Brineura (cerliponase alfa)
(Intraventricular)

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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 (1 kit containing 2 vials) every 14 days

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

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

Universal Criteria [1]

- 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 sign or symptom 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 † Φ [1,2,7,8]

- 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 (2) pathogenic variants/mutations in the 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); ‡ Compendia recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Coverage can be renewed based on the following criteria:

- 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].

V. Dosage/Administration [1]

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 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.

VI. 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

VII. References

1. Brineura [package insert]. Novato, CA; BioMarin Pharmaceutical Inc.; March 2020. Accessed January 2023.
2. Schulz A, Specchio N, Gissen P. Intracerebroventricular Cerliponase Alfa (BMN 190) in Children with CLN2 Disease: Interim Results from a Phase 1/2, Open-Label, Dose-Escalation Study. Neuropediatrics 2016; 47 - FV02-06. DOI: 10.1055/s-0036-1583718.
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. 2010 Oct 10. [Updated 2013 Aug 13]. GeneReviews® [Internet]. University of Washington, Seattle; 1993-2021. www.ncbi.nlm.nih.gov/books/NBK1428/. Accessed on December 30, 2021.
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.
8. 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 Sep;119(1-2):160-7. doi: 10.1016/j.ymgme.2016.07.011.

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 Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/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/LCA):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)
15	KY, OH	CGS Administrators, LLC