Xenpozyme™ (olipudase alfa)
(Intravenous)

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I. Length of Authorization

Coverage will be provided for 12 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Xenpozyme 20 mg single-dose vial: 17 vials per 14 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- 340 mg every 14 days

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Females of reproductive potential will have pregnancy status verified prior to start of therapy and will use effective contraception during treatment and for 14 days after the last dose if therapy is discontinued; AND
- Patient has documented baseline measures (necessary for renewal) of: percent predicted diffusion capacity of the lungs for carbon monoxide (DLco) or other age-appropriate pulmonary function testing, spleen volume, liver volume, plasma lyso-sphingomyelin, and/or platelet count (height Z-score and skeletal maturation are relevant for pediatric patients); AND

Universal Criteria [1]

- Documented baseline transaminase (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]) levels within 1 month prior to treatment initiation, within 72 hours prior to any infusion during dose escalation, and periodically throughout therapy; AND
- Patient should not require invasive ventilatory support OR non-invasive ventilatory support while awake and for >12 hours a day *(Note: Patients requiring ventilatory support will be reviewed on a case-by-case basis)*; AND

Acid Sphingomyelinase Deficiency (ASMD) (Niemann-Pick Disease) † Φ [1]

- Patient has a definitive diagnosis of ASMD as confirmed by the following:
  - Detection of biallelic pathogenic mutations in the *SMPD1* gene by molecular genetic testing; **OR**
  - Deficiency of acid sphingomyelinase enzyme activity <10% of controls as measured in peripheral leukocytes, cultured fibroblasts, or lymphocytes; **AND**
- Patient has a clinical diagnosis consistent with Niemann-Pick disease type B (NPD-B) or A/B (NPD-A/B) *(Note: NPD-A (infantile neurovisceral ASMD) has not been studied. Genotype-phenotype correlations as well as signs/symptoms may not be conclusive in infants therefore requests will be evaluated on a case-by-case basis)*; **AND**
- Therapy will be used for non-CNS manifestations of disease *(Note: Xenpozyme is not expected to cross the blood-brain barrier or modulate CNS manifestations of disease)*

† FDA-approved indication(s); ‡ Compendia recommended indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Coverage can be renewed based on the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include anaphylaxis and severe hypersensitivity reactions, severe infusion-associated reactions, severely elevated liver transaminases, etc.; **AND**
- Patient has not experienced progressive/irreversible severe cognitive impairment; **AND**
- Disease response with treatment as defined by improvement or stability from pre-treatment baseline by the following:
  - Improvement in or stability in the percent predicted diffusion capacity of the lungs for carbon monoxide (DLco) or other age-appropriate pulmonary function testing; **OR**
  - Improvement in or stability of spleen and/or liver volumes; **OR**
  - Reduction in plasma lyso-sphingomyelin; **OR**
  - Improvement in or stability of platelet count; **OR**
  - Improvement in linear growth progression as measured by mean height Z-scores *(pediatric patients only)*

V. Dosage/Administration [1]

Indication	Dose

Acid sphingomyelinase deficiency (ASMD)	Administer Xenpozyme via intravenous infusion every 2 weeks. **Adult Patients** ***(≥18 years)*** – First dose (Day 1/Week 0): 0.1 mg/kg – Second dose (Week 2): 0.3 mg/kg – Third dose (Week 4): 0.3 mg/kg – Fourth dose (Week 6): 0.6 mg/kg – Fifth dose (Week 8): 0.6 mg/kg – Sixth dose (Week 10): 1 mg/kg – Seventh dose (Week 12): 2 mg/kg – Eighth dose (Week 14): 3 mg/kg (recommended maintenance dose) **Pediatric Patients** ***(0 to <18 years)*** – First dose (Day 1/Week 0): 0.03 mg/kg – Second dose (Week 2): 0.1 mg/kg – Third dose (Week 4): 0.3 mg/kg – Fourth dose (Week 6): 0.3 mg/kg – Fifth dose (Week 8): 0.6 mg/kg – Sixth dose (Week 10): 0.6 mg/kg – Seventh dose (Week 12): 1 mg/kg – Eighth dose (Week 14): 2 mg/kg – Ninth dose (Week 16): 3 mg/kg (recommended maintenance dose) *Note: Prior to administration, consider pretreating all patients with antihistamines, antipyretics, and/or corticosteroids*
Weight-Based Dosing Information The recommended adult and pediatric dosages of Xenpozyme for the dose escalation and maintenance phases are based on body weight as follows for patients with a body mass index (BMI): • Less than or equal to 30, the dosage is based on actual body weight (kg) • Greater than 30, the dosage is based on adjusted body weight (kg). Calculate an adjusted body weight (kg) based on height in meters as described below: ○ Adjusted body weight (kg) = (actual height in m)^2 x 30	

VI. Billing Code/Availability Information

HCPCS Code:

- J3590 – Unclassified biologics

NDC:

- Xenpozyme 20 mg lyophilized powder for reconstitution in a single-dose vial: 58468-0050-xx

VII. References

1. Xenpozyme [package insert]. Cambridge, MA; Genzyme Corporation, Inc.; August 2022. Accessed September 2022.
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, vol 24, Iss 7, 2022, 1425-1436. ISSN 1098-3600, 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. Genet Med. 2021 Aug;23(8):1543-1550. doi: 10.1038/s41436-021-01156-3. Epub 2021 Apr 19.
4. Thurberg BL, Diaz GA, Lachmann RH, et al. Long-term efficacy of olipudase alfa in adults with acid sphingomyelinase deficiency (ASMD): Further clearance of hepatic sphingomyelin is associated with additional improvements in pro- and anti-atherogenic lipid profiles after 42 months of treatment. Mol Genet Metab. 2020 Sep - Oct;131(1-2):245-252. doi: 10.1016/j.ymgme.2020.06.010. Epub 2020 Jun 24.
5. Wasserstein MP, Diaz GA, Lachmann RH, et al. Olipudase alfa for treatment of acid sphingomyelinase deficiency (ASMD): safety and efficacy in adults treated for 30 months. J Inherit Metab Dis. 2018 Sep;41(5):829-838. doi: 10.1007/s10545-017-0123-6. Epub 2018 Jan 5.
6. Wasserstein MP, Schuchman EH. Acid Sphingomyelinase Deficiency. 2006 Dec 7 [Updated 2021 Feb 25]. In: Adam MP, Everman DB, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1370/.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
E75.241	Niemann-Pick disease type B
E75.244	Niemann-Pick disease type A/B

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

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