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
Scope: Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

I. Length of Authorization

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

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC unit]:

- Brineura 150 mg/5 mL single dose vial : 2 vials every 14 days

B. 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 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. Clinical trials evaluating the efficacy and safety of Brineura in patients with CLN2 disease have demonstrated significant benefits in slowing the decline of motor and language function, reducing the frequency of seizures, and improving overall quality of life. 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:

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

Universal Criteria

- Patient is at least 3 years of age; **AND**

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- Patient must not have acute intraventricular access device-related complications (e.g., leakage, extravasation of fluid, or device failure); **AND**
- Patient must not have ventriculoperitoneal shunts; **AND**
- Patient 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 †

- Patient 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 inthe TPP1/CLN2 gene on chromosome 11p15 ; **AND**
- Patient has mild to moderate 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**
- Patient is ambulatory; **AND**
- Patients with a history of bradycardia, conduction disorder, or with structural heart disease must have electrocardiogram (ECG) monitoring performed during the infusion

† FDA-labeled indication(s)

V. Renewal Criteria[1,5,7]

- Patient 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 III; **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, etc.; **AND**
- Patient has had a 12-lead ECG evaluation performed within the last 6 months (those with cardiac abnormalities require an ECG during each infusion); **AND**
- Patient 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	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

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	complete Brineura infusion, including the required infusion of Intraventricular Electrolytes, is approximately 4.5 hours. • Aseptic technique must be strictly observed during preparation and administration • Brineura should be administered by, or under the direction of a physician knowledgeable in intraventricular administration • Brineura is administered into the cerebrospinal fluid (CSF) by infusion via a surgically implanted reservoir and catheter (intraventricular access device). Brineura is intended to be administered via the Codman® HOLTER RICKHAM Reservoirs with the Codman® Ventricular Catheter. The intraventricular access device 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. • 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.; July 2020. Accessed January 2023.
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.

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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. 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, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
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.

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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 INTEGRITY (Medicare-Medicaid Plan) 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.

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