BRINEURA™ (CERLIPONASE ALFA) (FOR PENNSYLVANIA ONLY)

Policy Number: CS2019D0065D1

Effective Date: August 1, 2019

Table of Contents

<table>
<thead>
<tr>
<th>Table of Contents</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>APPLICATION</td>
<td>1</td>
</tr>
<tr>
<td>COVERAGE RATIONALE</td>
<td>1</td>
</tr>
<tr>
<td>APPLICABLE CODES</td>
<td>2</td>
</tr>
<tr>
<td>BACKGROUND</td>
<td>2</td>
</tr>
<tr>
<td>CLINICAL EVIDENCE</td>
<td>2</td>
</tr>
<tr>
<td>U.S. FOOD AND DRUG ADMINISTRATION</td>
<td>3</td>
</tr>
<tr>
<td>CENTERS FOR MEDICARE AND MEDICAID SERVICES</td>
<td>3</td>
</tr>
<tr>
<td>REFERENCES</td>
<td>3</td>
</tr>
<tr>
<td>POLICY HISTORY/REVISION INFORMATION</td>
<td>3</td>
</tr>
<tr>
<td>INSTRUCTIONS FOR USE</td>
<td>3</td>
</tr>
</tbody>
</table>

APPLICATION

This Medical Benefit Drug Policy only applies to the state of Pennsylvania. For all other states, 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**
  - Submission of medical records documenting baseline motor function as measured by the motor domain of the Clinical Scoring System for LINCL; 4 **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**
  - Patient is age 3 years or older; **and**
  - Submission of medical records documenting the patient’s disease has stabilized or improved based on the physician’s assessment; 4 **and**

Related Community Plan Policy
- Brineura™ (Cerliponase Alfa)

Commercial Policy
- Brineura™ (Cerliponase Alfa)
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.

<table>
<thead>
<tr>
<th>HCPCS Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J0567</td>
<td>Injection, cerliponase alfa, 1 mg</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-10 Diagnosis Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>E75.4</td>
<td>Neuronal ceroid lipofuscinosis</td>
</tr>
</tbody>
</table>

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.

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 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. 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.

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. 

**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. 

**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>
<thead>
<tr>
<th>Date</th>
<th>Action/Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>08/01/2019</td>
<td>Template Update: Reorganized policy template:</td>
</tr>
<tr>
<td></td>
<td>o Added Application section (content relocated from Coverage Rationale section)</td>
</tr>
<tr>
<td></td>
<td>o Relocated Background and FDA sections</td>
</tr>
</tbody>
</table>

**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.

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.