POLICY: Neurology – Brineura® (cerliponase alfa injection for intraventricular use – BioMarin)

DATE REVIEWED: 04/08/2020

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 neuronal ceroid lipofuscinoses (NCLs) sometimes referred to as Batten disease.[2] NCL diseases are a heterogenous 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 neurogeneration.[2] In CLN2 disease, symptom onset is typically between 2 and 4 years of age, and lifespan is to 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.

Clinical Efficacy

The efficacy of Brineura in CLN2 disease was assessed in patients 3 to 8 years of age and compared with a natural history cohort.[1] All patients had confirmed TPP1 deficiency. The Motor domain of the CLN2 Clinical Rating Scale assessed declining function, with scores ranging from 3 (indicating grossly normal) to 0 (profoundly impaired). Decline was defined as having an unreversed 2-category decline or an unreversed score of 0. At Week 96, the matched analysis demonstrated fewer patients declined in the Motor domain with Brineura-treated patients (n = 1/17) compared with untreated patients in the natural history cohort (n = 11/17).

Guidelines

Recently published expert recommendations state that patients with a suspected NCL disorder require NCL-specific diagnostic testing.[3] Patients require assessment by a metabolic specialist/geneticist, an NCL specialist, or a pediatric neurologist with experience in diagnosis NCL disorders. While there is no standardized method for identifying patients CLN2 disease, diagnosis is generally based on biochemical measurement of enzyme activity and genetic testing.[3-4]

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(s). 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.

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, and C):
   - **A)** The patient is ≥ 3 years of age; AND
   - **B)** The patient has a diagnosis of CLN2 disease as confirmed by ONE of the following (i or ii):
     - **i.** The patient has had a genetic test which confirms the diagnosis of CLN2 disease; OR
     - **ii.** The 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 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

Brineura has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

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 injection [prescribing information]. Novato, CA: BioMarin Pharmaceutical Inc.; December 2019.
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 SE and Williams RE. Neuronal ceroid-lipofuscinoses. GeneReviews® [Internet]. Updated: August 1, 2013. Accessed March 26, 2020. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1428/.

HISTORY

Type of Revision	Summary of Changes	Date Reviewed
Annual revision	No changes.	07/11/2018
Early annual revision	Early revision to align review date with new Brineura PA Policy. **Late Infantile Neuronal Ceroid Lipofuscinosis Type 2:** Update approval duration to be 1 year for all reviews (previously was 6 months for initial approval and 1 year for extended). Revise policy statement to require all reviews meet the Criteria section of the policy (previously only needed on initial authorizations).	04/10/2019
Annual revision	No changes to criteria.	04/08/2020