Neighborhood Health Plan OF RHODE ISLAND™
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Brineura (cerliponase alfa)
(Intraventricular)

Effective Date: 01/01/2020
Review Date: 12/4/2019, 1/29/20, 01/28/2021, 01/20/2022, 01/26/2023, 12/07/2023, 01/04/2024, 08/28/2024, 05/07/2025, 03/03/2026
Scope: Medicaid, Commercial, Medicare

I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

A. Max Units (per dose and over time) [HCPCS Unit]:

- 300 billable units (one kit containing 2 vials) every 14 days

III. Summary of Evidence

Brineura is a hydrolytic lysosomal N-terminal tripeptidyl peptidase indicated to slow the loss of ambulation in pediatric patients with neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency. Brineura efficacy was evaluated over 96 weeks in a non-randomized, single-arm clinical study with an extension phase in symptomatic pediatric patients aged 3 to 8 years with CLN2 disease confirmed by TPP1 deficiency. Patients received intraventricular infusions every other week, and their motor function was compared with that of untreated patients from an independent natural-history cohort using the Motor domain of the CLN2 Clinical Rating Scale. Among 24 enrolled patients, 23 continued treatments into the extension period, and analyses focused on 22 eligible treated patients versus 42 untreated controls. Logistic modeling showed that Brineura-treated patients had 13 times higher odds of not experiencing motor decline by 96 weeks compared with untreated patients (OR 13.1; 95% CI 1.2–146.9), demonstrating a significant delay in disease progression. Most common adverse reactions (>8%) include pyrexia, ECG abnormalities, decreased CSF protein, vomiting, seizures, hypersensitivity, increased CSF protein, hematoma, headache, irritability, pleocytosis, device-related infection, bradycardia, feeling jittery, and hypotension.

IV. Initial Approval Criteria[1,2,5,7]

Coverage is provided in the following conditions:

Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

Universal Criteria

- Member is at least 37 weeks post-menstrual age (gestational age at birth plus post-natal age) and weighs at least 2.5 kg years of age; **AND**
- Member must not have any acute intraventricular access device-related complications (e.g., leakage, extravasation of fluid, or device failure); **AND**
- Member must not have ventriculoperitoneal shunts; **AND**
- Member has no signs or symptoms of acute, unresolved localized infection on or around the device insertion site (e.g. cellulitis or abscess); or a suspected or confirmed CNS infection (e.g., cloudy CSF, positive CSF gram stain, or meningitis; **AND**

Late infantile neuronal ceroid lipofuscinosis type 2 (CLN2); tripeptidyl peptidase 1 (TPP1) deficiency †

- Member must have a definitive diagnosis of late infantile CLN2 confirmed by deficiency of the lysosomal enzyme tripeptidyl peptidase-1 (TPP1) and/or molecular analysis indicating two pathogenic variants/mutations in the TPP1/CLN2 gene on chromosome 11p15 ; **AND**
- Member has mild to moderate symptoms of disease documented by a two-domain score of 3 to 6 on the motor and language domains of the Hamburg CLN2 Clinical Rating Scale, with a score of at least 1 in each of these two domains; **AND**
- Member is ambulatory; **AND**
- Members with a history of bradycardia, conduction disorder, or with structural heart disease will have electrocardiogram (ECG) monitoring performed during each infusion

† FDA-labeled indication(s)

V. Renewal Criteria[1,5,7]

- Member continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section IV; **AND**
- Absence of unacceptable toxicity from the drug or complications from the device. Examples of unacceptable toxicity or complications include: meningitis and other intraventricular access device-related infections, intraventricular access device-related complications, severe hypersensitivity reactions including anaphylaxis, severe cardiovascular reactions, infusion-associated reactions (e.g., vomiting, seizure, rash, pyrexia, hypersensitivity, and anaphylactic reaction), etc.; **AND**
- Member has had a 12-lead ECG evaluation performed within the last 6 months [***Note:*** Members with cardiac abnormalities (e.g., a history of bradycardia, conduction disorder, or with structural heart disease) require an ECG during each infusion]; **AND**
- Member has responded to therapy compared to pretreatment baseline with stability/lack of decline in motor function/milestones on the Motor domain of the Hamburg CLN2 Clinical Rating Scale [Decline is defined as having an unreversed (sustained) 2-category decline or an unreversed score of 0].

VI. Dosage/Administration[1,2,5,7]

Indication	Dose
CLN2	**Dose by Age:** • **Birth to < 6 months**: 100 mg of Brineura (3.3 mL) administered once every other week by intraventricular infusion. • **6 months to < 1 year**: 150 mg of Brineura (5 mL) administered once every other week by intraventricular infusion. • **1 year to < 2 years**: For the first 4 doses, administer 200 mg of Brineura (6.7 mL) once every other week by intraventricular infusion. For subsequent doses, administer 300 mg of Brineura (10 mL) once every other week by intraventricular infusion. • **≥ 2 years**: 300 mg of Brineura (10 mL) administered once every other week by intraventricular infusion. **General Recommendations:** Administer Brineura first followed by infusion of the Intraventricular Electrolytes. For patients aged < 6 months, the recommended infusion rate of the Intraventricular Electrolytes is 1.25 mL/hr. For patients ≥ 6 months, the recommended infusion rate of the Intraventricular Electrolytes is 2.5 mL/hr.. The complete Brineura infusion, including the required infusion of Intraventricular Electrolytes, is approximately 4.5 hours. • Brineura should be administered by, or under the supervision of a physician experienced in intraventricular administration via a surgically implanted intraventricular access device system which consists of the reservoir and catheter components. • Brineura administration should be supervised by a healthcare provider knowledgeable in the management of hypersensitivity reactions including anaphylaxis and should be initiated in a healthcare setting with appropriate medical monitoring and support measures, including access to cardiopulmonary resuscitation equipment. • Brineura administration should be supervised by a healthcare provider knowledgeable in the management of hypersensitivity reactions including anaphylaxis and should be initiated in a healthcare setting with appropriate medical monitoring and support measures, including access to cardiopulmonary resuscitation equipment. • Brineura is administered into the cerebrospinal fluid (CSF) by infusion via a surgically implanted reservoir and catheter (the "intraventricular access device system"). Brineura is intended to be administered via the Codman® HOLTER RICKHAM Reservoirs with the Codman® Ventricular Catheter. The intraventricular access device reservoir must be implanted prior to the first infusion. It is recommended that the first dose be administered at least 5 to 7 days after device implantation.

	• Brineura is intended to be administered with the B Braun Perfusor® Space Infusion Pump System. Refer to the Brineura Prescribing Information for the essential performance syringe pump requirements in the event that an alternative pump must be used. • Pre-treatment of patients with antihistamines with or without antipyretics or corticosteroids is recommended 30 to 60 minutes prior to the start of infusion.

VII. Billing Code/Availability Information

HCPCS Code:

- J0567 – Injection, cerliponase alfa, 1 mg: 1 billable unit = 1 mg

NDC:

- Brineura 150 mg/5 mL (30 mg/mL) solution, two single-dose vials per carton co-packaged with Intraventricular Electrolytes Injection 5 mL in a single-dose vial: 68135-0811-xx

VIII. References

1. Brineura [package insert]. Novato, CA; BioMarin Pharmaceutical Inc.; August 2024. Accessed February 2026.
2. Schulz A, Specchio N, Gissen P. Intracerebroventricular cerliponase alfa (BMN 190) in children with CLN2 disease: Results from a Phase 1/2, open-label, dose-escalation study. J Inherit Metab Dis. 2016; 39 (Suppl. 1): S51.
3. Cherukuri A, Cahan H, Van Tuyl A, et al. Immunogenicity to cerliponase alfa, an enzyme replacement therapy for patients with CLN2 disease: results from a phase 1/2 study. Molecular Genetics and Metabolism. 2017 Jan 1;120(1):S35.
4. Schulz A, Specchio N, Gissen P, et al. Long-term safety and efficacy of intracerebroventricular enzyme replacement therapy with cerliponase alfa in children with CLN2 disease: interim results from an ongoing multicenter, multinational extension study. Molecular Genetics and Metabolism. 2017 Jan 1;120(1):S120.
5. Mole SE, Williams RE. Neuronal Ceroid-Lipofuscinoses. GeneReviews®. www.ncbi.nlm.nih.gov/books/NBK1428/. Initial Posting: October 10, 2001; Last Update: August 1,2013. Accessed on May 01, 2017.
6. Online Mendelian Inheritance in Man, OMIM®. Johns Hopkins University, Baltimore, MD. MIM Number: 204500: 9/18/2016. World Wide Web URL: https://omim.org/
7. Schulz A, Ajayi T, Specchio N, et al. Study of Intraventricular Cerliponase Alfa for CLN2 Disease. 1 N Engl J Med. 2018 May 17;378(20):1898-1907. doi: 10.1056/NEJMoa1712649. Epub 2018 Apr 24.

Appendix 1 – Covered Diagnosis Codes

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

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Articles may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/Article):N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)

Policy Rationale:
Brineura was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Brineura according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For Medicare members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.