BRINEURA™ (CERLIPONASE ALFA)

Policy Number: PHARMACY 300.4 T2 **Effective Date**: January 1, 2019

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Related Policy

- Acquired Rare Disease Drug Therapy Exception Process

INSTRUCTIONS FOR USE

This Clinical Policy provides assistance in interpreting Oxford benefit plans. Unless otherwise stated, Oxford policies do not apply to Medicare Advantage members. Oxford reserves the right, in its sole discretion, to modify its policies as necessary. This Clinical Policy is provided for informational purposes. It does not constitute medical advice. The term Oxford includes Oxford Health Plans, LLC and all of its subsidiaries as appropriate for these policies.

When deciding coverage, the member specific benefit plan document must be referenced. The terms of the member specific benefit plan document [e.g., Certificate of Coverage (COC), Schedule of Benefits (SOB), and/or Summary Plan Description (SPD)] may differ greatly from the standard benefit plan upon which this Clinical Policy is based. In the event of a conflict, the member specific benefit plan document supersedes this Clinical Policy. All reviewers must first identify member eligibility, any federal or state regulatory requirements, and the member specific benefit plan coverage prior to use of this Clinical Policy. Other Policies may apply.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines 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.

CONDITIONS OF COVERAGE

Applicable Lines of Business/Products	This policy applies to Oxford Commercial plan membership.
Benefit Type	Medical Benefit
Referral Required (Does not apply to non-gatekeeper products)	No
Authorization Required (Precertification always required for inpatient admission)	Yes
Precertification with Medical Director Review Required	Yes[1]
Applicable Site(s) of Service (If site of service is not listed, Medical Director review is required)	Office, Outpatient, Home
Special Considerations	[1]Precertification with review by a Medical Director or their designee is required.

BENEFIT CONSIDERATIONS

Before using this policy, please check the member specific benefit plan document and any federal or state mandates, if applicable.

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 titled Acquired Rare Disease Drug Therapy Exception Process.

Essential Health Benefits for Individual and Small Group

For plan years beginning on or after January 1, 2014, the Affordable Care Act of 2010 (ACA) requires fully insured non-grandfathered individual and small group plans (inside and outside of Exchanges) to provide coverage for ten categories of Essential Health Benefits ("EHBs"). Large group plans (both self-funded and fully insured), and small group ASO plans, are not subject to the requirement to offer coverage for EHBs. However, if such plans choose to provide coverage for benefits which are deemed EHBs, the ACA requires all dollar limits on those benefits to be removed on all Grandfathered and Non-Grandfathered plans. The determination of which benefits constitute EHBs is made on a state by state basis. As such, when using this policy, it is important to refer to the member specific benefit plan document to determine benefit coverage.

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; **or**
    - 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; **or**
    - 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; **or**
    - 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; **or**
    - 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.

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]

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]

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 may apply.

HCPCS Code	Description
J0567	Injection, cerliponase alfa, 1 mg

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

CLINICAL EVIDENCE

Proven/Medically Necessary

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 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.[5]

REFERENCES

The foregoing Oxford policy has been adapted from an existing UnitedHealthcare Pharmacy, Clinical Pharmacy Program that was researched, developed and approved by the UnitedHealth Group National Pharmacy & Therapeutics Committee. [*2017D0065A*]

1. Brineura [prescribing information]. Novato, CA: BioMarin Pharmaceutical Inc.; April 2017.
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 7, 2018.
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
01/01/2019	• Updated list of applicable HCPCS codes to reflect annual code edits: ○ Added J0567* ○ Removed C9014* and J3590 *(*annual code edit)* • Archived previous policy version PHARMACY 300.3 T2