09-J4000-34

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Reviewed: 11/13/24

Revised: 12/15/24

Subject: Olipudase Alfa-rpcp (Xenpozyme)

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Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Acid sphingomyelinase deficiency (ASMD) is a rare, progressive genetic disorder that results from a deficiency of the enzyme acid sphingomyelinase. Acid sphingomyelinase metabolizes sphingomyelin to prevent accumulation in the body's tissue. Previously, ASMD was broken down into two subgroups: (1) neuronopathic, or type A, and (2) non-neuronopathic, or Type B. In type A, patients experience severe, fatal neurodegenerative disease in infancy, while in type B, no neurodegenerative disease is noted, and patients usually survive into adulthood. Patients often experience hepatosplenomegaly, recurrent lung infections, thrombocytopenia, and delayed bone age causing short stature. There have been intermediate forms of the disorder reported; some refer to type B as any mild or intermediate form of ASMD, which can include more mild neurologic findings compared with type A. There is also an intermediate form referred to as Niemann-Pick disease type A/B, in which patients experience varying degrees of neurologic involvement.

On August 31, 2022, the FDA approved olipudase alfa (Xenpozyme) for the treatment of non-central nervous system (non-CNS) manifestations of ASMD in adult and pediatric patients. Olipudase alfa is an enzyme replacement therapy. The efficacy of olipudase alfa was evaluated in the ASCEND (NCT02004691) and ASCEND-Peds (NCT02292654) clinical trials and was found to improve lung function (measured by diffusing capacity of the lung for carbon monoxide) and reduce spleen and liver volumes.

ASCEND was a multicenter, randomized, double-blinded, placebo-controlled, repeat-dose phase II/III trial in adult patients with ASMD (clinical diagnosis consistent with ASMD type B and A/B). In this trial, patients received either olipudase alfa or placebo. Treatment was administered in both groups as an intravenous infusion once every 2 weeks. olipudase alfa was dosed as follows: 0.1 mg/kg (Day 1, Week 0), 0.3 mg/kg (Weeks 2 and 4), 0.6 mg/kg (Weeks 6 and 8), 1 mg/kg (Week 10), 2 mg/kg (Week 12), and then a maintenance dose of 3 mg/kg (Week 14 onwards). The trial was divided into 2 consecutive

periods: a randomized placebo-controlled, double-blinded primary analysis period (PAP) which lasted to Week 52, followed by an extension treatment period (ETP) for up to 4 years. Patients randomized to the placebo arm in the PAP crossed over to receive olipudase alfa treatment in the ETP to reach the targeted dose of 3 mg/kg, while patients in the original olipudase alfa arm continued treatment.

Patients enrolled in the trial had a diffusion capacity of the lungs for carbon monoxide (DLco) ≤70% of the predicted normal value and a spleen volume ≥6 multiples of normal (MN) measured by magnetic resonance imaging (MRI). Key efficacy endpoints included assessment of % predicted DLco, spleen volume, liver volume, and platelet count.

Five males and 13 females with a median age of 34 years (range: 18 to 66) were included in the placebo arm and 8 males and 5 females with a median age of 34 years (range: 20 to 59) were included in the olipudase alfa arm.

At Week 52 during the PAP, an increase of 21% in the mean percent change in % predicted DLco was observed in the olipudase alfa -treated patients compared to the placebo-treated patients. A reduction in spleen volume of 39% was observed in the olipudase alfa-treated patients compared to the placebo-treated patients. Seventeen of 18 patients previously receiving placebo and 13 of 13 patients previously treated with olipudase alfa for 52 weeks (in the PAP) started or continued treatment with olipudase alfa, respectively, for up to 4 years. At Week 104, patients initially randomized to placebo had received olipudase alfa for 52 weeks and demonstrated the following LS mean (SE) percent changes in clinical parameters from baseline (before first administration of olipudase alfa): increase in % predicted DLco was 26.8% (6.2); reduction in spleen volume (MN) was 36.5% (2.5); reduction in liver volume (MN) was 29.5 (2.6); and increase in platelet count was 19.5 (6.7). Patients in the previous olipudase alfa group demonstrated improvement from baseline to Week 104 in the following parameters: LS mean (SE) percent increase in % predicted DLco was 34.1% (7.9); LS mean (SE) percent reduction in spleen volume (MN) was 48.3 (2.9); LS mean (SE) percent reduction in liver volume (MN) was 31.7 (2.9); LS mean (SE) percent increase in platelet count was 24.0 (8.2).

ASCEND-Peds 2 was a multi-center, open-label, repeated-dose trial of olipudase alfa administered intravenously once every 2 weeks (via infusion) for 64 weeks in pediatric patients aged <18 years with a clinical diagnosis consistent with ASMD type B and A/B. Patients enrolled in the trial had a spleen volume ≥5 MN measured by MRI. Exploratory efficacy endpoints related to organomegaly, pulmonary and liver functions, and linear growth were evaluated at Week 52. olipudase alfa was dosed as follows: 0.03 mg/kg (Day 1, Week 0), 0.1 mg/kg (Weeks 2), 0.3 mg/kg (Weeks 4 and 6), 0.6 mg/kg (Week 8 and 10), 1 mg/kg (Week 12), 2 mg/kg (Week 14), and then a maintenance dose of 3 mg/kg (Week 16 onwards).

In the trial, 8 patients (7 patients from 2 to <12 years old, and 1 patient <2 years old) received an initial dose of 0.03 mg/kg olipudase alfa and all but one completed the dose escalation up to the maintenance dose of 3 mg/kg within 22 weeks. Treatment with olipudase alfa 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 as compared to baseline.

POSITION STATEMENT:

Initiation of olipudase alfa (Xenpozyme) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with acid sphingomyelinase deficiency (ASMD) – documentation from the medical record must be provided
2. Member has a mutation in the sphingomyelin phophodiesterase-1 (SMPD1) gene – laboratory documentation must be provided
3. Member has a deficiency of acid sphingomyelinase as measured in peripheral leukocytes, cultured fibroblasts, or lymphocytes – laboratory documentation must be provided
4. Member has a spleen volume greater than or equal to 5 multiples of normal (MN) measured by magnetic resonance imaging (MRI) – documentation from the medical record must be provided
5. Member has a diffuse capacity of the lung for carbon monoxide less than or equal to 70% of the predicted normal value – documentation from the medical record must be provided
6. Olipudase is prescribed by or in consultation with a provider specializing in the treatment of ASMD (e.g., neurologist, hepatologist, geneticist)
7. Dose does not exceed the following:
    a. Initiation: 0.1 mg/kg every 2 weeks
    b. Maintenance: 3 mg/kg every 2 weeks

Approval duration: 6 months

Continuation of olipudase alfa (Xenpozyme) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization has been previously approved by Florida Blue or another health plan in the past two years for treatment of ASMD (if another health plan, documentation of a health plan-paid claim for olipudase alfa during the 90 days immediately before the request must be submitted), OR the member has previously met all indication-specific criteria.
2. Olipudase is prescribed by or in consultation with a provider specializing in the treatment of ASMD (e.g., neurologist, hepatologist, geneticist)
3. Dose does not exceed 3 mg/kg every 2 weeks

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Adults: Recommended starting dose is 0.1 mg/kg administered as an intravenous infusion, titrate to 3 mg/kg.
- Pediatrics: Recommended starting dose is 0.03 mg/kg administered as an intravenous infusion, titrate to 3 mg/kg.

Dose Adjustments

- See product label for dose escalation.

Drug Availability

- For injection: 20 mg of olipudase alfa-rpcp as a lyophilized powder in a single-dose vial for reconstitution

PRECAUTIONS:

Boxed Warning

- Hypersensitivity Reactions Including Anaphylaxis
- Appropriate medical support measures, including cardiopulmonary resuscitation equipment, should be readily available. If a severe hypersensitivity reaction occurs, olipudase alfa should be discontinued immediately and appropriate medical treatment should be initiated

Contraindications

- None

Precautions/Warnings

- Infusion-Associated Reactions (IARs): If severe IARs occur, discontinue olipudase alfa and initiate appropriate medical treatment.
- Elevated Transaminases: Assess ALT and AST within one month prior to initiation of olipudase alfa, within 72 hours prior to any infusion during dose escalation, or prior to the next scheduled olipudase alfa infusion upon resuming treatment following a missed dose.
- Risk of Fetal Malformations During Dosage Initiation or Escalation in Pregnancy: olipudase alfa dosage 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. Advise females of reproductive potential to use effective contraception during treatment and for 14 days after the last dose if olipudase alfa is discontinued.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J0218	Injection, olipudase alfa-rpcp, 1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

E75.241	Niemann-Pick disease type B; also applicable to ASMD type B & Chronic visceral acid sphingomyelinase deficiency
E75.244	Niemann-Pick disease type A/B; ASMD type A/B & Chronic neurovisceral acid sphingomyelinase deficiency
E75.249	Niemann-Pick disease, unspecified

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

1. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2024 [cited 10/24/24]. Available from: http://www.clinicalpharmacology.com/.
2. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2000 Feb 29 - [cited 10/24/24]. Available from: http://clinicaltrials.gov/.
3. Cox GF, et al. Burden of illness in acid sphingomyelinase deficiency: A retrospective chart review of 100 patients. JIMD Rep. 2018; 41:119-129. doi:10.1007/89042018120.
4. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 10/24/24].
5. National Organization for Rare Disorders. Acid sphingomyelinase deficiency. 2022. https://rarediseases.org/rare-diseases/acid-sphingomyelinase-deficiency/.

6. Olipudase alfa demonstrated significant improvement in lung function and spleen volume in patients with ASMD. News release. Sanofi U.S.; October 27, 2020. https://www.news.sanofi.us/2020-10-27-Olipudase-alfa-demonstrated-significant-improvement-in-lung-function-and-spleen-volume-in-patients-with-ASMD.
7. Olipudase alfa shown to provide sustained improvement across multiple clinical manifestations of ASMD. News release. Sanofi U.S.; February 9, 2022. https://www.sanofi.com/en/media-room/press-releases/2022/2022-02-09-18-00-00-2382138.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 11/13/24.

GUIDELINE UPDATE INFORMATION:

01/01/23	New Medical Coverage Guideline.
04/01/23	Revision: Added HCPCS code J0218 and deleted code J3590.
12/15/23	Review and revision to guideline; updated references.
12/15/24	Review and revision to guideline; updated coding and references.