CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Neurology – Brineura Utilization Management Medical Policy
- Brineura® (cerliponase alfa intraventricular infusion – BioMarin)

REVIEW DATE: 04/02/2025

OVERVIEW

Brineura, a hydrolytic lysosomal N-terminal tripeptidyl peptidase, is indicated for **neuronal ceroid lipofuscinosis type 2** (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency, to slow the loss of ambulation in symptomatic pediatric patients.[1]

Brineura is a recombinant human TPP1 produced using recombinant DNA technology.[1] The recommended dose of Brineura is 300 mg administered once every other week (QOW) via intracerebroventricular (ICV) infusion. Following Brineura administration, the patient must also receive an infusion of intraventricular electrolytes. The drug is administered into the cerebral spinal fluid via a surgically implanted reservoir and catheter. It should only be administered by or under the direction of a physician who is knowledgeable in ICV administration.

Disease Overview

CLN2 disease is an extremely rare neurodegenerative disorder that is part of a group of neuronal ceroid lipofuscinoses (NCLs) sometimes referred to as Batten disease.[2] NCL diseases are a heterogeneous group of incurable neurodegenerative lysosomal storage diseases. They manifest as early impairment of vision, loss of cognitive and motor functions, seizures, and premature death. To date, 13 genetic variants have been discovered to cause the multiple variations of the disease (e.g., CLN1, CLN2, CLN3 etc.). Classic late infantile NCL disease is caused by a variant in the CLN2 gene, which encodes for lysosomal TPP1. Without TPP1, lysosomal storage materials accumulate, contributing to the progressive and persistent neurodegeneration.[2] In CLN2 disease, symptom onset is typically between 2 and 4 years of age, and lifespan is around 6 to 14 years. Other NCLs result in deficiencies in enzymes other than TPP1. As Brineura is human recombinant TPP1, its efficacy is specific to CLN2 disease.

Guidelines

Recently published expert recommendations state that patients with a suspected NCL disorder require NCL-specific diagnostic testing.[3-5] Patients require assessment by a metabolic specialist/geneticist, an NCL specialist, or a pediatric neurologist with experience in diagnosing NCL disorders. Expert recommendation from 2016 state that the recommended gold standard for laboratory diagnosis from experts was the demonstration of deficient TPP1 enzyme activity (in leukocytes, fibroblasts, or dried blood spots) and the identification of pathogenic variants in both alleles of the TPP1/CLN2 gene for confirmation of CLN2 disease.[4] When it is not possible to perform both analyses, either demonstration of deficient TPP1 enzyme activity in leukocytes or fibroblasts, or detection of two pathogenic variants in the CLN is diagnostic for CLN2 disease.[4] The 2021 guidelines established that the diagnosis of CLN2 can be confirmed by low levels of TPP1 enzyme activity and should be double confirmed by detecting two disease-causing mutations in the CLN2 gene.[5]

Safety

Brineura has a Boxed Warning for hypersensitivity reactions including anaphylaxis.[1] Initiation of Brineura should occur in a health care setting with appropriate monitoring.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Brineura. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Brineura as well as the monitoring required for adverse events and long-term efficacy, approval requires Brineura to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Brineura is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Neuronal Ceroid Lipofuscinosis Type 2 (CLN2).** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   - **A)** Patient has two pathogenic variants in the CLN2 gene as confirmed by genetic testing; AND
   - **B)** Patient has had a test which confirms reduced activity of tripeptidyl peptidase 1 (TPP1); AND
   - **C)** Brineura is prescribed by or in consultation with a metabolic specialist, geneticist, pediatric neurologist, or a physician specializing in the treatment of neuronal ceroid lipofuscinoses (NCLs).

   Dosing. Approve ONE of the following dosing (A, B, C, or D):
   - **A)** Birth to < 6 months: 100 mg via intracerebroventricular (ICV) infusion administered once every other week; OR
   - **B)** 6 months to < 1 year: 150 mg via ICV infusion administered once every other week; OR
   - **C)** 1 year to < 2 years: 200 mg via ICV infusion administered once every other week for the first 4 doses followed by 300 mg via ICV infusion administered once every other week; OR
   - **D)** ≥ 2 years of age 300 mg via ICV infusion administered once every other week.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Brineura is not recommended in the following situations:

1. **Neuronal Ceroid Lipofuscinoses (NCLs) other than neuronal ceroid lipofuscinosis type 2 (CLN2) [e.g., CLN1, CLN3, CLN10, CLN13, and others].** Brineura has not been studied for NCLs involving variants in genes other than CLN2.[1]

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Brineura® intraventricular infusion [prescribing information]. Novato, CA: BioMarin; July 2024.
2. Mukherjee AB, Appu AP, Sadhukhan T, et al. Emerging new roles of the lysosome and neuronal ceroid lipofuscinoses. *Mol Neurodegener*. 2019;14(1):4.
3. Williams RE, Adams HR, Blohm M, et al. Management strategies for CLN2 disease. *Pediatr Neurol*. 2017;69:102-112.

4. Fietz M, AlSayed M, Burke D, et al. Diagnosis of neuronal ceroid lipofuscinosis type 2 (CLN2 disease): expert recommendations for early detection and laboratory diagnosis. *Mol Genet Metab*. 2016;119(1-2):160-167.
5. Mole S, Schulz A, Badoe, E. Guidelines on the diagnosis, clinical assessments, treatment and management for CLN2 disease patients. *Orphanet J Rare Dis*. 2021;16:185.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Late Infantile Neuronal Ceroid Lipofuscinosis Type 2 (CLN2):** The requirement that the patient has had a genetic test which confirms the diagnosis of CLN2 disease OR patient has had a test which confirms reduced activity of tripeptidyl peptidase 1 (TPP1) was changed to "Patient has two pathogenic mutations in the CLN2 gene as confirmed by genetic testing AND patient has had a test which confirms reduced activity of tripeptidyl peptidase 1 (TPP1)."	04/12/2023
Annual Revision	No criteria changes	04/10/2024
Selected Revision	**Neuronal Ceroid Lipofuscinosis Type 2 (CLN2):** The condition name was changed to as listed; previously, the approval condition was titled Late Infantile Neuronal Ceroid Lipofuscinosis Type 2 (CLN2). The requirement that the patient is ≥ 3 years of age was removed from the criteria. For diagnosis confirmed by genetic testing, rephrased the term "mutation" to "pathogenic variant". **Dosing:** Age based dosing has been added from birth to ≥ 2 years of age. The requirement that each dose is followed by an infusion of intraventricular electrolytes (supplied in the Brineura package) has been removed from the criteria.	08/07/2024
Annual Revision	No criteria changes.	04/02/2025