Clinical Policy: Cerliponase Alfa (Brineura)

Reference Number: ERX.SPA.151
Effective Date: 09.01.17
Last Review Date: 08.21
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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

FDA Approved Indication(s)
Brineura is indicated for 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.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Brineura is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of late infantile neuronal CLN2;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 3 years;
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. Motor domain of the CLN2 Clinical Rating Scale score ≥ 1;
6. At the time of request, member does not have ventriculoperitoneal shunts;
7. 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 ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by a score of ≥ 1 on the CLN2 Clinical Rating Scale;
3. 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 (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. 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)
  - Patients with ventriculoperitoneal shunts
  - Acute intraventricular access device-related complications (e.g., leakage, device failure, or device-related infection)
- Boxed warning(s): none reported

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.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CLN2	300 mg administered once every other week as an intraventricular infusion followed by infusion of intraventricular electrolytes over approximately 4.5 hours	300 mg every other week

VI. Product Availability

Injection: 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

VII. References

1. Brineura Prescribing Information. Novato, CA: BioMarin Pharmaceutical Inc.; July 2020. Available at: https://www.brineura.com. Accessed May 4, 2021.
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. http://dx.doi.org/10.1016/j.ymgme.2016.07.011.
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

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	05.17	08.17
2Q 2018 annual review: Age added and contraindication of ventriculoperitoneal shunts; Continued approval duration modified from length of benefit to 12 months; In continued therapy modified positive response from no decline or decline or one category to a score ≥ 1. References reviewed and updated.	02.06.18	05.18
3Q 2018 annual review: no significant changes; references reviewed and updated.	06.15.18	08.18
3Q 2019 annual review: modified continued approval duration from 12 months to 6 months due to safety concerns for device access infections; references reviewed and updates.	05.19.19	08.19
3Q 2020 annual review: no significant changes; references reviewed and updated.	04.20.20	08.20
3Q 2021 annual review: no significant changes; references reviewed and updated.	05.04.21	08.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.