BRINEURA™ (CERLIPONASE ALFA)

Policy Number: CS2019D0065F

Effective Date: August 1, 2019

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APPLICATION

This Medical Benefit Drug Policy does not apply to the states of Kansas and Pennsylvania. For the state of Pennsylvania, refer to the related Community Plan policy section above.

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**
  - 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

   o Patient is age 3 years or older; and
   o Patient has a score of 1 or higher in the motor domain of the Clinical Scoring System for LINCL; and
   o 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

   o Brineura is to be administered intraventricularly by, or under the direction of, healthcare professionals
     experienced in performing intraventricular infusions via an intracerebroventricular catheter; and
   o 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
   o 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.

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<td>J0567</td>
<td>Injection, cerliponase alfa, 1 mg</td>
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<th>ICD-10 Diagnosis Code</th>
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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. A Clinical
Scoring System for late infantile neuronal ceroid lipofuscinoses has been developed as a method for quantitative
description of clinical courses over time. A

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. In

In a multicenter, open-label study, Schulz A. et al evaluated the effect of intraventricular infusion of cerliponase alfa
evory 2 weeks in pediatric patients with CLN2. 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
(±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 patients, 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) 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)

REFERENCES

5. AMCP Dossier for Brineura™ (cerliponase alfa), BioMarin Pharmaceutical, May 2017.

POLICY HISTORY/REVISION INFORMATION

<table>
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<tr>
<td>08/01/2019</td>
<td>Reorganized policy template:&lt;br&gt;• Simplified and relocated Application section; previously titled State Exceptions&lt;br&gt;• Relocated Background and FDA sections</td>
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Supporting Information

• Archived previous policy version CS2019D0065E

INSTRUCTIONS FOR USE

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

Brineura™ (Cerliponase Alfa)
UnitedHealthcare Community Plan Medical Benefit Drug Policy
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UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.