Effective Date **8/1/2022**
Next Review Date… **8/1/2023**
Coverage Policy Number **IP0175**

Cerliponase Alfa

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for cerliponase alfa (Brineura®).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Cerliponase alfa (Brineura) is considered medically necessary when the following are met:

1. **Late Infantile Neuronal Ceroid Lipofuscinosis Type 2 (CLN2).** Individual meets **ALL** of the following criteria (A, B, and C):
    A. 3 years of age or older
    B. Diagnosis of symptomatic late infantile neuronal ceroid lipofuscinosis type 2 (CLN2) documented by **ONE** of the following (i or ii):

i. Individual has had a genetic test which confirms the diagnosis of CLN2 disease (biallelic pathogenic or likely pathogenic variants in the *TPP1* gene)
ii. Individual has a deficiency of tripeptidyl peptidase 1 (TPP1) in dry blood spots, leukocytes or fibroblasts

C. Medication is prescribed by or in consultation with a metabolic specialist, geneticist, pediatric neurologist, or a physician specializing in the treatment of neuronal ceroid lipofuscinoses (NCLs)

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Cerliponase alfa (Brineura) is considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration is up to 12 months.

Reauthorization approval duration is up to 12 months.

Conditions Not Covered

Cerliponase alfa (Brineura) is considered experimental, investigational or unproven for **ANY** other use including the following (this list may not be all inclusive):

1. **Neuronal Ceroid Lipofuscinoses (NCLs) other than late infantile ceroid lipofuscinosis type 2 (CLN2) [e.g., CLN1, CLN3, CLN10, CLN13, and others].**
   Brineura has not been studied for NCLs involving mutations in genes other than CLN2.[1]

Coding / Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J0567	Injection, cerliponase alfa, 1 mg

Background

OVERVIEW
Brineura is indicated to slow the loss of ambulation in symptomatic pediatric patients ≥ 3 years of age with **late infantile neuronal ceroid lipofuscinosis type 2** (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency.[1]

Dosing and Administration
Brineura is recombinant human TPP1 produced using recombinant DNA technology.[1] The recommended dose of Brineura is 300 mg administered once every other week (QOW) via intracerebroventricular (ICV) infusion. Following Brineura administration, the patient must also receive an infusion of intraventricular electrolytes. The

drug is administered into the cerebral spinal fluid via a surgically implanted reservoir and catheter. It should only be administered by or under the direction of a physician who is knowledgeable in ICV administration.

The recommended dosage of Brineura in pediatric patients 3 years of age and older is 300 mg administered once every other week by intraventricular infusion. Administer Brineura first followed by infusion of the Intraventricular Electrolytes each at an infusion rate of 2.5 mL/hr. The complete Brineura infusion, including the required infusion of Intraventricular Electrolytes, is approximately 4.5 hours. Pre-treatment of patients with antihistamines with or without antipyretics or corticosteroids is recommended 30 to 60 minutes prior to the start of infusion.

Disease Overview
CLN2 disease is an extremely rare neurodegenerative disorder that is part of a group of neuronal ceroid lipofuscinoses (NCLs) sometimes referred to as Batten disease.[2] NCL diseases are a heterogeneous group of incurable neurodegenerative lysosomal storage diseases. They manifest as early impairment of vision, loss of cognitive and motor functions, seizures, and premature death. To date, 13 genetic mutations have been discovered to cause the multiple variations of the disease (e.g., CLN1, CLN2, CLN3 etc.). Classic late infantile NCL disease is caused by a mutation in the CLN2 gene, which encodes for lysosomal TPP1. Without TPP1, lysosomal storage materials accumulate, contributing to the progressive and persistent neurodegeneration.[2] In CLN2 disease, symptom onset is typically between 2 and 4 years of age, and lifespan is around 6 to 14 years. Other NCLs result in deficiencies in enzymes other than TPP1. As Brineura is human recombinant TPP1, its efficacy is specific to CLN2 disease.

Guidelines
Recently published expert recommendations state that patients with a suspected NCL disorder require NCL-specific diagnostic testing.[3] Patients require assessment by a metabolic specialist/geneticist, an NCL specialist, or a pediatric neurologist with experience in diagnosing NCL disorders. While there is no standardized method for identifying patients with CLN2 disease, diagnosis is generally based on biochemical measurement of enzyme activity and genetic testing.[3-4]

References

1. Brineura® intraventricular infusion [prescribing information]. Novato, CA: BioMarin; July 2020.
2. Mukherjee AB, Appu AP, Sadhukhan T, et al. Emerging new roles of the lysosome and neuronal ceroid lipofuscinoses. *Mol Neurodegener*. 2019;14(1):4.
3. Williams RE, Adams HR, Blohm M, et al. Management strategies for CLN2 disease. *Pediatr Neurol*. 2017;69:102-112.
4. Fietz M, AlSayed M, Burke D, et al. Diagnosis of neuronal ceroid lipofuscinosis type 2 (CLN2 disease): expert recommendations for early detection and laboratory diagnosis. *Mol Genet Metab*. 2016;119(1-2):160-167.