Brineura® (Cerliponase Alfa)

Policy Number: 2023D0065J
Effective Date: August 1, 2023

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Community Plan Policy

- Brineura® (Cerliponase Alfa)

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; and
  - Initial authorization will be for no more than 6 months

- For continuation of 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; 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; 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 the member specific benefit plan document 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 Guidelines may apply.

<table>
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<tr>
<th>HCPCS Code</th>
<th>Description</th>
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<tr>
<td>J0567</td>
<td>Injection, cerliponase alfa, 1 mg</td>
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<tr>
<th>Diagnosis Code</th>
<th>Description</th>
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<tr>
<td>E75.4</td>
<td>Neuronal ceroid lipofuscinosis</td>
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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-1 (TPP1). Deficiency in TPP1 activity results in the accumulation of lysosomal storage materials normally metabolized by this enzyme in the central nervous system (CNS), leading to progressive decline in motor function. 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. Within CLN2, two forms of disease evolution exist; classical CLN2 is where symptoms start earlier, between the ages of 3 and 5 years and the symptoms evolve faster. Non-classical CLN2 has a much slower disease evolution and symptoms appear as behavioral disorders, movement disorders and ataxia rather than seizures and blindness.

Cerliponase alfa (rhTTP1), a proenzyme, is taken up by target cells in the CNS and is translocated to the lysosomes through the Cation Independent Mannose-6-Phosphate Receptor (CI-MPR, also known as M6P/IGF2 receptor). Cerliponase alfa is activated in the lysosome and the activated proteolytic form of rhTTP1 cleaves tripeptides from the N-terminus of proteins.

### Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under
some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit
document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare
diseases may occur when certain conditions are met. Refer to the Policy and Procedure addressing the treatment of serious rare
diseases.

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 CLN2.6 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

Twenty-one international experts from seven different specialties developed guidelines on the diagnosis, clinical assessments,
treatment, and management for CLN2 disease patients that were published in 2021.7 From a consensus statement in these
guidelines, it is stated that initiation of long-term ERT with cerliponase alfa at 300 mg (or age-appropriate) dose every other
week through intraventricular infusion is suggested in non-classical TPP1 deficiency patients after confirmed diagnosis and
agreement between parents and provider, as long as no contraindications to therapy exist. Furthermore, initiation of long-term
ERT with cerliponase alfa at 300 mg (or age-appropriate) dose every other week through intraventricular infusion is
recommended in classical CLN2 patients with the potential to benefit from this therapy.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

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
References

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

Policy History/Revision Information

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<thead>
<tr>
<th>Date</th>
<th>Summary of Changes</th>
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<tbody>
<tr>
<td>08/01/20223</td>
<td>• Routine review; no change to coverage guidelines</td>
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<tr>
<td></td>
<td>• Archived previous policy version 2022D0065I</td>
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Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. 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.

This Medical Benefit Drug Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. 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.