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5.30.049

Section:	Prescription Drugs	**Effective Date:**	January 1, 2025
Subsection:	Endocrine and Metabolic Drugs	**Original Policy Date:**	July 28, 2017
Subject:	Brineura	**Page:**	1 of 5

Last Review Date: December 13, 2024

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 pediatric patients with neuronal ceroid lipofuscinosis type 2 (CLN2 disease), also known as tripeptidyl peptidase 1 (TPP1) deficiency (1).

Brineura contains a boxed warning regarding hypersensitivity reactions including anaphylaxis. Brineura should be initiated in a healthcare setting with appropriate medical monitoring and support measures, including access to cardiopulmonary resuscitation equipment (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

Brineura is not recommended in patients less than 37 weeks post-menstrual age (gestational age at birth plus post-natal age) or those weighing less than 2.5 kg due to physiologic immaturity (1).

In clinical studies, the inclusion criteria required mild to moderate disease documented using the Hamburg Scale and excluded those who had generalized motor status epilepticus within 4 weeks before the first dose (2).

Safety and effectiveness of Brineura have been established in pediatric patients (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** if the conditions indicated below are met.

Brineura may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 17 years of age or younger

Diagnosis

Patient must have the following:

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
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
4. Prescriber agrees to monitor patient for hypersensitivity reactions, including anaphylaxis and initiate appropriate medical treatment as needed

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 17 years of age or younger

Diagnosis

Patient must have the following:

Neuronal ceroid lipofuscinosis type 2 (CLN2)

AND ALL of the following:

1. Documentation confirming slowed loss of ambulation following first year of treatment
2. Prescriber agrees to monitor for hypersensitivity reactions, including anaphylaxis and initiate appropriate medical treatment as needed

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 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.; July 2024.
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.

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
March 2024	Annual review
August 2024	Per PI update, changed age requirement to 17 years of age or younger and removed “late infantile” from the diagnosis. Also

	removed initiation requirement for patients to be symptomatic and added requirement to monitor for hypersensitivity reactions
December 2024	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 13, 2024 and is effective on January 1, 2025.