VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION MANAGEMENT MEDICAL POLICY

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

REVIEW DATE: 04/12/2023

OVERVIEW

Brineura is indicated to slow the loss of ambulation in symptomatic pediatric patients ≥ 3 years of age with **late infantile neuronal ceroid lipofuscinosis type 2** (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency.[1]

Brineura is recombinant human TPP1 produced using recombinant DNA technology. 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 mutations 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 mutation 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 gold standard for laboratory diagnosis is 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]

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 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. **Late Infantile Neuronal Ceroid Lipofuscinosis Type 2 (CLN2).** Approve for 1 year if the patient meets ALL of the following (A, B, C and D):
   - **A)** Patient is ≥ 3 years of age; AND
   - **B)** Patient has two pathogenic mutations in the CLN2 gene as confirmed by genetic testing; AND
   - **C)** Patient has had a test which confirms reduced activity of tripeptidyl peptidase 1 (TPP1); AND
   - **D)** 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 the following dosing (A and B):
   - **A)** 300 mg via intracerebroventricular (ICV) infusion administered once every other week; AND
   - **B)** Each dose is followed by an infusion of intraventricular electrolytes (supplied in the Brineura package).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Brineura is not recommended in the following situations:

1. **Neuronal Ceroid Lipofuscinoses (NCLs) other than late infantile ceroid lipofuscinosis type 2 (CLN2) [e.g., CLN1, CLN3, CLN10, CLN13, and others].** Brineura has not been studied for NCLs involving mutations 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 2020.
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	No criteria changes.	03/23/2022

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