Xenpozyme®
(olipudase alfa-rpcp)
For Injection, 20 mg

ADMINISTERING XENPOZYME IN A HOME SETTING (MAINTENANCE PHASE ONLY)

This guide is a resource for healthcare providers administering XENPOZYME in the home setting during the maintenance phase, and includes requirements for home infusion, details on XENPOZYME administration, and information on managing potential infusion-associated reactions and medication errors.

INDICATION

XENPOZYME® (olipudase alfa-rpcp) is indicated for treatment of non–central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) in adult and pediatric patients.

IMPORTANT SAFETY INFORMATION

WARNING: HYPERSENSITIVITY REACTIONS INCLUDING ANAPHYLAXIS

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

Please see Important Safety Information and full Prescribing Information for complete details, including Boxed WARNING.

WHAT IS ASMD?[1]

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- ASMD—historically known as Niemann-Pick disease types A, A/B, and B—is a progressive disease with serious, multisystemic consequences.
- ASMD is caused by reduced activity of the enzyme acid sphingomyelinase (ASM).
- Insufficient ASM activity causes an accumulation of sphingomyelin, which can lead to multisystemic damage, morbidity, and early mortality.

WHAT IS XENPOZYME?[2]

XENPOZYME targets the underlying cause of ASMD. As an enzyme replacement therapy, XENPOZYME provides an exogenous source of ASM.

XENPOZYME is administered as an intravenous infusion in 2 phases:
- Initial dose escalation
- Maintenance phase (target dose of 3 mg/kg)

XENPOZYME administration should take place in a clinical setting throughout dose escalation, to enable management of potential severe reactions. Home infusion under the supervision of a healthcare provider may be an option during the maintenance phase, if recommended by the treating physician.

XENPOZYME is available as 4 mg or 20 mg of lyophilized powder in a single-dose vial for reconstitution.

ASMD=acid sphingomyelinase deficiency.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions Including Anaphylaxis

See Boxed WARNING. Prior to XENPOZYME administration, consider pretreating with antihistamines, antipyretics, and/or corticosteroids.

- If a *severe* hypersensitivity reaction occurs, discontinue XENPOZYME immediately and initiate appropriate medical treatment. Consider the risks and benefits of re-administering XENPOZYME following severe hypersensitivity reactions.
- If a *mild or moderate* hypersensitivity reaction occurs, consider temporarily holding the infusion, slowing the infusion rate, and/or reducing the XENPOZYME dose.

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CONSIDERATIONS FOR HOME INFUSION[2]

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WHEN MIGHT PHYSICIANS CONSIDER HOME INFUSIONS FOR PATIENTS WITH ASMD?

Home infusion under the supervision of a healthcare provider may be considered for patients in the maintenance phase who are tolerating their infusions well. The decision to have patients moved to home infusion should be made after evaluation and recommendation by the treating physician.

- Patients who have successfully completed the dose escalation regimen for a minimum of 14 weeks for adult patients and a minimum of 16 weeks for pediatric patients.
  - In the clinical trial in pediatric patients, all but 1 patient completed the dose escalation up to the maintenance dose of 3 mg/kg within 22 weeks.

MAKE SURE THE PATIENT FOLLOWS THE DOSING SCHEDULE

- If a patient is receiving home infusions and misses doses, their dose may be adjusted and/or they may need to return to a clinical setting for re-escalation.
- Dose escalation and any potential re-escalation infusions should take place in a supervised clinical setting and should not take place at home.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Infusion-Associated Reactions

Antihistamines, antipyretics, and/or corticosteroids may be given prior to XENPOZYME administration to reduce the risk of infusion-associated reactions (IARs). However, IARs may still occur in patients after receiving pretreatment.

- If *severe* IARs occur, discontinue XENPOZYME immediately and initiate appropriate medical treatment. Consider the risks and benefits of re-administering XENPOZYME following severe IARs.
- If a *mild or moderate* IAR occurs, the infusion rate may be slowed or temporarily withheld, and/or the XENPOZYME dosage may be reduced.

Acute phase reactions (APRs), acute inflammatory responses accompanied by elevations in inflammatory serum protein concentrations, have been observed. Most APRs occurred at 48 hours post infusion during the dose escalation period. APRs were managed similar to other IARs.

Please see Important Safety Information and full Prescribing Information for complete details, including Boxed WARNING.

MONITORING INFUSION-ASSOCIATED REACTIONS (IARs) AND HYPERSENSITIVITY[2]

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OBSERVE PATIENTS CLOSELY DURING AND FOR AN APPROPRIATE PERIOD OF TIME AFTER THE INFUSION, BASED ON CLINICAL JUDGMENT

PRIOR TO EACH INFUSION:

- Verify pregnancy status in females of reproductive potential.
- Inform patients and caregivers of the signs and symptoms of hypersensitivity reactions and IARs, and have them seek medical care should signs and symptoms occur.
- Antihistamines, antipyretics, and/or corticosteroids may be given prior to XENPOZYME administration to reduce the risk of IARs. However, IARs may still occur in patients after receiving pretreatment.
- Transaminase testing is recommended to be continued as part of routine clinical management.

DURING AND AFTER THE INFUSION:

- XENPOZYME dosage initiation or escalation, at any time during pregnancy, is not recommended.
  - Advise female patients of reproductive potential to use effective contraception during treatment with XENPOZYME and for 14 days after the last dose if XENPOZYME is discontinued.
- In the event of a ***severe*** hypersensitivity reaction or a ***severe*** IAR, immediately discontinue XENPOZYME administration and initiate appropriate medical treatment.
- In the event of a ***mild to moderate*** hypersensitivity reaction or IAR, consider temporarily holding or slowing the infusion rate, and/or reducing the XENPOZYME dose. If dose is reduced, re-escalate according to the dose escalation regimens for adult and pediatric patients, as applicable.
- Consider testing for immunoglobulin E antidrug antibodies, serum tryptase, and complement activation in patients who experience anaphylaxis.

Inform patients and caregivers that IARs may occur during or after XENPOZYME treatment. Advise them to watch for signs and symptoms of IARs and to seek medical care if they occur.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Elevated Transaminase Levels

XENPOZYME may be associated with elevated transaminases (ALT, AST, or both) within 24 to 48 hours after infusion. Levels generally returned to levels observed prior to the XENPOZYME infusion. To manage the risk of elevated transaminase levels, assess ALT and AST:

- within one month prior to initiation of XENPOZYME,
- within 72 hours prior to any infusion during dose escalation, which includes the first 3 mg/kg dose, or prior to the next scheduled XENPOZYME infusion upon resuming treatment following a missed dose.

Upon reaching the recommended maintenance dose, transaminase testing is recommended to be continued as part of routine clinical management of ASMD.

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REMINDERS FOR HCPs IN HOME INFUSION SETTINGS[2]

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THE MAINTENANCE PHASE OF XENPOZYME CAN TAKE PLACE AT HOME ONLY AFTER SUCCESSFUL DOSE ESCALATION AND BASED ON PHYSICIAN JUDGMENT

- Dose and infusion rates used in the home settings should remain the same as were used in the supervised clinical settings, and cannot be changed without supervision of a physician.

EXPLAIN THAT MISSED DOSE(S) MAY SET BACK TREATMENT

- A dose is considered missed when not administered within 3 days of the scheduled date.
- During the maintenance phase, 2 or more consecutive missed doses will require dose adjustment and may set back treatment.
- Depending on the number of doses missed, patients may need to return to a clinical setting for dose escalation.
- Remind the patient to report any missed infusions to the treating physician.

RISK OF POTENTIAL MEDICATION ERRORS IN THE HOME SETTING

- **Prior to treatment administration: please read all instructions carefully**, including both the preparation and administration instructions in the XENPOZYME full Prescribing Information and the preparation/infusion section in this guide.
- Ensure the availability of the following:
  - Cardiopulmonary resuscitation equipment
  - Patient information (prescribed maintenance dose, weight, etc.)
  - Physician contact information
  - Necessary supplies and environment (i.e., clean environment with electricity, water, telephone access, refrigeration, etc.)

In case of medication errors that have been identified, please contact the treating physician and report the case via the national reporting system: https://www.fda.gov/drugs/information-consumers-and-patients-drugs/working-reduce-medication-errors

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Risk of Fetal Malformations During Dosage Initiation or Escalation in Pregnancy

XENPOZYME dosage initiation or escalation, at any time during pregnancy, is not recommended as it may lead to elevated sphingomyelin metabolite levels that may increase the risk of fetal malformations. The decision to continue or discontinue XENPOZYME maintenance dosing in pregnancy should consider the female's need for XENPOZYME, the potential drug-related risks to the fetus, and the potential adverse outcomes from untreated maternal ASMD disease.

Verify pregnancy status in females of reproductive potential prior to initiating XENPOZYME treatment. Advise females of reproductive potential to use effective contraception during XENPOZYME treatment and for 14 days after the last dose if XENPOZYME is discontinued.

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INFUSION PREPARATION AND ADMINISTRATION[2]

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SUPPLIES NEEDED

- Refrigerated XENPOZYME (lyophilized powder for reconstitution)
- Sterile water for injection, USP: 1.1 mL (4 mg vial) or 5.1 mL (20 mg vial)
- Empty infusion bag
  - Appropriate infusion pump
- 0.9% sodium chloride injection, USP
- In-line low protein-binding 0.2-µm filter

RECONSTITUTION AND DILUTION

Note: The lyophilized powder must be reconstituted with sterile water for injection, USP, diluted with 0.9% sodium chloride injection, USP, and then administered by intravenous infusion.

- The reconstitution and dilution steps must be completed under aseptic conditions.

1 Determine the number of vials to be reconstituted based on the individual patient's weight and the prescribed dose.

Patient dose (mg)	**Vials required**
Patient weight (kg) **x dose** (mg/kg)	$\frac{\textbf{Patient dose (mg)}}{\textbf{X mg/vial}}$

If the number of vials includes a fraction, round up to the next whole number.

X = the vial size (either 4 mg or 20 mg, depending on which vial size is being used).

In patients with a body mass index (BMI) >30, the body weight that is used to calculate the dose of XENPOZYME is calculated via the following method: Body weight (kg) to be used for dose calculation = (actual height in m)^2 x 30.

2 Remove the required number of vials from refrigeration and set aside for approximately 20 to 30 minutes to allow them to reach room temperature.

3 Reconstitute each vial with sterile water for injection, USP, by directing the diluent flow to the inside wall of the vial to avoid foaming.
- 1.1 mL of sterile water for injection, USP, into the 4 mg vial
- 5.1 mL of sterile water for injection, USP, into the 20 mg vial

4 Tilt and roll each vial gently between the palms and avoid foaming. Each vial will yield a 4 mg/mL clear, colorless solution.

5 Visually inspect the reconstituted solution in the vials for particulate matter and discoloration. The solution should be clear and colorless. Discard if the solution is discolored or if visible particulate matter is present.

IMPORTANT RECONSTITUTION AND DILUTION NOTES

- The reconstitution and dilution steps must be completed under aseptic conditions.
- Avoid the formation of foam. Let any visible foam in the infusion bag dissipate before administration.

RECONSTITUTION AND DILUTION (CONTINUED)

INFUSION VOLUMES BASED ON BODY WEIGHT* FOR THE MAINTENANCE PHASE

	PEDIATRIC PATIENTS (0 TO 17 YEARS)			ADULT PATIENTS ≥18 YEARS
	BODY WEIGHT (≥2 kg to <10 kg)	BODY WEIGHT (≥10 kg to <20 kg)	BODY WEIGHT (≥20 kg)	BODY WEIGHT (≥20 kg)
XENPOZYME DOSE (mg/kg)	Total infusion volume (mL)	Total infusion volume (mL)	Total infusion volume (mL)	Total infusion volume (mL)
3.0	50	100	250	100

*Use actual or adjusted body weight per patient BMI. Use actual body weight (kg) for patients with a BMI ≤30. For patients with a BMI >30, calculate an adjusted body weight (kg) based on height in meters = (actual height in m)^2 x 30.

For infusion volumes during the dose escalation phase, see Table 4 in the XENPOZYME full Prescribing Information.

6 Withdraw the required volume of reconstituted solution and dilute to final volume with 0.9% sodium chloride injection, USP, in an infusion bag, based on body weight for adults or pediatric patients (see Section 2.6 and Table 4 in the XENPOZYME full Prescribing Information).

7 Gently invert the infusion bag to mix. Do not shake. Because this is a protein solution, slight flocculation (described as thin translucent fibers) occurs occasionally after dilution. The diluted solution must be filtered through an in-line low protein-binding 0.2-µm filter during administration.

8 Vials are for single dose only. Discard any unused solution.

INFUSION PREPARATION AND ADMINISTRATION (CONTINUED)[2]

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INFUSION RATES FOR ADULT PATIENTS*

DOSE (mg/kg)	INFUSION RATE			
	step 1	step 2	step 3	step 4
3.0	3.33 mL/hr	10 mL/hr	20 mL/hr	33.33 mL/hr

INFUSION RATES FOR PEDIATRIC PATIENTS*

DOSE (mg/kg)	INFUSION RATE			
	step 1	step 2	step 3	step 4
3.0	0.1 mg/kg/hr	0.3 mg/kg/hr	0.6 mg/kg/hr	1 mg/kg/hr

*In absence of IARs, increase infusion rate per the steps of infusion as indicated (+/- 5 min). Each step of infusion will last for 20 minutes with the exception of the final step, which should last until completion of the infusion volume.

9 After the infusion is complete, the infusion line should be flushed with 0.9% sodium chloride injection, USP, using the same infusion rate as the one used for the last part of the infusion.

10 Do not infuse XENPOZYME in the same intravenous line with other products.

- Reconstituted solution and diluted solution of XENPOZYME should be used immediately. This product contains no preservatives.
- If immediate use is not possible, the reconstituted solution may be stored for up to 24 hours refrigerated at 2 °C to 8 °C (36 °F to 46 °F) or up to 6 hours at controlled room temperature (20 °C to 25 °C [68 °F to 77 °F]).
- After dilution, the solution can be stored for up to 24 hours refrigerated at 2 °C to 8 °C (36 °F to 46 °F) or up to 12 hours (including infusion time) at controlled room temperature (20 °C to 25 °C [68 °F to 77 °F]), or discard.
- Do not freeze.

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WARNING: HYPERSENSITIVITY REACTIONS INCLUDING ANAPHYLAXIS

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

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions Including Anaphylaxis

See Boxed WARNING. Prior to XENPOZYME administration, consider pretreating with antihistamines, antipyretics, and/or corticosteroids.

- If a *severe* hypersensitivity reaction occurs, discontinue XENPOZYME immediately and initiate appropriate medical treatment. Consider the risks and benefits of re-administering XENPOZYME following severe hypersensitivity reactions.
- If a *mild or moderate* hypersensitivity reaction occurs, consider temporarily holding the infusion, slowing the infusion rate, and/or reducing the XENPOZYME dose.

Infusion-Associated Reactions

Antihistamines, antipyretics, and/or corticosteroids may be given prior to XENPOZYME administration to reduce the risk of infusion-associated reactions (IARs). However, IARs may still occur in patients after receiving pretreatment.

- If *severe* IARs occur, discontinue XENPOZYME immediately and initiate appropriate medical treatment. Consider the risks and benefits of re-administering XENPOZYME following severe IARs.
- If a *mild or moderate* IAR occurs, the infusion rate may be slowed or temporarily withheld, and/or the XENPOZYME dosage may be reduced.

Acute phase reactions (APRs), acute inflammatory responses accompanied by elevations in inflammatory serum protein concentrations, have been observed. Most APRs occurred at 48 hours post infusion during the dose escalation period. APRs were managed similar to other IARs.

Elevated Transaminase Levels

XENPOZYME may be associated with elevated transaminases (ALT, AST, or both) within 24 to 48 hours after infusion. Levels generally returned to levels observed prior to the XENPOZYME infusion. To manage the risk of elevated transaminase levels, assess ALT and AST:

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- within 72 hours prior to any infusion during dose escalation, which includes the first 3 mg/kg dose, or prior to the next scheduled XENPOZYME infusion upon resuming treatment following a missed dose.

Upon reaching the recommended maintenance dose, transaminase testing is recommended to be continued as part of routine clinical management of ASMD.

Please see full Prescribing Information for complete details, including Boxed WARNING.

WARNINGS AND PRECAUTIONS (CONTINUED)

Risk of Fetal Malformations During Dosage Initiation or Escalation in Pregnancy

XENPOZYME dosage initiation or escalation, at any time during pregnancy, is not recommended as it may lead to elevated sphingomyelin metabolite levels that may increase the risk of fetal malformations. The decision to continue or discontinue XENPOZYME maintenance dosing in pregnancy should consider the female's need for XENPOZYME, the potential drug-related risks to the fetus, and the potential adverse outcomes from untreated maternal ASMD disease.

Verify pregnancy status in females of reproductive potential prior to initiating XENPOZYME treatment. Advise females of reproductive potential to use effective contraception during XENPOZYME treatment and for 14 days after the last dose if XENPOZYME is discontinued.

ADVERSE REACTIONS

- Most frequently reported adverse drug reactions in adults (incidence ≥10%) were headache, cough, diarrhea, hypotension, and ocular hyperemia.
- Most frequently reported adverse drug reactions in pediatric patients (incidence ≥20%) were pyrexia, cough, diarrhea, rhinitis, abdominal pain, vomiting, headache, urticaria, nausea, rash, arthralgia, pruritus, fatigue, and pharyngitis.

10 STEPS TO PREPARE AND ADMINISTER XENPOZYME AT HOME[2]

1. Determine the number of vials to be reconstituted.
2. Remove the required number of vials from refrigeration and allow them to reach room temperature.
3. Reconstitute each vial.
4. Gently tilt and roll each vial.
5. Visually inspect the reconstituted solution in the vials for particulate matter and discoloration.
6. Determine the required volume of reconstituted solution and dilute to final volume.
7. Gently invert the infusion bag to mix. Do not shake.
8. Vials are for single dose only—discard any unused solution.
9. After the infusion is complete, the infusion line should be flushed.
10. Do not infuse XENPOZYME in the same intravenous line with other products.

- Monitor the patient in case of any signs and symptoms of IARs and hypersensitivity reactions, and inform the treating physician. Subsequent infusion in a clinical setting may be required.
- Remind the patient to report any missed infusions to the treating physician.
- Schedule regular follow-up consultations.

Please see Important Safety Information and full Prescribing Information for complete details, including Boxed WARNING.

VISIT XENPOZYME.COM/HCP FOR MORE INFORMATION.

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References: 1. McGovern MM, Avetisyan R, Sanson BJ, Lidove O. Disease manifestations and burden of illness in patients with acid sphingomyelinase deficiency (ASMD). *Orphanet J Rare Dis.* 2017;12(1):41. **2.** XENPOZYME. Prescribing Information.

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