Clinical Policy: Olipudase Alfa-rpcp (Xenpozyme)

Reference Number: CP.PHAR.586
Effective Date: 08.31.22
Last Review Date: 08.26
Line of Business: Commercial, HIM/ICHRA, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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 health plans affiliated with Centene Corporation® 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. For members aged ≥ 18 years, member has all of the following (a, b, and c):
   a. Diffuse capacity of the lung for carbon monoxide (DLco) ≤ 70%;
   b. Spleen volume ≥ 6 multiples of normal (MN) as measured by magnetic resonance imaging (MRI);
   c. Splenomegaly related score (SRS) ≥ 5;
5. For members aged < 18 years, member has both of the following (a and b):
   a. Spleen volume ≥ 5 MN as measured by MRI;
   b. Height Z-score ≤ -1;
6. Documentation of member's weight (in kg);
7. Dose does not exceed 3 mg/kg every two weeks.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Acid Sphingomyelinase Deficiency (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
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: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid, or evidence of coverage documents;

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	3 mg/kg every 2 weeks

Indication	Dosing Regimen	Maximum Dose
	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	

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 April 22, 2026.
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	P&T Approval Date
Policy created pre-emptively	05.17.22	08.22
RT4: drug is now FDA-approved – criteria updated per FDA labeling: no significant changes; references reviewed and updated.	09.08.22	
3Q 2023 annual review: no significant changes; added 4 mg vial; updated HCPCS code; references reviewed and updated.	04.07.23	08.23
3Q 2024 annual review: no significant changes; references reviewed and updated.	05.14.24	08.24
3Q 2025 annual review: no significant changes; references reviewed and updated.	06.05.25	08.25

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2026 annual review: no significant changes; updated Initial Approval and Continued Therapy authorization durations from 6 months to 12 months; added ICHRA line of business; references reviewed and updated.	04.22.26	08.26

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.