HAP CareSource™

PHARMACY POLICY STATEMENT
HAP CareSource™ Marketplace

DRUG NAME	Xenpozyme (olipudase alfa-rpcp)
BENEFIT TYPE	Medical
STATUS	Prior Authorization Required

Xenpozyme, approved by the FDA in 2022, is a hydrolytic lysosomal sphingomyelin-specific enzyme indicated for treatment of non–central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) in adult and pediatric patients. Xenpozyme provides the enzyme that is deficient or absent in ASMD. Without the enzyme acid sphingomyelinase (ASM), a complex lipid called sphingomyelin builds up in cells which can lead to multiorgan symptoms such as decreased lung function, enlarged liver and spleen, decreased platelet count, and growth delay in children, among many other manifestations. ASMD, a lysosomal storage disorder, is also known as Niemann-Pick disease and can be differentiated as type A, A/B, and B. Xenpozyme has not been studied in patients with ASMD type A. It is not expected to cross the blood-brain barrier or improve CNS manifestations. ASMD is an extremely rare genetic disease with fewer than 120 ASMD diagnoses in the U.S. Signs and symptoms may present in infancy, childhood, or adulthood with about two-thirds of diagnoses in the U.S. in pediatrics. Xenpozyme was the first approved treatment for ASMD.

Xenpozyme (olipudase alfa-rpcp) will be considered for coverage when the following criteria are met:

Acid Sphingomyelinase Deficiency (ASMD)

For **initial** authorization:

1. Medication must be prescribed by or in consultation with a physician knowledgeable in the management of ASMD, such as an endocrinologist, hepatologist, or pulmonologist; AND
2. Member has a confirmed diagnosis of ASMD with documentation of at least one of the following:
   a) ASM enzyme activity <10% of controls (in leukocytes or fibroblasts); OR
   b) Genetic test results showing two pathogenic mutations of the *SMPD1* gene; AND
3. Member has a clinical diagnosis of ASMD type A/B or type B with at least one of the following non-central nervous system manifestations with baseline measure(s): splenomegaly, hepatomegaly, decreased diffusing capacity of the lung (DLco), low platelets, delayed growth (pediatric); AND
4. Member does NOT have ASMD type A or rapidly progressing neurologic abnormalities; AND
5. Member has documented assessment of ALT and AST within one month prior to initiation.
6. **Dosage allowed/Quantity limit**:
   Administer as IV infusion every 2 weeks.
   Adults: Starting dose of 0.1 mg/kg then follow the dose escalation regimen in the prescribing information to the recommended maintenance dose of 3 mg/kg.
   Pediatrics: Starting dose of 0.03 mg/kg then follow the dose escalation regimen in the prescribing information to the recommended maintenance dose of 3 mg/kg.

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:

1. Chart notes must show improvement from baseline in at least one of the following: improved lung function (increased % predicted DLco), reduction of splenomegaly, reduction of hepatomegaly, increased platelet count, or improved z-score in children experiencing growth delay.

If all the above requirements are met, the medication will be approved for an additional 1 year.

HAP CareSource considers Xenpozyme (olipudase alfa-rpcp) not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
11/18/2022	New policy for Xenpozyme created.
04/25/2024	Updated references. Removed hematology, neuro from prescriber types. Simplified dosing info. Removed LFT monitoring from reauth. Specified <10% enzyme activity level and in leukocytes or fibroblasts. Reworded/clarified confirmed diagnosis vs. clinical diagnosis and asking for baseline clinical measure(s); removed dyslipidemia, bone density from list.

References:

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3. Diagnosing ASMD. ASMD. Updated March 2022. Accessed October 21, 2022. https://www.asmdfacts.com/hcp/diagnosing-asmd
4. 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. *Genetics in Medicine.* 2021; 23 (8): 1543-1550. doi:10.1038/s41436-021-01156-3
5. Wasserstein M, Lachmann R, Hollak C, et al. A randomized, placebo-controlled clinical trial evaluating olipudase alfa enzyme replacement therapy for chronic acid sphingomyelinase deficiency (ASMD) in adults: one-year results. *Genetics in Medicine.* 2022; 24 (7): 1425-1436. doi:10.1016/j.gim.2022.03.021
6. McGovern M, Dionisi-Vici C, Giugliani R, et al. Consensus recommendation for a diagnostic guideline for acid sphingomyelinase deficiency. *Genetics in Medicine.* 2017; 19: 967–974. doi:10.1038/gim.2017.7
7. Wasserstein MP, Schuchman EH. Acid Sphingomyelinase Deficiency. 2006 Dec 7 [Updated 2023 Apr 27]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1370/
8. 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;18(1):85. Published 2023 Apr 17. doi:10.1186/s13023-023-02686-6

Effective date: 01/01/2025
Revised date: 04/25/2024