# Clinical Policy: Cerliponasa alfa (Brineura)

Reference Number: PA.CP.PHAR.338
Effective Date: 01/2018
Last Review Date: 07/2025

**Description**
Cerliponase alfa (Brineura®) is a hydrolytic lysosomal N-terminal tripeptidyl peptidase.

**FDA approved indication**
Brineura is indicated to slow the loss of ambulation in pediatric patients with neuronal ceroid lipofuscinosis type 2 (CLN2 disease), also known as tripeptidyl peptidase 1 (TPP1) deficiency.

**Policy/Criteria**
*Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria*

It is the policy of PA Health and Wellness® that Brineura is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Neuronal Ceroid Lipofuscinosis Type 2** (must meet all)**:**

1. Diagnosis of neuronal CLN2;
2. Prescribed by or in consultation with a neurologist;
3. Member weighs ≥ 2.5 kg;
4. Confirmation of CLN2 with both of the following (a and b):
   a. TPP1 enzyme activity test demonstrating deficient TPP1 enzyme activity in leukocytes;
   b. Identification of 2 pathogenic mutations *in trans* in the TPP1/CLN2 gene;
5. At the time of request, member does not have acute intraventricular access device-related complications (e.g., leakage, device failure, or device-related infection) or ventriculoperitoneal shunts.
6. Dose does not exceed 300 mg administered once every other week as an intraventricular infusion;

**Approval duration: 6 months**

**B. Other diagnoses/indications**

1. Refer to PA.CP.PMN.53 if diagnosis is NOT specifically listed

**II. Continued Therapy**

**A. Neuronal Ceroid Lipofuscinosis Type 2** (must meet all)**:**

1. Currently receiving medication via of PA Health & Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy per the prescriber's clinical judgement (*see Appendix D*);

3. Member does not have acute intraventricular access device-related complications (e.g., leakage, device failure, or device-related infection) or ventriculoperitoneal shunts;
4. If request is for a dose increase, new dose does not exceed 300 mg administered once every other week as an intraventricular infusion.

**Approval duration: 6 months**

**B. Other diagnoses/indications** (1 or 2)**:**

1. Currently receiving medication via of PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;

**Approval duration: Duration of request or 6 months (whichever is less)**; or

2. Refer to PA.CP.PMN.53 if diagnosis is NOT specifically listed

## III. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*
CLN2: ceroid lipofuscinosis type 2
FDA: Food and Drug Administration
TPP1: tripeptidyl peptidase 1

*Appendix B: Therapeutic Alternatives*
Not applicable

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s):
  - Acute, unresolved localized infection on or around the device insertion site (e.g. cellulitis or abscess); or suspected or confirmed CNS infection (e.g. cloudy CSF or positive CSF gram stain, or meningitis)
  - Acute intraventricular access device-related complications (e.g., leakage, device failure, or device-related infection)
  - Patients with ventriculoperitoneal shunts
- Boxed warning(s): hypersensitivity reactions including anaphylaxis

*Appendix D: Motor Domain of CLN2 Clinical Rating Scale*

- The motor domain of the CLN2 Clinical Rating Scale is scored as follow: walks normally = 3, intermittent falls, clumsiness, obvious instability = 2, no unaided walking or crawling only = 1, immobile, mostly bedridden = 0.
- Decline was defined as having an unreversed (sustained) 2 category decline or an unreversed score of 0 in the motor domain of the CLN2 Clinical Rating Scale.

## IV. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| CLN2 | Brineura is administered once every other week as an intraventricular infusion with the following age-based dosages:<br>• Birth to < 6 months: 100 mg | 300 mg every other week |

| | | |
|---|---|---|
| | • 6 months to < 1 year: 150 mg<br>• 1 year to < 2 years: 200 mg (first 4 doses) followed by 300 mg (subsequent doses)<br>2 years and older: 300 mg | |

## V. Product Availability

Injection: 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

## VI. References

1. Brineura Prescribing Information. Novato, CA: BioMarin Pharmaceutical Inc.; July 2024. Available at: https://www.brineura.com. Accessed April 14, 2025.
2. Williams RE, Adama HR, Blohm M, et al. Management strategies for CLN2 disease. Pediatric Neurology. 2017 Apr;69:102-112. http://dx.doi.org/10.1016/j.pediatrneurol.2017.01.034.
3. 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. Molecular Genetics and Metabolism. 2016 Jul;119:160-167. doi: 10.1016/j.ymgme.2016.07.011. Epub 2016 Jul 25.
4. Kohlschütter A, Schulz A, Bartsch U, et al. Current and Emerging Treatment Strategies for Neuronal Ceroid Lipofuscinoses. CNS Drugs (2019) 33:315-325. https://doi.org/10.1007/s40263-019-00620-8.
5. Mole SE, Schulz A, Badoe E, et al. Guidelines on the diagnosis, clinical assessments, treatment, and management of CLN2 disease patients. Orphanet Journal of Rare Diseases. 2021 April 21; 16(1):185.

### Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

| HCPCS Codes | Description |
|---|---|
| J0567 | Injection, cerliponase alfa, 1 mg |

| Reviews, Revisions, and Approvals | Date |
|---|---|
| 2Q 2018 annual review: age added; modified continued therapy criteria to allow provider to determine presence of positive response instead of requiring no decline or decline or one category of CLN2 Clinical Rating Scale score and added requirement that member has at least a score of at least 1 to ensure continued ambulation; references reviewed and updated. | 02/2018 |
| References reviewed and updated. | 09/2018 |
| 3Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020 | 07/2019 |

| Reviews, Revisions, and Approvals | Date |
|---|---|
| 3Q 2020 annual review: added new contraindications; references reviewed and updated | 07/2020 |
| 3Q 2021 annual review: no significant changes; references reviewed and updated. | 07/2021 |
| 3Q 2022 annual review: no significant changes; references reviewed and updated. | 07/2022 |
| 3Q 2023 annual review: revised and added to continuation of therapy to ensure member does not have acute intraventricular access device-related complications (e.g., leakage, device failure, or device-related infection) or ventriculoperitoneal shunts; references reviewed and updated. | 07/2023 |
| 3Q 2024 annual review: removed age limit; references reviewed and updated. | 07/2024 |
| 3Q 2025 annual review: RT4: updated criteria to reflect the newly FDA-approved indication expansion to include symptomatic and presymptomatic patients younger than 3 years of age, including the following changes: removed any references to "late infantile" disease, replaced the age requirement with the 2.5 kg minimum weight requirement per dosing recommendations in the Prescribing Information; added the Boxed Warning re: hypersensitivity reactions including anaphylaxis; references reviewed and updated. | 07/2025 |