

- ▼ 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, events of medication errors, pregnancy and breastfeeding at www.tga.gov.au/reporting-problems.

Xenpozyme

(olipudase alfa)

HCP Guide Infusions at Home

(Maintenance Dose Only)

This Guide for HCPs contains important safety information you need to be aware of when preparing and administering treatment with olipudase alfa in a home setting.

Please refer to the Product Information for complete information.

1 – Objectives

- This Guide is designed to support HCPs in managing the following risks associated with the home infusion of olipudase alfa:
 - Immunogenicity: infusion associated reactions (IARs), systemic hypersensitivity including anaphylaxis, anti-drug antibody (ADA) mediated hypersensitivity
 - Medication errors in home infusion setting

2 – What is acid sphingomyelinase deficiency (ASMD)?

- ASMD is a rare and potentially life-threatening lysosomal storage disease that results from reduced activity of the enzyme acid sphingomyelinase (ASM), caused by pathogenic variants in the sphingomyelin phosphodiesterase 1 (SMPD1) gene. ASMD is historically known as Niemann-Pick Disease (NPD) types A and B
- The phenotype spectrum ranges from the severe infantile neurovisceral form (ASMD type A) to the chronic visceral form (ASMD type B), with an intermediate or chronic neurovisceral phenotypic presentation also being described (ASMD type A/B)
- ASM catalyses the hydrolysis of sphingomyelin to ceramide and phosphocholine; the enzymatic deficiency causes an accumulation of sphingomyelin (as well as cholesterol and other cell membrane lipids) in hepatocytes and in cells of the monocyte-macrophage lineage
- Organs in which sphingomyelin accumulates include spleen, liver, bone marrow, lungs, lymph nodes, and brain (in more severe phenotypes)

3 – What is Xenozyme (olipudase alfa)?

- Xenozyme is indicated as an enzyme replacement therapy for the treatment of non-central nervous system manifestations of ASMD in paediatric and adult patients with type A/B or type B
- Xenozyme is recombinant human ASM and it provides an exogenous source of ASM reducing the amount of sphingomyelin that accumulates in organs of patients with ASMD

4 – How to mitigate the important risks associated with olipudase alfa treatment?

4A. Immunogenicity: IARs, systemic hypersensitivity including anaphylaxis, ADA mediated hypersensitivity

- Olipudase alfa is **contraindicated** in patients with life-threatening hypersensitivity (anaphylactic reaction) to olipudase alfa or to any of the excipients
- Olipudase alfa administration **at home** should be **supervised by an HCP** who is trained in emergency measures and has access to appropriate medical support to manage severe reactions, such as those related to systemic hypersensitivity (eg, anaphylaxis)

MONITORING: The patient should be monitored for signs and symptoms of IARs, such as headache, urticaria, pyrexia, nausea and vomiting, and other signs or symptoms of hypersensitivity, closely **during infusion and for an appropriate period of time after the infusion, based on clinical judgment**

- If IARs or SYSTEMIC HYPERSENSITIVITY including ANAPHYLAXIS occur:
 - **Discontinue the infusion immediately** and initiate appropriate medical treatment
 - Seek the attention of a physician
 - Contact the treating physician
- Olipudase alfa treatment should **not be continued at home**
- Subsequent infusion should only occur in a clinical setting where resuscitation measures are available and re-escalation might be considered

4B. Risk of medication errors in home setting

- Prior to treatment administration:
 - Please read both the instructions for use in the Product information and the preparation/infusion manual included in this guide carefully
 - Ensure the availability of the following:
 - Resuscitative equipment
 - Patient information (prescribed maintenance dose, weight)
 - Prescriber contact information
 - Necessary supplies and environment (ie, clean environment with electricity, water, telephone access, refrigeration)
 - Carefully prepare the medication referencing the Product information and this Guide

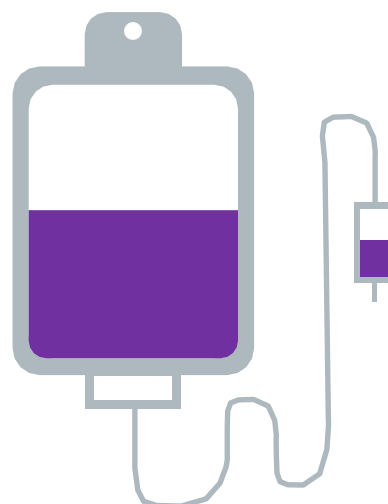
5 – What are the requirements for administration of olipudase alfa at home?

5A. Medical evaluation of the patient before moving to the home infusion setting

- The decision to have patients move to home infusion should be made after evaluation and recommendation by the treating physician.
- **Only patients on maintenance dose who are tolerating their infusions well can be considered for home infusions.**
- **Olipudase alfa can be administered at home only after successful dose escalation in the clinical setting and in agreement with the treating physician.**
- The patient and/or caregiver should be informed that home setting should be stopped and subsequent infusion may occur in a supervised setting for re-escalation:
 - If missed doses or delayed infusion
 - If mild, moderate, or severe IARs or systemic hypersensitivity including anaphylaxis occur

5B. Organisation of home infusion

- Administration of olipudase alfa should be supervised by HCP who is trained in emergency measures and has access to appropriate medical support to manage severe reactions.
- Clinical (treatment dose and scheduling) and logistical aspects should be discussed with the patient and/or caregiver by the treating physician before moving to the home setting.
- Prior to treatment administration, availability of the following should be ensured:
 - Resuscitative equipment
 - Patient information (ie, prescribed maintenance dose, weight, infusion rate, reconstituted volume, premedication, emergency medication)
 - Prescriber contact information (available on the patient card).
 - Necessary supplies and environment (ie, clean environment with electricity, water, telephone access, refrigeration).



5C. Equipment and supplies

- 1 infusion pump, adapted to syringe or infusion bag depending on olipudase alfa dose.
- Vials of olipudase alfa (4 mg or 20 mg per vial); must be stored in a clean refrigerator at a temperature of between 2°C and 8°C.
- Sterile water for injection to reconstitute olipudase alfa vials.
- Sterile NaCl 0.9% solution, infusion bag size depending on olipudase alfa dose, to prepare the final solution for intravenous (IV) administration.
- Sterile NaCl 0.9% solution, to flush infusion line pre- and post-infusion
- In-line low protein-binding 0.2µm filter.
- Infusion-administration set (infusion line).
- Pretreatment medication (if applicable as prescribed).
- Emergency medication (as prescribed).

5D. Pretreatment and emergency treatment

- Appropriate pretreatment and emergency treatment should be provided based on the patient-specific prescription.

6 – How to administer olipudase alfa?

- Olipudase alfa is for IV use only.
- Olipudase alfa should be administered every 2 weeks. In case of missed dose or delayed infusion (i.e. a delay of >3 days), the treating physician should be contacted as subsequent infusions may need to occur in a clinical setting.
- Prior to administration, please follow instructions on reconstitution and dilution (see **Sections 7 and 8**)
- The infusion solution must be filtered through an in-line low protein-binding 0.2µm filter during administration.
- After the infusion is complete, the infusion line should be flushed with NaCl 0.9% solution for injection using the same infusion rate as the one used for the last part of the infusion.

What are the requirements for administration of olipudase alfa at home?

How to administer olipudase alfa?

7 – How to reconstitute and dilute olipudase alfa?

7A. Before reconstitution

- Assess patient's clinical condition on the day of infusion.
 - If the patient presents with an unresolved adverse effect from the previous infusion or has an acute illness, please contact the treating physician.
 - The infusion may be postponed, based on the prescriber's clinical judgment.
- Prepare an IV line.
- Calculate the patient dose (mg) and determine the number of vials to be reconstituted based on the individual patient's weight and the prescribed dose.

Patient dose (mg) = patient weight (kg) x dose (mg/kg)

Number of vials to reconstitute:

- If using 4 mg vial = patient dose (mg) divided by 4 mg/vial
- If using 20 mg vial = patient dose (mg) divided by 20 mg/vial

- If the number of vials includes a fraction, round up to the next whole number.
- Leave the required number of olipudase alfa vials at room temperature for 20–30 minutes.

7B. Reconstitution procedure

- Aseptic technique should be used during reconstitution. Do NOT use any filters during the reconstitution.
- **IMPORTANT: Prevent formation of foam – it will reduce the amount of active enzyme!**



1. For preparation of injectables, inject slowly against the wall of the olipudase alfa vial:

- If using 4 mg vial = 1.1 mL of sterile water
- If using 20 mg vial = 5.1 mL of sterile water



2. Mix gently by rotating the vial between the palms



3. The resulting solution should be transparent, colourless, and clear. Any vials exhibiting opaque particles or discolouration should not be used

4. The resulting solution contains 4 mg of olipudase alfa per 1 mL.

- From a microbiological point of view, the reconstituted solution should be used immediately. If not used for dilution immediately, in-use storage times and conditions prior to dilution should normally not be longer than 24 hours at temperatures between 2°C to 8°C, or 6 hours at room temperature (up to 25°C).

7C. Preparation of the infusion solution (calculation)

- Calculate the volume of reconstituted olipudase alfa needed for the infusion, using the following formula:

$$\bullet \text{ Volume (mL)} = \text{patient dose (mg)} \div 4 \text{ (mg/mL)}$$

- Example 1: A child with body weight of 10 kg on maintenance dose of 3 mg/kg
 - Dose of olipudase alfa needed per infusion is $10 \text{ kg} \times 3 \text{ mg} = 30 \text{ mg}$
 - Therefore, volume of reconstituted olipudase alfa needed per infusion is $30 \text{ mg} \div 4 \text{ mg/mL} = 7.5 \text{ mL}$
- Example 2: An adult with body weight of 65 kg on maintenance dose of 3 mg/kg
 - Dose of olipudase alfa needed per infusion is $65 \text{ kg} \times 3 \text{ mg} = 195 \text{ mg}$
 - Therefore, volume of reconstituted olipudase alfa needed per infusion is $195 \text{ mg} \div 4 \text{ mg/mL} = 48.75 \text{ mL}$
- **Note**: for adults with **body mass index (BMI) > 30 kg/m²**, the amount of olipudase alfa needed for infusion is determined based on theoretical, not actual, body weight
 - The theoretical body weight is calculated as follows: **30 (kg/m²) x height (m²)**
 - For example, an individual who is 1.7 m tall and has BMI = 35 kg/m²; has the actual body weight of 101.2 kg ($35 \text{ kg/m}^2 \times 1.7 \text{ m}^2$), but their **theoretical body weight** is 86.7 kg ($30 \text{ kg/m}^2 \times 1.7 \text{ m}^2$)
 - Dose of olipudase alfa needed per infusion is $86.7 \text{ kg} \times 3 \text{ mg/kg} = 260 \text{ mg}$
 - Therefore, volume of reconstituted olipudase alfa needed per infusion is $260 \text{ mg} \div 4 \text{ mg/mL} = 65 \text{ mL}$

7D. Preparation of infusion solution

- Aseptic technique should be used during reconstitution. Do NOT use any filters during the dilution.
- **Avoid foaming during the dilution steps.**
- If **pre-filled infusion bags** with 0.9% NaCl solution are used:

1. Determine the total infusion volume (see Section 8) and use the pre-filled infusion bag of appropriate size
2. Remove the volume of 0.9% NaCl solution that is equal to the calculated volume of reconstituted olipudase alfa (eg, if 10 mL of reconstituted solution is needed for infusion, first remove and discard 10 mL of NaCl solution)



3. Carefully, collect the calculated amount of reconstituted olipudase alfa solution using a syringe



4. Gently, inject the reconstituted olipudase alfa solution into the infusion bag

- If **empty infusion bags** are used:

1. Determine the total infusion volume (see Section 8) and use the sterile infusion bag of appropriate size
2. Carefully collect the calculated amount of reconstituted olipudase alfa solution using a syringe
3. Gently, inject the reconstituted olipudase alfa solution into the infusion bag



4. Add slowly the sufficient quantity of 0.9% NaCl solution for injection to obtain the required total infusion volume

- **Gently invert infusion bag to mix.** Do not shake. Because this is a protein solution, slight flocculation (described as thin translucent fibres) occurs occasionally after dilution.
- From a microbiological point of view, the diluted solution should be used immediately. If not used immediately after dilution, in-use storage times and conditions should normally not be longer than 24 hours at temperatures between 2°C to 8°C followed by 12 hours (including infusion time) at room temperature (up to 25°C).

8 – Which infusion volumes and infusion rates should be used in children and adults?

CHILDREN

- Determine the total volume of infusion solution and an appropriate delivery container (infusion bag), as described in **Table 1**:
 - Infusion bags: 50, 100, or 250 mL **prefilled with 0.9% NaCl solution** (see **Section 7D**)
 - **Whenever possible, use soft infusion bags to minimise foam formation**
- For children, total infusion volume for the maintenance dose of **3mg/kg** can range from **50 to 250 mL**, depending on the child's body weight

Table 1. Volume of the final olipudase alfa infusion solution to deliver the maintenance dose in children (3mg/kg)

Body weight (kg)	Maintenance dose (mg/kg)	Total infusion volume (mL)	Delivery container
≥3 and <10	3	50	Infusion bag, 50 mL
≥10 and <20	3	100	Infusion bag, 100 mL
≥20	3	250	Infusion bag, 250 mL

- Follow the instructions for calculation of the volume of reconstituted olipudase alfa needed (see **Section 7C**) and for preparation of infusion bags for infusion (see **Section 7D**)
- After preparing infusion solution in the infusion bag, use the following infusion rates to deliver the appropriate maintenance dose (**Table 2**):

Table 2. Olipudase alfa infusion rates: maintenance dose, children (3 mg/kg if no IARs)

Dose (mg/kg)	Infusion steps			Approximate infusion duration (minutes)
	Step	Rate (mg/kg/hour)	Duration (minutes)	
3	1	0.1	20 ± 5	220
	2	0.3	20 ± 5	
	3	0.6	20 ± 5	
	4	1	160 ± 5	

How to reconstitute and dilute Xenpozyme (olipudase alfa)?

Which infusion volumes and rates should be used in children and adults?

ADULTS

- For adults, the maintenance doses are delivered using **100mL infusion bags** only
- Follow the instructions for calculation of the volume of reconstituted olipudase alfa needed (see **Section 7C**) and for preparation of infusion bags for infusion (see **Section 7D**).
- Once the 100 mL infusion bags have been prepared, use the infusion rates outlined in **Table 3**.

Table 3. Olipudase alfa infusion rates: maintenance dose, adults (3 mg/kg if no IARs)

Dose (mg/kg)	Infusion steps			Approximate infusion duration (minutes)
	Step	Rate (mL/hour)	Duration (minutes)	
3	1	3.3	20 ± 5	220
	2	10	20 ± 5	
	3	20	20 ± 5	
	4	33.3	160 ± 5	

9 – Reminders for the HCP in home infusion setting

- Olipudase alfa administration should be supervised by an HCP **who is trained in emergency measures and has access to appropriate medical support** to manage severe reactions, such as those related to systemic hypersensitivity (eg, anaphylaxis).
- **Dose and infusion** rate should remain the same as were used in the supervised clinical setting and should not be changed without the supervision of the treating physician.
- **Monitor the patient** in case of any signs and symptoms of IARs or systemic hypersensitivity including anaphylaxis and **contact the treating physician**. Subsequent infusion should only occur in a setting where resuscitation measures are available.
- **Contact the treating physician** if infusion is missed (ie, a delay of >3 days). Re-escalation in the supervised clinical setting may be required if doses have been missed.
- Check if you have sufficient supplies and request orders as necessary.

XENPOZYME® Prescribing Information

PBS Information: This product is not listed on the PBS.
This product is funded by the Life Savings Drug Program

Please review full XENPOZYME Product Information before prescribing. To access full Product Information, visit <https://qr.medsinfo.com.au/tx/sw.cfm?h=swcxenpo>, scan the QR code or call 1800 818 806.



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