **recommended dosages of 20 mg/kg every other week for late-onset Pompe disease (LOPD) and 40 mg/kg every other week for infantile-onset Pompe disease (IOPD).** Round up to the nearest whole vial.

DOSE CALCULATION				
		CALCULATION	EXAMPLES	
			LOPD	IOPD
DOSE	=	Total patient weight (kg) × dose by phenotype (mg/kg)	42 kg × 20 mg/kg = 840 mg	11 kg × 40 mg/kg = 440 mg
VIALS TO RECONSTITUTE (round up to the nearest whole vial)	=	$\frac{\text{Total patient dose (mg)}}{\text{vial concentration (100 mg/vial)}}$	$\frac{840\text{ mg}}{100\text{ mg/vial}} = 8.4$ vials round up to 9 total vials	$\frac{440\text{ mg}}{100\text{ mg/vial}} = 4.4$ vials round up to 5 total vials
RECONSTITUTED VOLUME	=	$\frac{\text{Total patient dose (mg)}}{10\text{ mg/mL}}$	$\frac{840\text{ mg}}{10\text{ mg/mL}} = 84$ mL	$\frac{440\text{ mg}}{10\text{ mg/mL}} = 44$ mL

STEP 2

Remove required number of vials from refrigerator and allow to reach room temperature (approximately 30 minutes).

Reconstitute each vial by slowly injecting 10 mL of sterile water along the glass wall in each vial. Avoid forceful impact of the sterile water on the powder and avoid foaming. Each vial will yield 100 mg/10 mL (10 mg/mL).

Tilt and roll each vial gently. Do not invert, swirl, or shake.

Please see the Full Summary of Product Characteristics for more information on Nexviadyme.

STEP 3

Perform an immediate visual inspection on the reconstituted vials. Do not use if the solution is discolored or if opaque particles are observed.

Acceptable
Clear, colorless to pale yellow

Not acceptable
Discolored, opaque particles, or foreign matter

STEP 4

Reconstituted Nexviadyme solution should be diluted in 5% glucose in water to a final concentration of 0.5 mg/mL to 4 mg/mL (see infusion volumes/rates in tables 1 and 2).

A

Remove the volume of Nexviadyme solution to be diluted from the 5% glucose in water for infusion bag.

B

Slowly withdraw the volume of reconstituted solution from each vial.

C

Add the reconstituted solution slowly and directly into the 5% glucose in water.

D

Gently invert or massage the infusion bag to mix. Do not shake. Protect from light.

E

It is recommended to use an in-line filter to administer Nexviadyme. After infusion, flush the infusion line with 5% glucose in water.

All images shown are for illustrative purposes. The actual images of product and supplies may vary due to local country's approval and regulations.

ADMINISTRATION

Infusion rate overview

Nexviadyme should be administered incrementally as determined by patient response and comfort over approximately 4 to 5 hours for patients with LOPD and 5 hours for patients with IOPD.

For patients with LOPD and IOPD, it is recommended that the infusion begins at an initial rate of 1 mg/kg/hour and is gradually increased every 30 minutes if there are no signs of infusion-associated reactions (IARs), until a maximum rate of 7 mg/kg/hour (for patients with LOPD) and 10 mg/kg/hour (for patients with IOPD) is reached (see tables 1 and 2).[a] Vital signs should be obtained at each step before increasing the infusion rate.

Patients with an acute underlying illness at the time of Nexviadyme infusion appear to be at greater risk of IARs. Careful consideration should be given to the patient's clinical status prior to administration of Nexviadyme.

NOTE: Do not infuse Nexviadyme in the same IV line with other products.

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

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

Infusion process

1. Explain the administration procedure to the patient.
2. Obtain vital signs prior to and during the infusion.
3. Obtain IV access.
4. Complete any required blood work; flush line with 5% glucose in water.
5. Initiate primary infusion line of 5% glucose in water to maintain patency of IV access.
6. Set up and prime the administration set with the Nexviadyme infusion solution. Use care to prevent the appearance of air bubbles in the tubing.
7. Connect the Nexviadyme solution administration set to the 0.2 µm, low-protein-binding, in-line filter set and prime the line to minimize air bubbles.
8. Connect the Nexviadyme solution line to the lowest additive port on the patient's primary administration set.
9. Administer infusions in a stepwise manner using an infusion pump.[b]
10. When the infusion is complete, flush with 5% glucose in water to ensure that entire dose of Nexviadyme is administered.
11. Remove the administration set; dispose in accordance with local requirements.

Faster preparation with twice as much medication per vial in Nexviadyme vs MYOZYME® (alglucosidase alfa)

Nexviadyme® (avalglucosidase alfa)

Infusion volumes and rates

Table 1: LOPD — Recommended infusion volumes and infusion rates for 20 mg/kg dose[a]

RECOMMENDED INFUSION VOLUME				RECOMMENDED RATES OF INFUSION			
PATIENT WEIGHT (kg)	DOSE (mg/kg)	TOTAL INFUSION VOLUME (mL)	PROTEIN CONCENTRATION (mg/mL)	STEP 1 1 mg/kg/hour (mL/hour)	STEP 2 3 mg/kg/hour (mL/hour)	STEP 3 5 mg/kg/hour (mL/hour)	STEP 4 7 mg/kg/hour (mL/hour)
1.25 to 10	20	50	0.5-4	3	8	13[b]	18[b]
10.1 to 20	20	100	2.02-4	5	15	25	35
20.1 to 30	20	150	2.68-4	8	23	38	53
30.1 to 35	20	200	3.01-3.5	10	30	50	70
35.1 to 50	20	250	2.81-4	13	38	63	88
50.1 to 60	20	300	3.34-4	15	45	75	105
60.1 to 100	20	500	2.40-4	25	75	125	175
100.1 to 120	20	600	3.34-4	30	90	150	210
120.1 to 140	20	700	3.43-4	35	105	175	245
140.1 to 160	20	800	3.5-4	40	120	200	280
160.1 to 180	20	900	3.56-4	45	135	225	315
180.1 to 200	20	1000	3.60-4	50	150	250	350

Table 2: IOPD — Recommended infusion volumes and infusion rates for 40 mg/kg dose[a]

RECOMMENDED INFUSION VOLUME				RECOMMENDED RATES OF INFUSION				
PATIENT WEIGHT (kg)	DOSE (mg/kg)	TOTAL INFUSION VOLUME (mL)	PROTEIN CONCENTRATION (mg/mL)	STEP 1 1 mg/kg/ hour (mL/hour)	STEP 2 3 mg/kg/ hour (mL/hour)	STEP 3 6 mg/kg/ hour (mL/hour)	STEP 4 8 mg/kg/ hour (mL/hour)	STEP 5 10 mg/kg/ hour (mL/hour)
1.25 to 5	40	50	1-4	1.25	3.75	7.5	10	12[c]
5.1 to 10	40	100	2.04-4	2.5	7.5	15	20	25
10.1 to 20	40	200	2.02-4	5	15	30	40	50
20.1 to 30	40	300	2.68-4	7.5	22.5	45	60	75
30.1 to 35	40	400	3.01-3.5	10	30	60	80	100
35.1 to 50	40	500	2.81-4	12.5	37.5	75	100	125
50.1 to 60	40	600	3.34-4	15	45	90	120	150
60.1 to 100	40	1000	2.40-4	25	75	150	200	250
100.1 to 120	40	1200	3.34-4	30	90	180	240	300
120.1 to 140	40	1400	3.43-4	35	105	210	280	350
140.1 to 160	40	1600	3.5-4	40	120	240	320	400
160.1 to 180	40	1800	3.56-4	45	135	270	360	450
180.1 to 200	40	2000	3.60-4	50	150	300	400	500

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

[b]For patients with LOPD with a body weight of 1.25 to 5 kg, a maximum infusion rate of 4.8 mg/kg/hour can be applied.

[c]For patients with IOPD with a body weight of 1.25 to 5 kg, a maximum infusion rate of 9.6 mg/kg/hour can be applied.

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 alleviate symptoms.
- If any questions, please contact our local medical service

Helsepersonell oppfordres til å melde enhver mistenkt bivirkning. Dette gjøres via meldeskjema som finnes på nettsiden til Statens legemiddelverk: www.legemiddelverket.no/meldeskjema.

Du kan i tillegg også kontakte Sanofi på pharmacovigilance. norway@sanofi.com eller på tlf.nr: 46 91 80 01 (kl. 10-14).

Before prescribing the product always refer to your full local prescribing information as this information may vary from country to country.

Nexviadyme (avalglucosidase alfa) - Abbreviated Prescribing Information

Product composition: Nexviadyme 100 mg, powder for concentrate for solution for infusion. Each vial contains 100 mg of avalglucosidase alfa. After reconstitution, each vial contains a total extractable volume of 10.0 ml at a concentration of 10 mg of avalglucosidase alfa per ml. **Indication:** Nexviadyme is indicated for long-term enzyme replacement therapy for the treatment of patients of all ages with Pompe disease (acid α-glucosidase deficiency). **Dosage and administration:** Nexviadyme treatment should be supervised by a physician experienced in the management of patients with Pompe disease or other inherited metabolic or neuromuscular diseases. Patients may be pre-treated with antihistamines, antipyretics, and/or corticosteroids to prevent or reduce allergic reactions. The recommended dose of avalglucosidase alfa is 20 mg/kg of body weight administered once every 2 weeks as an intravenous infusion. Infusion of Nexviadyme at home may be considered for patients who are tolerating their infusions well and have no history of moderate or severe IARs for a few months. ***Special populations:*** Please see full SPC for more information. **Contraindications:** Life-threatening hypersensitivity to the active substance or to any of the excipients listed when re-challenge was unsuccessful. **Special warnings and precautions for use:** *Hypersensitivity reactions (including anaphylaxis):* hypersensitivity reactions, including anaphylaxis, have been reported in Nexviadyme-treated patients. If severe hypersensitivity or anaphylaxis occur, Nexviadyme should be discontinued immediately, and appropriate medical treatment should be initiated. *Infusion-associated reactions (IARs):* in clinical studies, IARs were reported to occur at any time during and/or within a few hours after the infusion of Nexviadyme and were more likely with higher infusion rates. Patients with an acute underlying illness at the time of Nexviadyme infusion appear to 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. Antihistamines, antipyretics, and/or corticosteroids can be given to prevent or reduce IARs. However, IARs may still occur in patients after receiving pre-treatment. If severe IARs occur, immediate discontinuation of the administration of Nexviadyme should be considered and appropriate medical treatment should be initiated. The benefits and risks of re-administering Nexviadyme following severe IARs should be considered. *Immunogenicity:* For warning precautions regarding immunogenicity and risk of acute cardiorespiratory failure, cardiac arrythmia and sudden death during general anesthesia cv catheter placement, please see full SPC. *Risk of acute cardiorespiratory failure:* caution should be exercised when administering Nexviadyme to patients susceptible to fluid volume overload or patients with acute underlying respiratory illness or compromised cardiac and/or respiratory function for whom fluid restriction is indicated. These patients may be at risk of serious exacerbation of their cardiac or respiratory status during infusion. Appropriate medical support and monitoring measures should be readily available during Nexviadyme infusion, and some patients may require prolonged observation times that should be based on the individual needs of the patient. *Cardiac arrhythmia and sudden death during general anaesthesia for central venous catheter placement:* caution should be used when administering general anaesthesia for the placement of a central venous catheter or for other surgical procedures in patients with IOPD with cardiac hypertrophy. Cardiac arrhythmia, including ventricular fibrillation, ventricular tachycardia, and bradycardia, resulting in cardiac arrest or death, or requiring cardiac resuscitation or defibrillation, have been associated with the use of general anaesthesia in IOPD patients with cardiac hypertrophy. Please see full SPC for more information regarding special warnings and precautions for use. **Fertility, pregnancy and lactation:** There are no available data on the use of Nexviadyme in pregnant women or on the presence of Nexviadyme in human milk or the effects of Nexviadyme on milk production or the breast-fed infant. Nexviadyme should be used during pregnancy or breast-feeding only if the potential benefits to the mother outweigh the potential risks, including those to the foetus or breast-fed child. **Undesirable Effects:** Very common (≥10%): Hypersensitivity. Common (≥1% to <10%): Anaphylaxis, Headache, Dizziness, Tremor, Ocular hyperaemia, Hypertension, Cough, Dyspnoea, Nausea, Diarrhoea, Vomiting, Lip swelling, Swollen tongue, Pruritus, Rash, Urticaria, Erythema, Palmer erythema, Muscle spasms, Myalgia, Fatigue, Chills, Chest discomfort, Pain, Influenza-like illness, Infusion site pain, Blood pressure increased and Oxygen saturation decreased. Due to the small patient population, an adverse reaction reported in 2 patients is classified as common. Refer to the full prescribing information for the complete list of undesirable effects, including post-marketing undesirable effects. Health care professionals are asked to report any suspected adverse reactions via their national reporting system.

LEGAL CLASSIFICATION: Prescription only medicine.
Marketing authorisation holder: Genzyme Europe B.V., Paasheuvelweg 25, 1105 BP Amsterdam, The Netherlands. Abbreviated Prescribing Information based on the EU clean product information of June 2022.

Reseptstatus: C. Pakninger og priser: Hetteglass 100 mg, NOK 14,667.62. Refusjon: Nexviadyme er til vurdering i nye metoder. Lokal representant: sanofi-aventis Norge AS, Prof. Kohts vei 5-17, 1325 Lysaker. Fullstendig preparatomtale finnes på www.legemiddelsok.no

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