MEDICAL COVERAGE POLICY	
SERVICE:	**Cerliponase alfa (Brineura®)**
Policy Number:	**238**
Effective Date:	**1/1/2025**
Last Review:	**10/14/2024**
Next Review:	**10/14/2025**

Important note: *Unless otherwise indicated, medical policies will apply to all lines of business. Medical necessity as defined by this policy does not ensure the benefit is covered. This medical policy does not replace existing federal or state rules and regulations for the applicable service or supply. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan documents. See the member plan specific benefit plan document for a complete description of plan benefits, exclusions, limitations, and conditions of coverage. In the event of a discrepancy, the plan document always supersedes the information in this policy.*

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PRIOR AUTHORIZATION: Required

POLICY: Please review the plan's EOC (Evidence of Coverage) or Summary Plan Description (SPD) for details.

For Medicare plans, please refer to appropriate Medicare NCD (National Coverage Determination) or LCD (Local Coverage Determination). Medicare NCD or LCD specific InterQual criteria may be used when available. If there are no applicable NCD or LCD criteria, use the criteria set forth below.

For Medicaid plans, please confirm coverage as outlined in the Texas Medicaid Provider Procedures Manual | TMHP (TMPPM). Texas Mandate HB154 is applicable for Medicaid plans.

BSWHP may consider cerliponase alfa (Brineura™) medically necessary for the treatment of late infantile neuronal ceroid lipofuscinosis type 2 (CLN2) disease when the following criteria are met:

For initial requests:

1. Member has a diagnosis of neuronal ceroid lipofuscinosis type 2 (CLN2) documented by EITHER of the following:
    a. Deficiency of tripeptidyl peptidase 1 (TPP1) in leukocytes or fibroblasts; **OR**
    b. Demonstration of biallelic pathogenic or likely pathogenic variants in the TPP1 gene

AND

2. Combined score of 3 – 6 on motor and language domains of the CLN2 clinical rating scale (CRS) and at least 1 in each of the 2 domains
3. Cerliponase alfa will be administered by, or under the direction of a physician knowledgeable in intraventricular administration and management of hypersensitivities (e.g. anaphylaxis); **AND**
4. Dosage of cerliponase alfa will not exceed 300 mg once every other week; **AND**
5. The member does not have any of the following:
    a. Age less than 37 weeks post-menstrual age (gestational age at birth plus post-natal age)
    b. Weight less than 2.5 kg
    c. Sign or symptom of acute or unresolved localized infection on or around the device insertion site (e.g. cellulitis or abscess)
    d. Suspected or confirmed CNS infection (e.g. cloudy CSF or positive CSF gram stain, or meningitis)
    e. Acute intraventricular access device-related complications (e.g., leakage, device failure, or extravasation of fluid)

f. A ventriculoperitoneal shunt
g. Other FDA-labeled contraindications to cerliponase alfa

For renewal requests, documentation must be submitted showing all of the following:

1. Continued use of the drug is consistent with initial request criteria
2. Documentation of efficacy as evidenced by one of the following:
    a. No loss of ambulation; **OR**
    b. Member's loss of ambulation has slowed from baseline
3. Manageable adverse effects

ALL requests for Brineura™ (cerliponase alfa) will be reviewed by both a clinical pharmacist and a medical director.

Brineura™ (cerliponase alfa) is considered experimental, investigational and/or unproven for all other indications.

BACKGROUND:

Cerliponase alfa is the first FDA-approved treatment to slow loss of walking ability in symptomatic pediatric patients aged 3 years and older with late infantile neuronal ceroid lipofuscinosis type 2 (CLN2). CLN2 disease is a rare inherited disorder that primarily affects the nervous system and currently has no cure. CLN2 disease is very rare, with estimates of incidence ranging from 0.15 per 100,000 live births in Portugal, 0.46 per 100,000 live births in West Germany, 0.78 per 100,000 live births in the United Kingdom, and 9.0 per 100,000 live births in Newfoundland. The late infantile form of the disease, for which signs and symptoms generally begin between aged 2 years and 4 years, features initial symptoms including language delay, recurrent seizures, and ataxia.

The recommended dose of cerliponase in pediatric patients 3 years of age and older is 300 mg administered once every other week by intraventricular infusion, followed by an infusion of electrolytes. The complete Brineura infusion, including infusion of intraventricular electrolytes, lasts approximately 4.5 hours.

The efficacy of cerliponase was assessed over 96 weeks in a non-randomized single-arm dose escalation clinical study with extension in symptomatic pediatric patients with CLN2 disease confirmed by TPP1 deficiency. Twenty-four cerliponase-treated patients, aged 3 to 8 years were enrolled in the single-arm clinical study and compared to 42 untreated patients from a natural history cohort. The Motor domain of a CLN2 Clinical Rating Scale was used to assess disease progression at weeks 48, 72, and 96. Baseline cores ranged from 3 (grossly normal) to 0 (profoundly impaired) with unit decrements representing milestone events in the loss of motor function (ability to walk or crawl). 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. The median time until a 2-point decline in the motor–language score was not reached for treated patients and was 345 days for historical controls. The 2021 Guidelines on the diagnosis, clinical assessments, treatment and management for CLN2 disease patients recommends initiation of enzyme replacement therapy Brineura (cerliponase alfa) in patients with CLN2.

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Cerliponase received an expanded indication for children of all ages with CLN2 disease based on Study 190-203, a Phase 2, open-label, multicenter trial evaluating cerliponase treatment over the span of approximately three years in children aged 1-6 years at baseline, including eight children less than 3 years of age. Results from Study 190-203, which were presented at the 20th Annual We're Organizing Research on Lysosomal Diseases meeting (WORLDSymposium) in February 2024, showed that intraventricular (intracerebroventricular, ICV)-administered cerliponase slowed the decline in motor function and delayed disease onset in children with CLN2 disease, including those who were under 3 years of age. Decline was defined as having a sustained two-point loss or an unreversed score of zero. In the children below 3 years of age treated with cerliponase, none (0%) had a two-point decline or score of zero in the motor score by the final assessment (week 169) compared to 11 out of 18 (61%) of the natural history cohort.

CODES:

Important note: *Due to the wide range of applicable diagnosis codes and potential changes to codes, an inclusive list may not be presented, but the following codes may apply. Inclusion of a code in this section does not guarantee that it will be reimbursed, and patient must meet the criteria set forth in the policy language.*

CPT Codes:	
HCPCS Codes:	J0567 - Injection, cerliponase alfa, 1 mg
ICD10 codes:	E75.4 - Neuronal ceroid lipofuscinosis
ICD10 Not covered:	

POLICY HISTORY:

Status	Date	Action
New	5/16/2017	New policy
Updated	12/13/2017	Updated policy with codes effective 1/1/18
Reviewed	04/10/2018	No changes
Reviewed	04/25/2019	Changed status to coverage with criteria
Reviewed	02/27/2020	Criteria updated
Updated	04/22/2021	Medicaid instructions added
Reviewed	04/21/2022	Medicare instructions added
Reviewed	04/27/2023	No changes
Updated	09/28/2023	Updated Medicare and Medicaid instructions
Updated	08/12/2024	Renamed policy for drug name only. Applied new format and layout. Updated FDA labeled contraindications and background information. Removed age criteria with expanded FDA indication.

REFERENCES:

The following scientific references were utilized in the formulation of this medical policy. BSWHP will continue to review clinical evidence related to this policy and make modifications based upon the evolution of the published clinical evidence. Should additional scientific studies become available, and they are not included in the list, please forward the reference(s) to BSWHP so the information can be reviewed by the Medical Coverage Policy Committee (MCPC) and the Quality Improvement Committee (QIC) to determine if a modification of the policy is in order.

1. FDA Label Brineura™ (cerliponase alfa). Food and Drug Administration
2. Brineura (cerliponase alfa) [prescribing information]. Novato, CA: BioMarin Pharmaceutical Inc; March 2020.
3. Mole, S.E., Schulz, A., Badoe, E. et al. Guidelines on the diagnosis, clinical assessments, treatment and management for CLN2 disease patients. Orphanet J Rare Dis 16, 185 (2021). https://doi.org/10.1186/s13023-021-01813-5
4. Schulz A, et. al. for CLN2 Study Group. Study of Intraventricular Cerliponase Alfa for CLN2 Disease. N Engl J Med 2018;378:1898-907. DOI: 10.1056/NEJMoa1712649.
5. Williams, Ruth E et al. “Management Strategies for CLN2 Disease.” Pediatric neurology vol. 69 (2017): 102-112. doi:10.1016/j.pediatrneurol.2017.01.034.

***Note**:*
Health Maintenance Organization (HMO) products are offered through Scott and White Health Plan dba Baylor Scott & White Health Plan, and Scott & White Care Plans dba Baylor Scott & White Care Plan. Insured PPO and EPO products are offered through Baylor Scott & White Insurance Company. Scott and White Health Plan dba Baylor Scott & White Health Plan serves as a third-party administrator for self-funded employer-sponsored plans. Baylor Scott & White Care Plan and Baylor Scott & White Insurance Company are wholly owned subsidiaries of Scott and White Health Plan. These companies are referred to collectively in this document as Baylor Scott & White Health Plan.

RightCare STAR Medicaid is offered through Scott and White Health Plan in the Central Texas Medicaid Rural Service Area (MRSA); FirstCare STAR is offered through SHA LLC dba FirstCare Health Plans (FirstCare) in the Lubbock and West MRSAs; and FirstCare CHIP is offered through FirstCare in the Lubbock Service Area.