Clinical Policy: Olipudase Alfa-rpcp (Xenpozyme)

Reference Number: PA.CP.PHAR.586
Effective Date: 08/2023
Last Review Date: 07/2025

Description
Olipudase alfa-rpcp (Xenpozyme®) is a hydrolytic lysosomal sphingomyelin-specific enzyme.

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

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Xenpozyme is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Acid Sphingomyelinase Deficiency (must meet all)**:**

1. Diagnosis of ASMD confirmed by one of the following (a or b):
    a. Enzyme assay demonstrating a deficiency of acid sphingomyelinase activity;
    b. DNA testing;
2. A diagnosis of Gaucher disease has been ruled out by determination of glucocerebrosidase activity;
3. Member has ASMD Type B or Type A/B;
4. Documentation of member's weight (in kg);
5. Dose does not exceed 3 mg/kg every two weeks.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Acid Sphingomyelinase Deficiency (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy as evidenced by improvement in, but not limited to, any of the following parameters: lung function, reduced or stabilized spleen volume, or (in pediatrics only) improved height Z-scores *(see Appendix D for examples of individual patients' ASMD disease manifestation profiles)*;
3. Documentation of member's weight (in kg);
4. If request is for a dose increase, new dose does not exceed 3 mg/kg every two weeks.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53;

B. ASMD Type A.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ASMD: acid sphingomyelinase deficiency
DLco: diffuse capacity of the lung for carbon monoxide
FDA: Food and Drug Administration
MN: multiples of normal
MRI: magnetic resonance imaging
SRS: splenomegaly related score

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s): life-threatening hypersensitivity reactions including anaphylaxis

Appendix D: General Information

- Individual patient manifestations of ASMD may include hepatomegaly, splenomegaly, bleeding/bruising, thrombocytopenia, dyslipidemia, interstitial lung disease (with decreased DLco), delayed growth and puberty, osteoporosis/osteopenia, liver dysfunction with progressive fibrosis, and cardiac disease.
- ASMD Type A (infantile neurovisceral disease) includes severe neurologic symptoms and is uniformly fatal in early childhood. Olipudase alfa does not cross the blood-brain barrier and thus is not appropriate for the treatment of patients with ASMD Type A.
- ASMD and Gaucher disease have several clinical manifestations in common. Simultaneous determination of acid sphingomyelinase activity and glucocerebrosidase activity to distinguish ASMD from Gaucher disease is recommended.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
ASMD Type B and Type A/B	Pediatrics: IV dosing every 2 weeks starting with 0.03 mg/kg/dose titrated to a final target maintenance dose by Week 16 of 3 mg/kg every 2 weeks Adults: IV dosing every 2 weeks starting with 0.1 mg/kg/dose titrated to a final target maintenance dose by Week 14 of 3 mg/kg every 2 weeks	3 mg/kg every 2 weeks

VI. Product Availability

Vials with lyophilized powder for reconstitution: 4 mg, 20 mg

VII. References

1. Xenpozyme Prescribing Information. Cambridge, MA: Genzyme Corporation; December 2024. Available at: https://products.sanofi.us/xenpozyme/xenpozyme.pdf. Accessed June 5, 2025
2. 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;1-12. https://doi.org/10.1016/j.gim.2022.03.021.
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. Genetics in Medicine. 2021;23:1543-50. https://doi.org/10.1038/s41436-021-01156-3.
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 of Rare Diseases. 2023;18:85. https://doi.org/10.1186/s13023-023-02686-6.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0218	Injection, olipudase alfa-rpcp, 1 mg

Reviews, Revisions, and Approvals	Date
Policy created	07/2023
3Q 2024 annual review: removed lab requirements; references reviewed and updated.	07/2024
3Q 2025 annual review: no significant changes; references reviewed and updated.	07/2025