BRINEURA® (CERLIPONASE ALFA)

Policy Number: CS2020D0065G **Effective Date**: TBD

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Commercial Policy
- Brineura® (Cerliponase Alfa)

APPLICATION

This Medical Benefit Drug Policy only applies to the state of Louisiana

COVERAGE RATIONALE

Brineura is proven and medically necessary for slowing the loss of ambulation in symptomatic pediatric patients with late infantile neuronal ceroid lipofuscinosis (LINCL) type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency, when ALL of the following criteria are met: [1-6,10-15]

- For initial therapy, **all** of the following:
  - **One** of the following:
    - Diagnosis of late infantile neuronal ceroid lipofuscinosis type 2 (CLN2) by a neurologist with expertise in the diagnosis of CLN2
    - Diagnosis of late infantile neuronal ceroid lipofuscinosis type 2 (CLN2) by a physician in consultation with a neurologist with expertise in the diagnosis of CLN2;

    and
  - Patient is age 3 years or older; **and**
  - **All** of the following scores on the Clinical Scoring System for LINCL: [4]
    - Combined score of 3 to 6 in the motor and language domains
    - Score of at least 1 in the motor domain
    - Score of at least 1 in the language domain;

    and
  - **One** of the following:
    - Brineura is prescribed by a neurologist with expertise in the treatment of CLN2
    - Brineura is prescribed by a physician in consultation with a neurologist with expertise in the treatment of CLN2;

    and
  - Brineura is to be administered intraventricularly by, or under the direction of, healthcare professionals experienced in performing intraventricular infusions via an intracerebroventricular catheter; **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling: 300 mg administered once every other week as an intraventricular infusion; **and**

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- Initial authorization will be for no more than 6 months

- For continuation therapy, **all** of the following:
  - **One** of the following:
    - Diagnosis of late infantile neuronal ceroid lipofuscinosis type 2 (CLN2) by a neurologist with expertise in the diagnosis of CLN2
    - Diagnosis of late infantile neuronal ceroid lipofuscinosis type 2 (CLN2) by a physician in consultation with a neurologist with expertise in the diagnosis of CLN2;

    and
  - Patient is age 3 years or older; **and**
  - Patient has a score of 1 or higher in the motor domain of the Clinical Scoring System for LINCL; [4] **and**
  - **One** of the following:
    - Brineura is prescribed by a neurologist with expertise in the treatment of CLN2
    - Brineura is prescribed by a physician in consultation with a neurologist with expertise in the treatment of CLN2;

    and
  - Brineura is to be administered intraventricularly by, or under the direction of, healthcare professionals experienced in performing intraventricular infusions via an intracerebroventricular catheter; **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling: 300 mg administered once every other week as an intraventricular infusion; **and**
  - Reauthorization will be for no more than 6 months

Brineura (cerliponase alfa) is unproven and not medically necessary for other forms of neuronal ceroid lipofuscinosis.

APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Coverage Determination Guidelines may apply.

HCPCS Code	Description
J0567	Injection, cerliponase alfa, 1 mg

ICD-10 Diagnosis Code	Description
E75.4	Neuronal ceroid lipofuscinosis

BACKGROUND

Neuronal ceroid lipofuscinosis type 2 (CLN2), is a neurodegenerative lysosomal storage disorder caused by deficient activity of the enzyme tripeptidyl peptidase. CLN2 is autosomal recessive and pediatric-onset, and is characterized by seizures, language delay, movement disorders, motor deterioration, dementia, blindness, and early death.[2,3] A Clinical Scoring System for late infantile neuronal ceroid lipofuscinoses has been developed as a method for quantitative description of clinical courses over time. [4]

CLINICAL EVIDENCE

Proven

Ceroid Lipofuscinosis Type 2 (CLN2) / Tripeptidyl Peptidase 1 (TPP1) Deficiency

Cerliponase alfa is 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]

In a multicenter, open-label study, Schulz A. et al evaluated the effect of intraventricular infusion of cerliponase alfa every 2 weeks in pediatric patients with CLN2. [5] The primary outcome compared the duration until a 2-point decline in the score on the motor and language domains of the CLN2 Clinical Rating Scale in study patients to the rate of decline in 42 historical controls. In addition, the rate of decline in the motor-language score was compared between the two groups. Of the 24 patients enrolled, 23 constituted the efficacy population. The median time until a 2-point decline in the motor-language score was not reached for treated patients and was 345 days for historical controls. The mean

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(±SD) unadjusted rate of decline in the motor-language score per 48-week period was 0.27±0.35 points in treated patients and 2.12±0.98 points in 42 historical controls (mean difference, 1.85; P<0.001). Common adverse events included convulsions, pyrexia, vomiting, hypersensitivity reactions, and failure of the intraventricular device. Infections developed in the intraventricular device for administration in 2 pateints, required antibiotic treatment and device replacement. The authors conclude that intraventricular infusion of cerliponase alfa in patients with CLN2 disease resulted in less decline in motor and language function than that in historical controls.

Clinical evidence for the safety and efficacy of cerliponase alfa for the treatment of late infantile neuronal ceroid lipofuscinosis type 2 (CLN2) was demonstrated in a prospective Phase 1/2 Open-Label Dose-Escalation Study and Extension. The objective of the study was to evaluate the safety and tolerability of cerliponase alfa administered to patients with CLN2 disease by intraventricular administration. There were 5 study centers involved. Patients were treated with intraventricular infusion of cerliponase alfa with doses ranging from 30 to 300 mg every 14 days in the dose escalation study and were maintained at 300 mg every 14 days in the extension study. The primary endpoint was response rate, defined as the absence of an unreversed two-point decline or score of zero in the CLN2 score at 48 weeks. 24 patients were enrolled, with 23 patients completing the study. By motor/language CLN2 scores measured from baseline, 87% (20/23) of treated patients responded to treatment, defined as an absence of an unreversed two-point decline or score of zero by Week 48, compared to an expected response rate of 50% (P-value=0.0002). Sixty-five percent of treated patients experienced no progression in their CLN2 score. Of all points lost, approximately 80% occurred within four months of treatment initiation. The proportion of patients with a response to treatment was 87% at Week 48 and 63% at Week 96. [6]

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Brineura (cerliponase alfa) 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]

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Medicare does not have a National Coverage Determination (NCD) for Brineura® (cerliponase alfa). Local Coverage Determinations (LCDs) do not exist.

~~Medicare does not have a National Coverage Determination (NCD) specifically for Brineura® (cerliponase alfa). Local Coverage Determinations (LCDs) do not exist at this time.~~

In general, Medicare covers outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. Refer to the Medicare Benefit Policy Manual, Chapter 15, §50 - Drugs and Biologicals. (Accessed ~~April 22, 2019~~June 20 2020)

REFERENCES

1. Brineura [prescribing information]. Novato, CA: BioMarin Pharmaceutical Inc.; ~~December 2018~~ **March 2020**.
2. Williams RE, Adams HR, Blohm M, Cohen-Pfeffer JL, de Los Reyes E, Denecke J, et al. Management Strategies for CLN2 Disease. Pediatr Neurol. 2017 Apr;69:102-112.
3. http://www.cln2connection.com/overview/cln2-disease. Accessed May 30, 2019.
4. Steinfeld R, Heim P, von Gregory H, et al. Late infantile neuronal ceroid lipofuscinosis: quantitative description of the clinical course in patients with CLN2 mutations. Am J Med Genet. 2002;112:347-354.
5. AMCP Dossier for Brineura™ (cerliponase alfa), BioMarin Pharmaceutical, May 2017.
6. Schulz A, et al. Study of Intraventricular Cerliponase Alfa for CLN2 Disease. N Engl J Med. 2018 Apr 24.

POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
TBD	**Annual review. No changes to coverage criteria. Updated CMS statement and reference**

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