Background statement: Xenpozyme is a recombinant human acid sphingomyelinase enzyme initially approved by the FDA in 2022 for the treatment of non-central nervous system (non-CNS) manifestations of acid sphingomyelinase deficiency (ASMD) in adult and pediatric patients. Xenpozyme received fast track, breakthrough therapy, priority review, and orphan drug designations. Xenpozyme provides the enzyme that is deficient or absent in ASMD. Without the enzyme acid sphingomyelin (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 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. Xenpozyme is not expected to cross the blood-brain barrier or improve CNS manifestations of ASMD. 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 is currently the only approved treatment for ASMD.

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

**Acid Sphingomyelinase Deficiency: Treatment of non-CNS manifestations of acid sphingomyelinase deficiency (ASMD)**

For *initial* authorization:
1. Medication must be prescribed by or in consultation with any specialist with experience treating acid sphingomyelinase deficiency ASMD, such as a hepatologist, pulmonologist, hematologist, neurologist, or endocrinologist; AND
2. Member has a diagnosis of ASMD type A/B or type B supported by clinical presentation with at least one of the following: splenomegaly, hepatomegaly, decreased diffusing capacity of the lung assessed by DLco, dyslipidemia, low platelets, delayed growth, and decreased bone density assessed by T-scores; AND
3. Member has a diagnosis of ASMD type A/B or type B, confirmed by one of the following:
   a) ASM biochemical enzyme assay showing low levels of ASM; OR
   b) Genotyping showing two pathogenic mutations of the SMPD1 gene; AND
4. Member does not have ASMD type A or rapidly progressing neurologic abnormalities (Xenpozyme was not studied in ASMD type A and is not expected to modulate CNS manifestations of the disease); AND
5. Member has documented assessment of ALT and AST within one month prior to initiation of Xenpozyme; AND
6. **Dosage allowed/Quantity limit:**
   - **Initial dose:** Recommended starting dose is 0.1 mg/kg for adults and 0.03 mg/kg for pediatrics administered as an intravenous infusion. Xenpozyme is administered via intravenous infusion every 2 weeks following the dose escalation regimen in the package insert.
**Maintenance dose:** The recommended maintenance dose of Xenpozyme in pediatrics and adults is 3 mg/kg via intravenous infusion every 2 weeks.

*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 improvement in children experiencing growth delay; AND
2. Chart notes must show that ALT and AST are continuing to be monitored.

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

**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.**

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<th>DATE</th>
<th>ACTION/DESCRIPTION</th>
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<tbody>
<tr>
<td>11/18/2022</td>
<td>New policy for Xenpozyme created.</td>
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**References:**


**Effective date:** 04/01/2023
**Revised date:** 11/18/2022

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