Medical Policy:

Xenpozyme (olipudase alfa-rpcp), intravenous infusion

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.366	January 2, 2025	November 10, 2022

The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Definitions

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

Length of Authorization

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

Dosing Limits [Medical Benefit]

Dosing is weight-based. For patients with a body mass index (BMI) of ≤ 30 kg/m2, actual body weight is used. For patients with a BMI > 30 kg/m2 adjusted body weight is used (adjusted body weight in kg = [actual height in meters]2 x 30). Home infusion of Xenpozyme under the supervision of a healthcare provider may be considered for patients on a maintenance dose and who are tolerating the infusion well. The decision to have patients moved to home infusion should be made after evaluation and recommendation by a physician.

The recommended starting dose in adults is 0.1 mg/kg via intravenous (IV) infusion. The dose is titrated every

2 weeks over a period of 14 weeks to a maintenance dose of 3 mg/kg every 2 weeks (Table 1). In pediatric patients, the recommended starting dose is 0.03 mg/kg via IV infusion.1 The dose is titrated every 2 weeks over a period of 16 weeks to a maintenance dose of 3 mg/kg every 2 weeks (Table 2). To reduce the risk of hypersensitivity and infusion-related reactions or elevated transaminase levels, the dose escalation regimen outlined in Tables 1 and 2 below should be followed. A dose is considered "missed" when it is not administered within 3 days of the scheduled date.1 Refer to Table 3 for missed doses.

Table 1. Xenpozyme Dose Escalation Regimen for Adults (≥ 18 Years of Age).[1]

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

† The dose escalation phase includes the first 3 mg/kg dose.

Table 2. Xenpozyme Dose Escalation Regimen for Pediatric Patients.[1]

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

† The dose escalation phase includes the first 3 mg/kg dose.

Table 3. Dosing Recommendations for Xenpozyme Missed Doses*.[1]

Consecutive Missed Doses In:	Escalation Phase	Maintenance Phase
1 missed dose	First dose after a missed dose: Administer last tolerated dose. Second and subsequent doses after missed dose: Resume dose escalation at next infusion according to Table 1 for adult patients or Table 2 for pediatric patients.	First and subsequent doses after missed dose: Administer maintenance dose.
2 consecutive missed doses	First dose after missed dose: Administer 1 dose below the last tolerated dose. Second and subsequent doses after missed dose: Resume dose escalation according to Table 1 for adults or Table 2 for pediatric patients.	First dose after missed dose: Administer 1 dose below the maintenance dose. Second and subsequent doses after missed dose: Resume the maintenance dose.
≥ 3 consecutive missed doses	First and subsequent doses after missed doses: Resume dose escalation at 0.3 mg/kg and follow Table 1 for adults or Table 2 for pediatric patients.	First and subsequent doses after missed doses: Restart dosing at 0.3 mg/kg and follow Table 1 for adult patients or Table 2 for pediatric patients.

*At scheduled infusion after a missed dose, if the dose administered is 0.3 mg/kg or 0.6 mg/kg, administer that dose twice as per Table 1 and 2.

Limit: 3mg/kg every 2 weeks; 340 billable units (340 mg) every 14 days

Guideline

I. INITIAL CRITERIA

1. **Acid Sphingomyelinase Deficiency (ASMD).** Approve if the patient meets the following criteria (A, B, C, and D):
    A. The diagnosis of ASMD meets ALL of the following (i, ii, and iii):
        i. The diagnosis of ASMD has been established by acid sphingomylinase (ASM) enzymatic assay testing; **AND**
        ii. The diagnosis of ASMD has been confirmed by genetic testing demonstrating biallelic pathogenic variants in the sphingomyelin phosphodiesterase-1(SMPD1) gene; **AND**
        iii. A diagnosis of Gaucher disease has been excluded; **AND**

        Note: ASMD has historically been known as Niemann-Pick Disease.
    B. Patient meets **ONE** of the following criteria (i or ii):
        i. Patient has ASMD type B; **OR**
        ii. Patient has ASMD type A/B; **AND**
    C. Patient has **TWO** or more non-central nervous system signs of ASMD type B or type A/B according to the prescriber; **AND**

    Note: Examples of non-central nervous system signs of ASMD type B or type A/B include but are not limited to hepatosplenomegaly, interstitial lung disease, decreased diffusing capacity of the lungs, progressive liver disease with cirrhosis or fibrosis, dyslipidemia, osteopenia, thrombocytopenia, anemia, leukopenia.
    D. The medication is prescribed by or in consultation with a geneticist, endocrinologist, a metabolic disorder sub-specialist, or a physician who specializes in the treatment of lysosomal storage disorders

II. RENEWAL CRITERIA

A. Patient continues to meet criteria such as identified in Initial Criteria; **AND**
B. 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**
C. Patient has not experienced progressive/irreversible severe cognitive impairment; **AND**
D. Disease response with treatment as defined by improvement or stability from pre-treatment baseline by the following:
    i. 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**
    ii. Improvement in or stability of spleen and/or liver volumes; **OR**
    iii. Reduction in plasma lyso-sphingomyelin; **OR**
    iv. Improvement in or stability of platelet count; **OR**
    v. Improvement in linear growth progression as measured by mean height Z-scores *(pediatric patients only)*

Applicable Procedure Codes

Code	Description
J0218	Injection, olipudase alfa-rpcp, 1 mg; 1 billable unit = 1 mg

Applicable NDCs

Code	Description
58468-0050-01	Xenpozyme (olipudase alfa-rpcp) 20mg vial

ICD-10 Diagnoses

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

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	1/2/2025	Annual Review: Initial Criteria: Acid Sphingomyelinase Deficiency (ASMD). Removed verbiage "mutation testing" and replaced with the following: "The diagnosis of ASMD has been confirmed by genetic testing demonstrating biallelic pathogenic variants in the sphingomyelin phosphodiesterase-1(SMPD1) gene "Added renewal criteria
EmblemHealth & ConnectiCare	1/2/2024	Annual Review: No criteria changes
EmblemHealth & ConnectiCare	5/02/2023	Annual Review: Added code J0218, removed code J3590, Removed ICD-10 coses E75.29 and E75.24, added E75.241 and E75.244. Under ASMD initial Criteria- Removed the Statement "A.The diagnosis of ASMD is established by enzymatic assay; AND" and replaced it with the statement "A) The diagnosis of ASMD meets ALL of the following (i, ii, and iii): i.The diagnosis of ASMD has been established by acid sphingomylinase (ASM) enzymatic assay testing; AND ii.The diagnosis of ASMD has been confirmed by mutation testing; AND iii.A diagnosis of Gaucher disease has been excluded; AND Note: ASMD has historically been known as Niemann-Pick Disease." Removed the statement "C.Patient has signs of ASMD type B or type A/B (e.g., hepatosplenomegaly, decreased diffusing capacity of the lungs, progressive liver disease with cirrhosis or fibrosis, dyslipidemia, osteopenia, and thrombocytopenia), according to the prescriber; AND" and replaced it with "C) Patient has two or more non-central nervous system signs of ASMD type B or type A/B according to the prescriber; AND Note: Examples of non-central nervous system signs of ASMD type B or type A/B include but are not limited to hepatosplenomegaly, interstitial lung disease, decreased diffusing capacity of the lungs, progressive liver disease with cirrhosis or fibrosis, dyslipidemia, osteopenia, thrombocytopenia, anemia, leukopenia."
EmblemHealth & ConnectiCare	11/10/2022	New Policy

References

1. Xenpozyme™ intravenous infusion [prescribing information]. Cambridge, MA: Genzyme; August 2022.