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| **Section:** | Prescription Drugs | **Effective Date:** | April 1, 2023 |
| **Subsection:** | Endocrine and Metabolic Drugs | **Original Policy Date:** | July 28, 2017 |
| **Subject:** | Brineura | **Page:** | 1 of 4 |

***Last Review Date:*** March 10, 2023

# Brineura

## Description

### Brineura (cerliponase alfa)

**Background**
Late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency, is a neurodegenerative disease caused by a deficiency of the lysosomal enzyme tripeptidyl peptidase-1 (TPP1), which catabolizes polypeptides in the CNS. Deficiency in TPP1 activity leads to an accumulation of lysosomal storage materials in the CNS, leading to a progressive decline in motor function. Brineura (cerliponase alfa) is a proenzyme that is taken up by target cells and activated in the lysosome. It subsequently cleaves tripeptides from the N-terminus of proteins in order to slow the loss of ambulation (1).

**Regulatory Status**
FDA-approved indication: Brineura is a hydrolytic lysosomal N-terminal tripeptidyl peptidase indicated to slow the loss of ambulation in symptomatic pediatric patients 3 years of age and older with late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency (1).

Brineura is contraindicated in patients with: (1)

- Any sign or symptom of acute or unresolved localized infection on or around the device insertion site (e.g. cellulitis or abscess); or suspected or confirmed CNS infection (e.g. cloudy CSF or positive CSF gram stain, or meningitis)
- Any acute intraventricular access device-related complication (e.g., leakage, extravasation of fluid, or device failure)

- Ventriculoperitoneal shunts

In the clinical studies that were conducted the exclusion criteria were children less than 3 or older than 16 years of age old at time of enrollment (2-3).

Safety and efficacy of Brineura have not been established in pediatric patients less than 3 years of age (1).

**Related policies**

## Policy

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Brineura may be considered **medically necessary** in patients 3 to 16 years of age for the treatment of late infantile neuronal ceroid lipofuscinosis type 2 (CLN2) and if the conditions indicated below are met.

Brineura may be considered **investigational** for patients less than 3 or older than 16 years of age and for all other indications.

## Prior-Approval Requirements

**Age** 3 to 16 years of age

**Diagnosis**

Patient must have the following:

Late infantile neuronal ceroid lipofuscinosis type 2 (CLN2)

**AND ALL** of the following:

1. Diagnosis of CLN2 was confirmed by enzyme assay demonstrating a deficiency of tripeptidyl peptidase 1 (TPP1) activity or by genetic testing
2. Medication is being used to slow the loss of ambulation in symptomatic patients

3. Patients have mild to moderate disease documented by a two-domain score of 3-6 on motor and language domains of the Hamburg CLN2 Clinical Rating Scale, with a score of at least 1 in each of these two domains

**AND NONE** of the following:

1. Acute intraventricular access device-related complications including:
    a. Leakage
    b. Device failure
    c. Device-related infection
2. Ventriculoperitoneal shunt
3. Generalized motor status epilepticus prior to 4 weeks of first dose

## Prior – Approval *Renewal* Requirements

**Age** 3 to 16 years of age

**Diagnosis**

Patient must have the following:

Late infantile neuronal ceroid lipofuscinosis type 2 (CLN2)

**AND** the following:

1. Documentation confirming slowed loss of ambulation following first year of treatment

## Policy Guidelines

### Pre - PA Allowance

None

### Prior – Approval Limit

**Duration** 12 months

### Prior – Approval *Renewal* Limits

Same as above

## Rationale

**Summary**
Brineura is a hydrolytic lysosomal N-terminal tripeptidyl peptidase that works by decreasing the accumulation of lysosomal storage materials in patients with late infantile neuronal ceroid lipofuscinosis type 2 (CLN2). As a result, Brineura slows the progressive decline in motor function and loss of ambulation (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Brineura while maintaining optimal therapeutic outcomes.

**References**
1. Brineura [package insert]. Novato, CA: BioMarin Pharmaceutical Inc.; March 2020.
2. ClinicalTrials.gov. A Phase 1/2 Open-Label Dose-Escalation Study to Evaluate Safety, Tolerability, Pharmacokinetics, and Efficacy of Intracerebroventricular BMN 190 in Patients with Late-Infantile Neuronal Ceroid Lipofuscinosis (CLN2) Disease. Available at: https://clinicaltrials.gov/ct2/results?term=bmn+190&Search=Search.
3. ClinicalTrials.gov. A Multicenter, Multinational, Extension Study to Evaluate the Long-Term Efficacy and Safety of BMN 190 in Patients with CLN2 Disease. Available at: https://clinicaltrials.gov/ct2/show/NCT02485899?term=bmn+190&rank=3.

## Policy History

| Date | Action |
|---|---|
| July 2017 | Addition to PA |
| September 2017 | Annual review |
| November 2018 | Annual review and reference update |
| December 2019 | Annual editorial review and reference update |
| December 2020 | Annual review and reference update |
| March 2021 | Annual editorial review and reference update |
| March 2022 | Annual review |
| March 2023 | Annual review. Changed policy number to 5.30.049 |

## Keywords

**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 10, 2023 and is effective on April 1, 2023.**