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

DOSING WITH XENPOZYME

THE FIRST AND ONLY DISEASE-SPECIFIC TREATMENT FOR ASMD[1]

A STEP-BY-STEP GUIDE TO XENPOZYME DOSING AND PREPARATION

20 mg vial pictured.
XENPOZYME is available in 4 mg or 20 mg vials.

ASMD=acid sphingomyelinase deficiency.

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.

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WHAT IS ASMD?[2]

- 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?[1]

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.

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.

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

PRETREATMENT AND DOSING

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

STEPS TO TAKE PRIOR TO TREATMENT INITIATION[1]

- **Verify pregnancy status in females of reproductive potential.**
  - 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.
- **Consider administering pretreatment medication.**
  - 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.
- **Assess baseline transaminase (ALT and AST) levels** in all patients within 1 month prior to treatment initiation.

WHY DOSE ESCALATION IS NECESSARY

- XENPOZYME provides an exogenous source of ASM. When infused, it metabolizes accumulated sphingomyelin into ceramide and phosphocholine components.[1]
- At the start of treatment with XENPOZYME, the rapid metabolism of accumulated sphingomyelin generates pro-inflammatory breakdown products, which may induce IARs and/or transient transaminase elevations. A dose escalation regimen may reduce the risk of IARs or transient transaminase elevations at treatment initiation.[1,3]

DOSE ESCALATION REGIMEN[1]

Please follow the directions in the XENPOZYME full Prescribing Information and in this guide.

- The recommended starting dose is 0.1 mg/kg for adult patients and 0.03 mg/kg for pediatric patients (under age 18).
- Dose escalation takes at least 14 weeks for adults and at least 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.

MAINTENANCE PHASE[1]

- The maintenance phase of XENPOZYME can take place every 2 weeks, after the patient has successfully completed the dose escalation regimen.
- **XENPOZYME target maintenance dose: 3 mg/kg.**
- Home administration under the supervision of a healthcare provider may be considered for patients who are receiving the maintenance dose and tolerating their infusions well.

ALT=alanine aminotransferase; AST=aspartate aminotransferase.

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.

DOSE ESCALATION[1]

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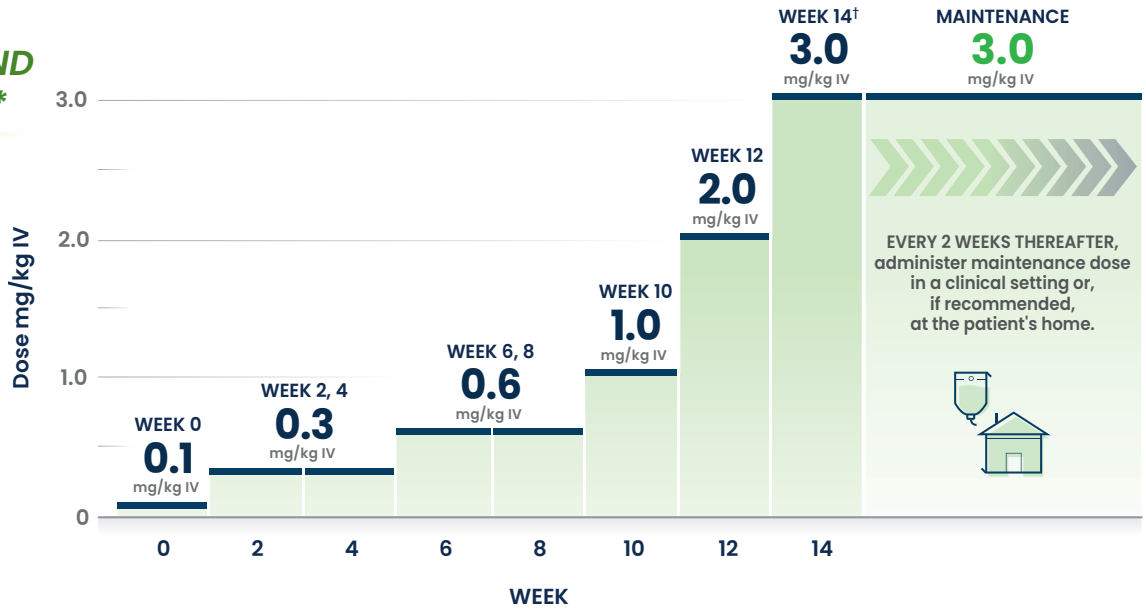
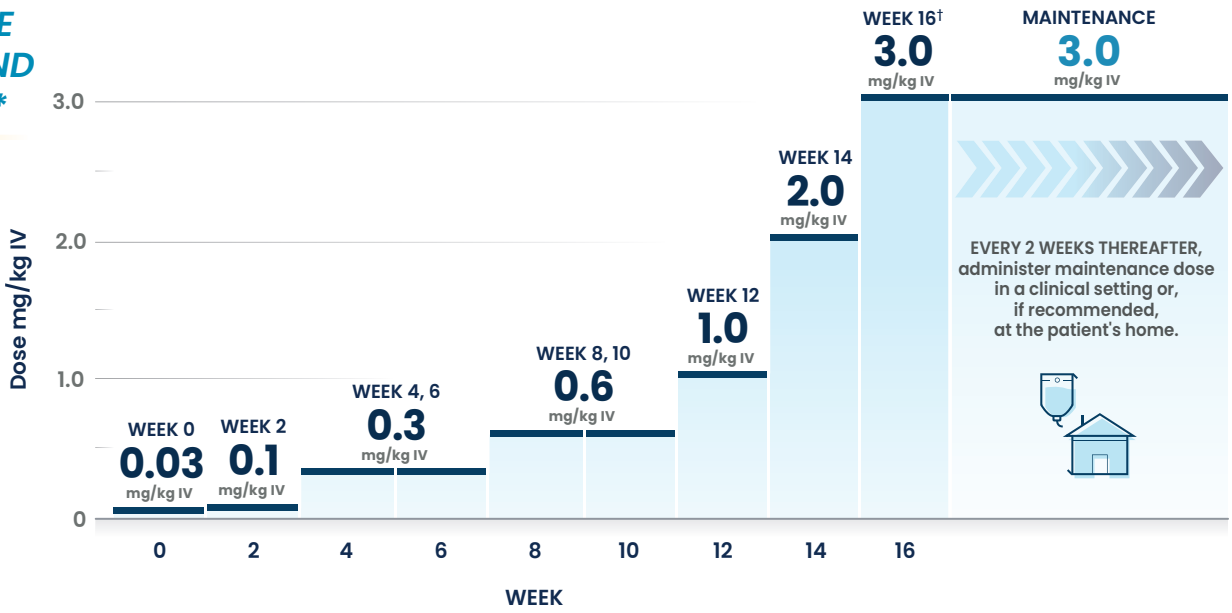
Throughout the dose escalation phase, XENPOZYME administration should take place in a clinical setting.

ADULT DOSE ESCALATION AND MAINTENANCE*



PEDIATRIC DOSE ESCALATION AND MAINTENANCE*



*Use actual body weight for patients with a body mass index (BMI) ≤30. For patients with a BMI >30, calculate adjusted body weight (kg) = (actual height in m)^2 x 30.
†The dose escalation phase includes the first 3 mg/kg dose.

Follow the dose escalation regimen before infusing at the maintenance dose level. If doses are missed, re-escalation may be necessary.

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

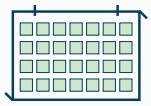
MONITORING TRANSIENT TRANSAMINASE (ALT AND AST) ELEVATIONS[1]

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

- XENPOZYME may be associated with transaminase elevations within 24 to 48 hours after infusion. Transaminase elevations generally returned to pre-infusion levels at the time of the next scheduled infusion.

During dose escalation or upon resuming treatment following a missed dose, transaminase (ALT and AST) levels should be assessed within 72 hours prior to the next scheduled XENPOZYME infusion.

THE FOLLOWING MONITORING GUIDANCE MUST BE FOLLOWED TO MANAGE THE RISK OF TRANSIENT TRANSAMINASE ELEVATIONS:

WITHIN 1 MONTH PRIOR TO TREATMENT INITIATION:	DURING DOSE ESCALATION OR UPON RESUMING TREATMENT FOLLOWING A MISSED DOSE:	DURING THE MAINTENANCE PHASE:
		

• Assess baseline ALT and AST levels.	• Assess transaminase levels within 72 hours prior to any infusion during dose escalation, or prior to the next scheduled XENPOZYME infusion upon resuming treatment following a missed dose.
	  ◦ If transaminase levels are elevated above baseline and >2 times the ULN, the XENPOZYME dose can be adjusted (prior dose repeated or reduced) or treatment can be temporarily withheld until the liver transaminases return to the patient's baseline value.
	  ◦ If either the baseline or pre-infusion transaminase level (during the dose escalation phase) is >2 times the ULN, repeat assessment of transaminase levels within 72 hours after the end of the infusion to monitor trends in transaminase elevations.
		• Transaminase testing is recommended to be continued as part of routine clinical management.

ULN=upper limit of normal.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (CONTINUED)

Infusion-Associated Reactions (continued)

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 IARs AND HYPERSENSITIVITY[1]

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

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

DURING AND AFTER THE INFUSION:

- 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 IgE ADA, serum tryptase, and complement activation in patients who experience anaphylaxis.

COUNSELING PATIENTS AND CAREGIVERS

- 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 help if they occur.

ADA=antidrug antibody; IgE=immunoglobulin E.

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.

INFUSION PREPARATION[1]

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

SUPPLIES NEEDED

20 mg vial pictured.
XENPOZYME is available in 4 mg or 20 mg vials.

- 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 syringe or infusion bag, depending on infusion volume
  - Appropriate infusion pump (for syringe or infusion bag)
- 0.9% sodium chloride injection, USP
- In-line low protein-binding 0.2-µm filter

- **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 the XENPOZYME Home Infusion Guide.
- Ensure the availability of cardiopulmonary resuscitation equipment.
- Carefully prepare the medication in accordance with the XENPOZYME full Prescribing Information and the XENPOZYME Home Infusion Guide.

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

RECONSTITUTION AND DILUTION[1]

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

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 BMI >30, the body weight that is used to calculate the dose of XENPOZYME is calculated via the following method (for dose escalation and maintenance phases): 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.

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

7 Gently invert the syringe or 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.

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 syringe or infusion bag dissipate before administration.

RECONSTITUTION AND DILUTION[1] (continued)

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

INFUSION VOLUMES BASED ON BODY WEIGHT*

	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)
0.03	Actual volume will vary‡ (0.6 mL to 3 mL)	Actual volume will vary‡ (3 mL to 6 mL)	5	NA
0.1	Actual volume will vary‡ (2 mL to 10 mL)	5	10	20
0.3	5	10	20	100
0.6	10	20	50	100
1.0	20	50	100	100
2.0	50	75	200	100
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 a total volume of infusion ≤20 mL, prepare a syringe for infusion. For a total volume of ≥50 mL, prepare an infusion bag.
‡Volume will vary to achieve a final concentration of 0.1 mg/mL.

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.

VISIT XENPOZYME.COM/HCP FOR MORE INFORMATION.

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

ADMINISTRATION INSTRUCTIONS[1]

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

INFUSION RATES FOR ADULT PATIENTS*

DOSE (mg/kg)	INFUSION RATE			
	step 1	step 2	step 3	step 4
0.1	20 mL/hr	60 mL/hr	NA	NA
0.3 to 3	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
0.03	0.1 mg/kg/hr for the full length of the infusion	NA	NA	NA
0.1	0.1 mg/kg/hr	0.3 mg/kg/hr	NA	NA
0.3	0.1 mg/kg/hr	0.3 mg/kg/hr	0.6 mg/kg/hr	NA
0.6	0.1 mg/kg/hr	0.3 mg/kg/hr	0.6 mg/kg/hr	1 mg/kg/hr
1.0				
2.0				
3.0				

*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.

- Do not infuse XENPOZYME in the same intravenous line with other products.
- After the infusion is complete, the infusion line should be flushed with 0.9% sodium chloride injection, USP.
- 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.

HOME INFUSION[1]

HOME INFUSION UNDER THE SUPERVISION OF A HEALTHCARE PROVIDER MAY BE CONSIDERED FOR PATIENTS IN THE MAINTENANCE PHASE WHO ARE TOLERATING THEIR INFUSIONS WELL

- Dose and infusion rates should remain constant while at home and cannot be changed without supervision of a treating physician.
- 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 the XENPOZYME Home Infusion Guide.
- Ensure the availability of the following:
  - Cardiopulmonary resuscitation equipment
  - Patient information (prescribed maintenance dose, weight, etc.)
  - Treating 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

The next step may be home infusion.

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.

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.

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

HELPING PATIENTS ADHERE TO THE DOSING SCHEDULE[1]

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

EXPLAIN THAT MISSED DOSE(S) MAY SET BACK TREATMENT

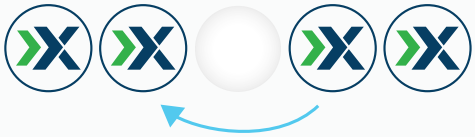
- During the dose escalation phase, more than 1 missed dose will delay time to the maintenance phase and possible home infusion.
- During the maintenance phase, 2 or more consecutive missed doses will require dose adjustment.
  - If a patient is receiving home infusions and misses doses, they may need to return to a clinical setting for dose escalation.
  - Remind the patient to report any missed infusions to the treating physician.
  - Schedule regular follow-up consultations.

RE-ESCALATION MAY BE NECESSARY IF A PATIENT MISSES 1 OR MORE DOSES*

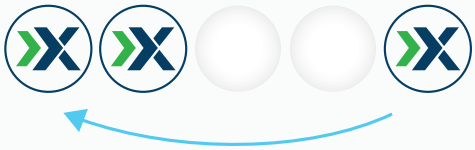
A dose is considered missed when not administered within 3 days of the scheduled date. When a dose of XENPOZYME is missed, administer the next dose as described below as soon as possible. Thereafter, administration should be scheduled every 2 weeks from the date of the last administration.

DURING THE DOSE ESCALATION PHASE:

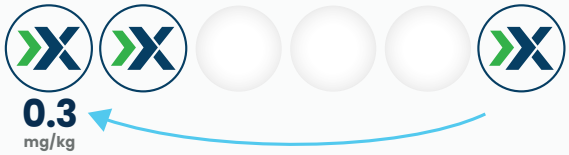
If 1 infusion is missed, administer the last tolerated dose before resuming dose escalation, according to the dose escalation regimens for adult and pediatric patients (see page 5).



If 2 consecutive infusions are missed, administer 1 dose below the last tolerated dose before resuming dose escalation, according to the dose escalation regimens for adult and pediatric patients (see page 5).



If 3 or more consecutive infusions are missed, resume dose escalation at 0.3 mg/kg, according to the dose escalation regimens for adult and pediatric patients (see page 5).

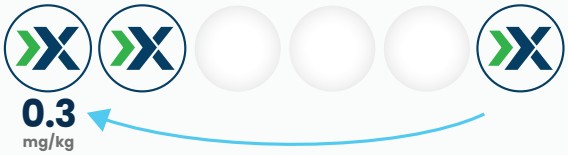


DURING THE MAINTENANCE PHASE:

If 1 maintenance infusion is missed, administer the maintenance dose and adjust the treatment schedule accordingly.

If 2 consecutive maintenance infusions are missed, administer 1 dose below the maintenance dose before resuming the maintenance dose.

If 3 or more consecutive maintenance infusions are missed, restart dosing at 0.3 mg/kg, according to the dose escalation regimens for adult and pediatric patients (see page 5).



*At the next scheduled infusion after a missed dose, if the dose administered is 0.3 mg/kg or 0.6 mg/kg, that dose should be administered twice per Tables 1 and 2 in the XENPOZYME full Prescribing Information. For complete dose escalation regimens for adult and pediatric patients, please see page 5 of this guide and Tables 1 and 2 in the XENPOZYME full Prescribing Information.

IMPORTANT SAFETY INFORMATION

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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:

- 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.

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.

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

10 STEPS TO PREPARE AND ADMINISTER XENPOZYME[1]

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 syringe or 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.
- 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.

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

References: 1. XENPOZYME. Prescribing Information. **2.** 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. **3.** Wasserstein MP, Jones SA, Soran H, et al. Successful within-patient dose escalation of olipudase alfa in acid sphingomyelinase deficiency. *Mol Genet Metab*. 2015;116(1-2):88-97.

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