

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

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 37 weeks post-menstrual age (gestational age at birth plus post-natal age) and weighs at least 2.5 kg; **AND**

Universal Criteria ¹

- Patient must not have any 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 ^{1,2,6-7}

- 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 will have electrocardiogram (ECG) monitoring performed during each infusion

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Ⓞ Orphan Drug

IV. Renewal Criteria ¹

Coverage may be renewed based on the following criteria:

- Patient continues to meet the 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 (e.g., device leakage, device failure extravasation of CSF fluid, or bulging of the scalp around or above the access device), severe hypersensitivity reactions including anaphylaxis, severe cardiovascular reactions, infusion-associated reactions (e.g., vomiting, seizure, rash, pyrexia, hypersensitivity, and anaphylactic reaction), etc.; **AND**
- Patient has had a 12-lead ECG evaluation performed within the last 6 months [*Note: Patients with cardiac abnormalities (e.g., a history of bradycardia, conduction disorder, or with structural heart disease) 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	Brineura is administered once every other week by intraventricular infusion as noted in the table below:		
	Age groups	Brineura dose administered every other week	Infusion Rate
	Birth to < 6 months	100 mg	1.25 mL/hr
	6 months to < 1 year	150 mg	2.5 mL/hr
	1 year to < 2 years	200 mg (first 4 doses) 300 mg (subsequent doses)	2.5 mL/hr
	2 years and older	300 mg	2.5 mL/hr
NOTE:			
<ul style="list-style-type: none"> • Administer Brineura first followed by infusion of the Intraventricular Electrolytes at the infusion rate noted in the table above. The complete Brineura infusion, including the 			

	<p>required infusion of Intraventricular Electrolytes, is approximately 2 to 4.5 hours, depending on the dose and volume administered.</p> <ul style="list-style-type: none"> • 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 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. • Premedication of patients with antihistamines with or without antipyretics or corticosteroids is recommended 30 to 60 minutes prior to the start of infusion. • 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.
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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.; July 2024. Accessed February 2025.
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. Online Mendelian Inheritance in Man, OMIM®. Johns Hopkins University, Baltimore, MD. MIM Number: 204500: 9/18/2016. World Wide Web URL: <https://omim.org/>
6. 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.
7. 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.
8. Mole SE, Schulz A, Badoe E, et al. Guidelines on the diagnosis, clinical assessments, treatment and management for CLN2 disease patients. *Orphanet J Rare Dis*. 2021 Apr 21;16(1):185. doi: 10.1186/s13023-021-01813-5.

Appendix 1 – Covered Diagnosis Codes

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

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

The preceding information is intended for non-Medicare coverage determinations. 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 Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications, including any preceding information, may be applied 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.

Medicare Part B Administrative Contractor (MAC) Jurisdictions

Jurisdiction	Applicable State/US Territory	Contractor
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)
15	KY, OH	CGS Administrators, LLC