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Section:	Prescription Drugs	**Effective Date:**	April 1, 2021
Subsection:	Endocrine and Metabolic Drugs	**Original Policy Date:**	July 28, 2017
Subject:	Brineura	**Page:**	1 of 4

Last Review Date: March 12, 2021

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 ALL of 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. Accessed on February 22, 2021.
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. Accessed on February 22, 2021.

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

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 12, 2021 and is effective on April 1, 2021.