Original Effective Date: 02/25/2023
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Last P&T Approval/Version: 07/30/2025
Next Review Due By: 07/2026
Policy Number: C24670-A

Xenpozyme (olipudase alfa-rpcp)

PRODUCTS AFFECTED

Xenpozyme (olipudase alfa-rpcp)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Acid sphingomyelinase deficiency (ASMD)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. ACID SPHINGOMYELINASE DEFICIENCY (ASMD):
1. Documented diagnosis of acid sphingomyelinase deficiency (ASMD) type A/B, or B (also known as Niemann-Pick disease)
AND
2. Documentation diagnosis was confirmed by deficiency of acid sphingomyelinase enzyme AND

genetic testing of the SMPD1 gene [DOCUMENTATION REQUIRED]
NOTE: Peripheral Blood Leukocytes or cultured skin fibroblast assessment of acid sphingomyelinase (ASM) activity of less than 10% of control sample demonstrates deficiency
AND

3. Documentation that Xenpozyme (olipudase alfa-rpcp) is not being used to treat neurologic manifestations, if present
   AND
4. Documentation of member's therapeutic goals based on their individual non-neurologic baseline symptoms (e.g., hepatosplenomegaly, liver and spleen volume, pulmonary function, platelet count, height z-scores [for pediatrics]), overall health, and quality of life [DOCUMENTATION REQUIRED]
   AND
5. Documentation of member's current dosing weight including weight, height, and body mass index (BMI), within the last 30 days
   NOTE: Dosing for BMI greater than 30 should be based on adjusted body weight (see Appendix)

CONTINUATION OF THERAPY:

A. ACID SPHINGOMYELINASE DEFICIENCY (ASMD):

1. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity, including severe hypersensitivity reactions (i.e., anaphylaxis)
   AND
2. Documentation of positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms (e.g., liver and spleen volume, pulmonary function, platelet count, height z-scores [for pediatrics])
   AND
3. Documentation of member's current weight including weight, height, and body mass index (BMI), within the last 30 days
   NOTE: Dosing for BMI greater than 30 should be based on adjusted body weight (see Appendix)

DURATION OF APPROVAL:

Initial authorization: 12 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a board-certified geneticist, hematologist, pulmonologist, hepatologist, pediatric metabolic specialist, or physician experienced in the management of ASMD or Niemann-Pick or enzyme deficiency disorders. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

No restriction

QUANTITY:

Adults: Maintenance dose of 3 mg/kg every 2 weeks
Pediatrics: Maintenance dose of 3 mg/kg every 2 weeks
See Appendix for Dose Escalation Phase

PLACE OF ADMINISTRATION:
The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-hospital facility-based location as per the Molina Health Care Site of Care program.

Note: Site of Care Utilization Management Policy applies for Xenpozyme (olipudase alfa-rpcp). For information on site of care, see Specialty Medication Administration Site of Care Coverage Criteria (molinamarketplace.com)

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Intravenous

DRUG CLASS:
Acid Sphingomyelinase Deficiency (ASMD) - Agents

FDA-APPROVED USES:
Indicated for the treatment of non–central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) in adult and pediatric patients

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
Dose Escalation Phase

Adult Patients (18 years and older)	
First dose (Day 1/Week 0)	0.1mg/kg
Second dose (Week 2)	0.3mg/kg
Third dose (Week 4)	0.3mg/kg
Fourth dose (Week 6)	0.6mg/kg
Fifth dose (Week 8)	0.6mg/kg
Sixth dose (Week 10)	1mg/kg
Seventh dose (Week 12)	2mg/kg
Eighth dose (Week 14)^{†}	3mg/kg (recommended maintenance dose)

*Use actual body weight for patients with a BMI less than or equal to 30. For patients with a BMI greater than 30, calculate adjusted body weight (kg) = (actual height in m)2 × 30
†The dose escalation phase includes the first 3 mg/kg dose.

Pediatric Patients (0 to 17 years)	
First dose (Day 1/Week 0)	0.03mg/kg
Second dose (Week 2)	0.1mg/kg
Third dose (Week 4)	0.3mg/kg
Fourth dose (Week 6)	0.3mg/kg
Fifth dose (Week 8)	0.6mg/kg
Sixth dose (Week 10)	0.6mg/kg
Seventh dose (Week 12)	1mg/kg

Eighth dose (Week 14)	2mg/kg
Ninth dose (Week 16)^{†}	3mg/kg (recommended maintenance dose)

*Use actual body weight for patients with a BMI less than or equal to 30. For patients with a BMI greater than 30, calculate adjusted body weight (kg) = (actual height in m)2 × 30
†The dose escalation phase includes the first 3 mg/kg dose.

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
ASMD is a lysosomal storage disease that results from reduced activity of the enzyme acid sphingomyelinase (ASM), caused by pathogenic variants in the sphingomyelin phosphodiesterase 1 (SMPD1) gene. ASM degrades sphingomyelin. The deficiency of ASM causes an intra-lysosomal accumulation of sphingomyelin (as well as cholesterol and other cell membrane lipids) in various tissues. Xenpozyme provides an exogenous source of ASM. Xenpozyme is not expected to cross the blood-brain barrier or modulate the CNS manifestations of ASMD. Xenpozyme was not studied in ASMD Type A. Type A is considered the most severe form and is characterized by marked CNS involvement.

The approval of Xenpozyme was based on efficacy of Xenpozyme for the treatment of non-neurologic ASMD evaluated in 3 clinical trials. Studies enrolled only those with ASMD type A/B or type B. ASCEND was a placebo-controlled trial in adults (n=31) and ASCEND-Peds was a single-arm study in pediatric patients <18 years of age (n=8). Both trials evaluated the efficacy and safety of Xenpozyme over 52 weeks. In ASCEND, Xenpozyme was found to significantly improve percent predicted diffusion capacity of the lungs for carbon monoxide (DLco), spleen volume, liver volume, and platelet count compared to placebo. In ASCEND-Peds, Xenpozyme resulted in improvements in mean percent change in % predicted DLco, spleen and liver volumes, platelet counts, and linear growth progression (as measured by height Z-scores) at Week 52 compared to baseline.
Trial 3 is a long-term pediatric extension trial. The 8 patients from ASCEND-Peds continued in this open-label long-term trial. Efficacy analyses showed continued improvements in the three patients evaluated for percent predicted DLco, the six patients evaluated for platelet counts, and the eight patients evaluated for spleen and liver volumes, compared to baseline, over an additional 6 months of treatment. The height Z-score increased by 1.3 from baseline when evaluated through 24 months of treatment. Bone age, as assessed by hand X-ray, was delayed by a mean of 26.4 months at baseline in the seven pediatric patients enrolled in ASCEND-Peds in whom it was measured in Trial 3. The mean bone age improved to within 12 months of the chronological age at month 24.
Most frequently reported adverse drug reactions in adults (incidence ≥10%) were headache, cough, diarrhea, hypotension, and ocular hyperemia. Most frequently reported adverse drug reactions in pediatric patients (incidence ≥20%) were pyrexia, cough, diarrhea, rhinitis, abdominal pain, vomiting, headache, urticaria, nausea, rash, arthralgia, pruritus, fatigue, and pharyngitis. Anaphylactic reaction was reported in 2 (25%) of treated pediatric patients. Xenpozyme (olipudase alfa-rpcp) has a black box warning for severe hypersensitivity reactions.
Infusion-associated reactions (IARs) occurred in approximately 75% of pediatric and 50% of adult treated patients. A severe IAR occurred in one (12.5%) of the pediatric patients. The most frequent IARs in adults (incidence ≥10%) were headache, pruritus, vomiting, and urticaria. The most frequent IARs in pediatric patients (incidence ≥20%) were urticaria, erythema, headache, nausea, pyrexia, and vomiting. Antihistamines, antipyretics, and/or corticosteroids may be given prior to Xenpozyme administration to reduce the risk of IARs.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Xenpozyme (olipudase alfa-rpcp) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Xenpozyme (olipudase alfa-rpcp) include: No labeled contraindications.

Exclusions/Discontinuation:

Initiation or escalation, at any time during pregnancy, is not recommended as it may lead to elevated sphingomyelin metabolite levels that may increase the risk of fetal malformations.

OTHER SPECIAL CONSIDERATIONS:

Xenpozyme (olipudase alfa-rpcp) has a Black Box Warning for severe hypersensitivity reactions. If a severe hypersensitivity reaction (e.g., anaphylaxis) occurs, discontinue Xenpozyme immediately and initiate appropriate medical treatment. Consider the risks and benefits of re-administering Xenpozyme following severe hypersensitivity reactions (including anaphylaxis).

There is a risk of fetal malformations which can be due to elevated sphingomyelin metabolite levels which occur during dose initiation or dosage escalation. At any time during pregnancy, dose initiation or escalation is not recommended. Female patients of reproductive potential should be counseled to use effective contraception during treatment and for 14 days after the last dose.

Xenpozyme may be associated with elevated transaminases (ALT, AST, or both) within 24 to 48 hours after infusion. To manage the risk of elevated transaminase levels, assess ALT and AST within one month prior to initiation of Xenpozyme, within 72 hours prior to any infusion during dose escalation.

If a dose is not administered within 3 days of scheduled date, follow dosing recommendations for Xenpozyme missed doses per label.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
J0218	Injection, olipudase alfa-rpcp, 1 mg

AVAILABLE DOSAGE FORMS:

Xenpozyme SOLR 20MG single-dose vial
Xenpozyme SOLR 4MG single-dose vial

REFERENCES

1. Xenpozyme (olipudase alfa-rpcp) for injection, for intravenous use. [prescribing information]. Cambridge, MA: Genzyme Corporation; December 2024.
2. McGovern, M. M., Dionisi-Vici, C., Giugliani, R., Hwu, P., Lidove, O., Lukacs, Z., Wasserstein, M. P. (2017). Consensus recommendation for a diagnostic guideline for acid sphingomyelinase deficiency. Genetics in Medicine, 19(9), 967-974. doi:10.1038/gim.2017.7

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Duration of Approval Contraindications/Exclusions/Discontinuation Other Special Considerations References	Q3 2025
REVISION- Notable revisions: Required Medical Information Appendix Available Dosage Forms References	Q4 2024
REVISION- Notable revisions: Required Medical Information Coding/Billing Information References	Q3 2023
REVISION- Notable revisions: Required Medical Information Coding/Billing Information References	Q2 2023
NEW CRITERIA CREATION	Q1 2023