Reference number(s)
5561-A

Standard Medicare Part B Management
Xenpozyme

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Xenpozyme	olipudase alfa-rpcp

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-approved Indications[1]

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

All other indications will be assessed on an individual basis. Submissions for indications other than those listed in this criteria should be accompanied by supporting evidence from Medicare approved compendia.

Documentation

The following documentation must be available, upon request, for all submissions:

Initial Requests

- Acid sphingomyelinase enzyme assay or genetic testing results supporting the diagnosis.

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Continuation Requests

- Documentation (e.g., chart notes, lab results) of a response to therapy (e.g., improvement in lung function, reduction in spleen volume, reduction in liver volume, improvement in platelet count, improvement in linear growth progression).

Coverage Criteria

Acid Sphingomyelinase Deficiency (ASMD)[1,2]

Authorization of 12 months may be granted for treatment of non-central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) when the diagnosis is confirmed by either of the following:

- A documented deficiency of acid sphingomyelinase as measured in peripheral leukocytes, cultured fibroblasts, or lymphocytes, or
- Genetic testing results documenting pathogenic variant(s) in the sphingomyelin phosphodiesterase-1 (SMPD1) gene.

Continuation of Therapy

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Authorization for 12 months may be granted when all of the following criteria are met:

- The member is currently receiving therapy with the requested medication.
- The requested medication is being used to treat an indication in the coverage criteria section.
- The member is receiving benefit from therapy (e.g., improvement in lung function, reduction in spleen volume, reduction in liver volume, improvement in platelet count, improvement in linear growth progression).

Summary of Evidence

The contents of this policy were created after examining the following resources:

- The prescribing information for Xenpozyme.
- The available compendium
    - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    - Micromedex DrugDex
    - American Hospital Formulary Service- Drug Information (AHFS-DI)
    - Lexi-Drugs

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    - Clinical Pharmacology
- Acid sphingomyelinase deficiency. GeneReviews.

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Xenpozyme are covered.

Explanation of Rationale

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using an enzyme assay to confirm the diagnosis of ASMD prior to initiating treatment with Xenpozyme can be found in the clinical trials cited in the prescribing information. To be included in the trial, the patient must have had a documented deficiency of acid sphingomyelinase as measured in peripheral leukocytes, cultured fibroblasts, or lymphocytes.

Support for using genetic testing to confirm the diagnosis of ASMD prior to initiating treatment with Xenpozyme can be found in the GeneReviews article by Wasserstein Et al. The diagnosis of ASMD is established by detection of biallelic pathogenic variants in SMPD1 by molecular genetic testing and residual acid sphingomyelinase enzyme activity that is less than 10% of controls (in peripheral blood lymphocytes or cultured skin fibroblasts).

References

1. Xenpozyme [package insert]. Cambridge, MA: Genzyme Corporation; December 2024.
2. Wasserstein MP, Schuchman EH. Acid sphingomyelinase deficiency. 2006 Dec 7 [Updated 2023 Apr 27]. In: Adam MP, Everman DB, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1370/ (Accessed on November 18, 2025).

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