Xenpozyme™ (olipudase alfa-rpcp intravenous infusion)

When requesting Xenpozyme™ (olipudase alfa-rpcp intravenous infusion), the individual requiring treatment must be diagnosed with the following FDA-approved indication and meet the specific coverage guidelines and applicable safety criteria for the covered indication.

FDA-approved indication

Xenpozyme is indicated for the treatment of non-central nervous system (CNS) manifestations of acid sphingomyelinase deficiency (ASMD) in adult and pediatric patients.

Coverage Guidelines

Acid Sphingomyelinase Deficiency (ASMD)

The individual must meet all of the following criteria for authorization:

- Diagnosis is established by acid sphingomyelinase (ASM) enzymatic assay and genetic testing demonstrating biallelic pathogenic variants in the sphingomyelin phosphodiesterase-1 *(SMPD1)* gene;
- A diagnosis of Gaucher disease is excluded;
- Has ASMD type B OR ASMD type A/B;
- Has two or more non-central nervous system signs of ASMD type B or type A/B (e.g., hepatosplenomegaly, interstitial lung disease, decreased diffusing capacity of the lungs, progressive liver disease with cirrhosis or fibrosis, dyslipidemia, osteopenia, thrombocytopenia, anemia, leukopenia);
- Medication is prescribed by or in consultation with a geneticist, endocrinologist, a metabolic disorder sub-specialist, or a physician who specializes in the treatment of lysosomal storage disorders.

Approval duration: 12 months

Dosing Recommendations

Recommended starting dose of Xenpozyme in adults is 0.1mg/kg via intravenous infusion every 2 weeks. Dose escalation is as follows:

Table 1: XENPOZYME Dose Escalation Regimen for Adult Patients*

Adult Patients (18 years and older)	
First dose (Day 1/Week 0)	0.1 mg/kg
Second dose (Week 2)	0.3 mg/kg
Third dose (Week 4)	0.3 mg/kg
Fourth dose (Week 6)	0.6 mg/kg
Fifth dose (Week 8)	0.6 mg/kg
Sixth dose (Week 10)	1 mg/kg
Seventh dose (Week 12)	2 mg/kg
Eighth dose (Week 14)†	3 mg/kg (recommended maintenance dose)

*Use actual body weight for patients with a BMI less than or equal to 30. For patients with a BMI greater than 30, calculate adjusted body weight (kg) = (actual height in m)^2 × 30.
†The dose escalation phase includes the first 3 mg/kg dose.

Recommended starting dose of Xenpozyme in pediatric patients is 0.03 mg/kg via intravenous infusion every 2 weeks. Dose escalation is as follows:

Table 2: XENPOZYME Dose Escalation Regimen for Pediatric Patients*

Pediatric Patients (0-17 years)	
First dose (Day 1/Week 0)	0.03 mg/kg
Second dose (Week 2)	0.1 mg/kg
Third dose (Week 4)	0.3 mg/kg
Fourth dose (Week 6)	0.3 mg/kg
Fifth dose (Week 8)	0.6 mg/kg
Sixth dose (Week 10)	0.6 mg/kg
Seventh dose (Week 12)	1 mg/kg
Eighth dose (Week 14)†	2 mg/kg
Ninth dose (Week 16)†	3 mg/kg (recommended maintenance dose)

*Use actual body weight for patients with a BMI less than or equal to 30. For patients with a BMI greater than 30, calculate adjusted body weight (kg) = (actual height in m)^2 × 30.
†The dose escalation phase includes the first 3 mg/kg dose.

References

1. Xenpozyme™ intravenous infusion [prescribing information]. Cambridge, MA: Genzyme; December 2024.
2. Wasserstein M, Lachmann R, Hollack C, et al. A randomized, placebo-controlled clinical trial evaluating olipudase alfa enzyme replacement for chronic acid sphingomyelinase deficiency (ASMD) in adults: One-year results. *Genet Med.* 2022;24(7):1425-1436.
3. Diaz GA, Jones SA, Scarpa M, et al. One-year results of a clinical trial of olipudase alfa enzyme replacement therapy in pediatric patients with acid sphingomyelinase deficiency. *Genet Med.* 2021;23:154-1550.
4. Geberhiwot T., Wasserstein M, Wanninayake, S. et al. Consensus clinical management guidelines for acid sphingomyelinase deficiency (Niemann-Pick disease types A, B, and A/B). *Orphanet J Rare Dis* 2023 Apr;18(1),85.