olipudase alfa-rpcp (Xenpozyme®)

Policy # 00848
Original Effective Date: 09/11/2023
Current Effective Date: 09/11/2023

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider olipudase alfa-rpcp (Xenpozyme®)‡ for the treatment of acid sphingomyelinase deficiency (ASMD) to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for olipudase alfa-rpcp (Xenpozyme) will be considered when the following criteria are met:

- Patient has a diagnosis of acid sphingomyelinase deficiency (ASMD or Niemann-Pick disease) confirmed by one of the following:
  - Absence or deficiency of acid sphingomyelinase (ASM) enzyme activity; OR
  - Molecular genetic testing demonstrating mutation in the *SMPD1* gene; AND
- Patient has at least one of the following non-central nervous system manifestations of ASMD:
  - Splenomegaly (as evidenced by a spleen volume ≥6 multiples of normal for adults or ≥5 multiples of normal for patients less than 18 years of age); OR
  - Hepatomegaly; OR
  - Interstitial lung disease as evidenced by a diffusion capacity of the lungs for carbon monoxide (DL_{CO}) ≤70% of predicted normal; OR
  - Thrombocytopenia; AND
- Prescriber attests that the patient has a clinical diagnosis consistent with Type B or Type A/B ASMD; AND
- Patient does NOT have ANY of the following:
  - Use of invasive ventilatory support; OR

- Use of noninvasive ventilatory support while awake and for >12 hours a day; OR
- Platelet count <60 x10^3 µL (average of two screening samples obtained up to 24 hours apart); OR
- INR >1.5; OR
- AST or ALT >250 IU/L; OR
- Total bilirubin >1.5 mg/dL (unless there is a diagnosis of Gilbert Syndrome); OR
- Previous major organ transplant; OR
- Acute or rapidly progressive neurologic abnormalities; AND

*(Note: These specific patient selection criteria are additional requirements for coverage eligibility and will be denied as not medically necessary** if not met)*

- Dose does not exceed 3 mg/kg every 2 weeks.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of olipudase alfa-rpcp (Xenpozyme) when the patient has any of the following attributes to be **not medically necessary.****

- Use of invasive ventilatory support; OR
- Use of noninvasive ventilatory support while awake and for >12 hours a day; OR
- Platelet count<60 x10^3 µL (average of two screening samples obtained up to 24 hours apart); OR
- INR >1.5; OR
- AST or ALT >250 IU/L; OR
- Total bilirubin >1.5 mg/dL (unless there is a diagnosis of Gilbert Syndrome); OR
- Previous major organ transplant; OR
- Acute or rapidly progressive neurologic abnormalities

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of olipudase alfa-rpcp (Xenpozyme) when the patient selection criteria are not met (except those denoted above as **not medically necessary****) to be **investigational.***

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Background/Overview

Xenpozyme is an enzyme replacement therapy indicated for the treatment of non-central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) in adult and pediatric patients. It provides an exogenous source of acid sphingomyelinase (ASM), the enzyme that has reduced activity in patients with ASMD. Because it does not cross the blood-brain barrier or modulate the CNS manifestations of the disease, it is not indicated for the treatment of CNS symptoms. It is administered via intravenous injection, and the dose should be titrated to 3 mg/kg following a 14-16-week dose escalation regimen. The package insert contains a black box warning for hypersensitivity reactions including anaphylaxis that may occur following administration of the product.

ASMD, historically known as Niemann-Pick disease type A and type B, is a rare, progressive, potentially fatal lysosomal storage disease that is caused by mutations in the sphingomyelin phosphodiesterase-1 (*SMPD1*) gene. ASMD is considered a disease spectrum that is divided into three types with varying levels of severity, clinical manifestations, and rates of progression. Symptoms typical to all ASMD types include hepatosplenomegaly, thrombocytopenia, interstitial lung disease causing a decreased diffusing capacity of the lungs, progressive liver disease with cirrhosis and fibrosis, cardiac disease, dyslipidemia, and osteopenia.

- ASMD type A: the most severe form with onset in infancy; associated with rapidly progressing neurodegeneration and is often fatal by 3 years of age due to respiratory failure.
- ASMD type B: significant phenotypic variability with later onset of disease; most patients present with non-neurologic symptoms; patients frequently live into adulthood.
- ASMD type A/B: considered an intermediate form; associated with mild to severe neurologic manifestations that progress more slowly and onset later than in ASMD type A.

An ASMD diagnosis is suspected in patients who present with characteristic symptoms but must be confirmed through acid sphingomyelinase enzyme activity and genetic testing of the *SMPD1* gene. Prior to the approval of Xenpozyme, the only available treatments for ASMD were supportive therapies that address specific symptoms as they occur, including lipid-lowering therapies, growth hormone treatment, oxygen, blood transfusions, and physical and occupational therapy, as appropriate for each patient.

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FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Xenpozyme was approved in August 2022 for the treatment of non-central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) in adult and pediatric patients.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Xenpozyme for the treatment of non-central nervous system manifestations of ASMD has been evaluated in 3 clinical trials involving a total of 61 patients with ASMD.

Trial 1 was a multicenter, randomized, double-blinded, placebo controlled, repeat-dose, phase II/III trial in adult patients with ASMD. In this trial, patients received either Xenpozyme or placebo. Treatment was administered in both groups as an intravenous infusion once every 2 weeks. 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 Xenpozyme treatment in the ETP to reach the targeted dose of 3 mg/kg, while patients in the original Xenpozyme arm continued treatment. Patients enrolled in the trial had a $DL_{CO} \leq 70\%$ of the predicted normal value and a spleen volume $\geq$6 multiples of normal measured by MRI. The Xenpozyme arm included 13 patients and the placebo arm included 18 patients. Key efficacy endpoints included % of predicted DL_{CO}, spleen volume, liver volume, and platelet count. At Week 52 during the PA, an increase of 21% in the mean percent change in % predicted DL_{CO} was seen in the Xenpozyme treated patients compared to the placebo-treated patients. A reduction in spleen volume of 39% was observed in the Xenpozyme-treated patients compared to the placebo-treated patients. A decrease in mean liver volume and an increase in mean platelet count were also noted in the Xenpozyme treated patients compared to the placebo-treated patients.

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Trial 2 was a multi-center, open-label, repeated-dose trial of Xenpozyme administered intravenously once every 2 weeks for 64 weeks in pediatric patients aged <18 years with a clinical diagnosis consistent with ASMD type B and A/B. The trial included 8 patients and all but one completed the dose escalation up to the maintenance dose of 3 mg/kg within 22 weeks. Treatment with Xenpozyme resulted in improvements in mean percent change in % predicted DL_{CO}, spleen and liver volumes, platelet counts, and linear growth progression at Week 52 as compared to baseline.

The 8 patients from Trial 2 continued treatment in an open label long-term trial (Trial 3) and were treated with Xenpozyme for 2.5 to 3.2 years. Efficacy analyses showed continued improvements in the 3 patients evaluated for % predicted DL_{CO}, 6 patients evaluated for platelet counts, and all 8 patients evaluated for spleen and liver volumes, compared to baseline, during the additional 6 months extension. In addition, the height Z-score increased by 1.3 from baseline when evaluated through 24 months of Xenpozyme treatment.

References

1. Xenpozyme [package insert]. Genzyme Corporation. Cambridge, MA. Updated July 2023.
2. Xenpozyme New Drug Review. IPD Analytics. Updated October 2022.

Policy History

Original Effective Date: 09/11/2023
Current Effective Date: 09/11/2023
08/03/2023 Medical Policy Committee review
08/09/2023 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 08/2024

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2022 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J0218
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or

diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

1. Consultation with technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.