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Section:	Prescription Drugs	**Effective Date:**	April 1, 2025
Subsection:	Endocrine and Metabolic Drugs	**Original Policy Date:**	September 23, 2022
Subject:	Xenpozyme	**Page:**	1 of 4

Last Review Date: March 7, 2025

Xenpozyme

Description

Xenpozyme (olipudase alfa-rpcp)

Background
Acid sphingomyelinase deficiency (ASMD) is a rare progressive genetic disorder. Sphingomyelinase is an enzyme that is required to break down sphingomyelin, a fatty substance that surrounds nerve cell axons. Deficiency of sphingomyelinase leads to the buildup of sphingomyelin in different tissues of the body and the symptoms and outcomes can be highly variable between patients. Xenpozyme is a replacement for endogenous sphingomyelinase that can help control non-central nervous system (CNS) manifestations of the disease, as Xenpozyme is not expected to enter the CNS through the blood brain barrier (1).

Regulatory Status
FDA-approved indication: Xenpozyme is indicated for treatment of non-central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) in adult and pediatric patients (1).

Xenpozyme has a boxed warning regarding the risk of hypersensitivity reactions including anaphylaxis. Prior to administration, pretreatment with antihistamines, antipyretics, and/or corticosteroids should be considered. Appropriate medical support and equipment should be readily available during Xenpozyme infusion. In severe reactions, infusion of Xenpozyme should be discontinued and appropriate medical treatment initiated. Rechallenge may be considered for these patients. In cases of mild to moderate infusion rela+ted reaction, the infusion rate may be slowed and/or withheld and the dose reduced (1).

Elevated transaminases have also occurred in patients treated with Xenpozyme. To manage this risk, patients should have ALT and AST measured within one month prior to initiation of Xenpozyme treatment and within 72 hours prior to any infusion during the dose escalation phase of treatment. The dose should be reduced or withheld if baseline or pre-treatment AST or ALT levels are greater than twice the upper limit of normal (ULN). When the maintenance phase of dosing has been reached, transaminases should be assessed routinely (1).

Xenopozyme may cause drug-related risks to a fetus. The pregnancy status of females of reproductive potential should be verified prior to initiating Xenpozyme treatment. Females of reproductive potential should be advised to use effective contraception during treatment and for 14 days after the last dose of Xenpozyme (1).

The safety and effectiveness of Xenpozyme has been established in pediatric patients (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Xenpozyme may be considered **medically necessary** if the conditions indicated below are met.

Xenpozyme may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnosis

Patient must have the following:

Acid sphingomyelinase deficiency (ASMD)

AND ALL of the following:

1. Sphingomyelin phosphodiesterase 1 (SMPD1) gene mutation
2. Prescriber agrees to monitor patient for infusion related reactions, such as anaphylaxis, and provide appropriate medical treatment if necessary
3. Prescriber agrees to monitor liver transaminases (ALT and AST) prior to and during treatment

4. Females of reproductive potential **only:** patient will be advised to use effective contraception during treatment with Xenpozyme and for 14 days after the last dose

Prior–Approval *Renewal* Requirements

Diagnosis

Patient must have the following:

Acid sphingomyelinase deficiency (ASMD)

AND ALL of the following:

1. Prescriber agrees to monitor patient for infusion related reactions, such as anaphylaxis, and provide appropriate medical treatment if necessary
2. Prescriber agrees to monitor liver transaminases (ALT and AST) during treatment
3. Females of reproductive potential **only:** patient will be advised to use effective contraception during treatment with Xenpozyme and for 14 days after the last dose

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 2 years

Prior–Approval *Renewal* Limits

Same as above

Rationale

Summary

Acid sphingomyelinase deficiency (ASMD) is a rare progressive genetic disorder. Sphingomyelinase is an enzyme that is required to break down sphingomyelin, a fatty substance

that surrounds nerve cell axons. Xenpozyme is administered to replace this enzyme and mitigate non-CNS manifestations of the condition. Xenpozyme has a boxed warning regarding severe infusion related reactions and patients should be monitored closely during infusion, and prescribers prepared to manage severe reactions, including anaphylaxis.

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Xenpozyme while maintaining optimal therapeutic outcomes.

References

1. Xenpozyme [Package Insert]. Cambridge, MA: Genzyme Corporation; September 2024.

Policy History

Date	Action
September 2022	Addition to PA
December 2022	Annual review. Per SME, added initiation requirement for SMPD1 gene mutation and added “such as anaphylaxis” to patient monitoring requirement
December 2023	Annual review and reference update
March 2024	Annual review and reference update
March 2025	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 7, 2025 and is effective on April 1, 2025.