MEDICAL COVERAGE POLICY	
SERVICE:	**Cerliponase alfa (Brineura) for Batten Disease**
Policy Number:	**238**
Effective Date:	**05/01/2021**
Last Review:	**04/22/2021**
Next Review Date:	**04/22/2022**

Important note
Unless otherwise indicated, this policy will apply to all lines of business.
Even though this policy may indicate that a particular service or supply may be considered medically necessary and thus covered, this conclusion is not based upon the terms of your particular benefit plan. Each benefit plan contains its own specific provisions for coverage and exclusions. Not all benefits that are determined to be medically necessary will be covered benefits under the terms of your benefit plan. You need to consult the Evidence of Coverage (EOC) or Summary Plan Description (SPD) to determine if there are any exclusions or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and your plan of benefits, the provisions of your benefits plan will govern. However, applicable state mandates will take precedence with respect to fully insured plans and self-funded non-ERISA (e.g., government, school boards, church) plans. Unless otherwise specifically excluded, Federal mandates will apply to all plans. With respect to Medicare-linked plan members, this policy will apply unless there are Medicare policies that provide differing coverage rules, in which case Medicare coverage rules supersede guidelines in this policy. Medicare-linked plan policies will only apply to benefits paid for under Medicare rules, and not to any other health benefit plan benefits. CMS's Coverage Issues Manual can be found on the CMS website. Similarly, for Medicaid-linked plans, the Texas Medicaid Provider Procedures Manual (TMPPM) supersedes coverage guidelines in this policy where applicable.

SERVICE: Cerliponase alfa (Brineura)™

PRIOR AUTHORIZATION: Required

POLICY:

For Medicaid plans, please confirm coverage as outlined in the Texas Medicaid TMPPM.

For all other plans, Cerliponase alfa (Brineura™) may be considered medically necessary for the treatment of late infantile neuronal ceroid lipofuscinosis type 2 (CLN2) disease (Batten Disease) when the following criteria are met:

- Individual is 3 years of age or older
- Diagnosis of symptomatic late infantile neuronal ceroid lipofuscinosis type 2 (CLN2) documented by EITHER of the following:
  - ✓ Deficiency of tripeptidyl peptidase 1 (TPP1) in leukocytes or fibroblasts
  - ✓ Demonstration of biallelic pathogenic or likely pathogenic variants in the TPP1 gene
- Member is ambulatory
- Cerliponase alfa will be administered by, or under the direction of a physician knowledgeable in intraventricular administration
- Dosage of cerliponase alfa will not exceed 300 mg once every other week
- The member does not have acute intraventricular access device-related complications (e.g., leakage, device failure, or device-related infection) or a ventriculoperitoneal shunt
- Member has no FDA-labeled contraindications to Brineura™ (cerliponase alfa).

Continuation of therapy with Cerliponase alfa may be medically necessary when the following criteria are met:

- Member's loss of ambulation has slowed from baseline;

- The member does not have acute intraventricular access device-related complications (e.g., leakage, device failure, or device-related infection) or a ventriculoperitoneal shunt

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.

OVERVIEW:

Cerliponase alfa (Brineura—BioMarin Pharmaceutical) was recently approved by FDA as a treatment for a particular form of Batten disease. This disease is very rare with incidence estimates ranging from 0.15 per 100,000 births to 9.0 per 100,000 births in different parts of the world. There is no cure for this disease. Cerliponase 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. 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. A single-arm dose escalation clinical study involving 22 symptomatic pediatric patients with CLN2 disease and 42 untreated patients with CLN2 disease from a natural history cohort who were at least 3 years old and had motor or language symptoms found that patients who received cerliponase alfa had fewer declines in walking ability compared with the untreated patients. The drug's safety was evaluated in 24 patients with CLN2 disease aged 3–8 years who received at least one dose of cerliponase alfa in clinical studies.

The recommended dose of Brineura 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.

There is insufficient published evidence to evaluate the safety and efficacy of Brineura for the treatment of CLN2 disease; no clinical trials have been published to date. The unpublished phase I/II trial that served as the basis for FDA approval has been presented at conference proceedings; investigators reported that participants treated with Brineura experienced a lower rate of decline in motor and language function at 48 weeks compared with a 42-patient untreated natural history cohort. Quality clinical trials are needed to determine the clinical efficacy of this drug.

CODES:

Important note:
CODES: 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:	
CPT Not Covered:	
ICD10 codes:	E75.4
HCPCS	J0567 - cerliponase alpha, Brineura

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CMS:

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
Review	04/25/2019	Changed status to coverage with criteria
Review	02/27/2020	Criteria updated
Updated	04/22/2021	Medicaid instructions added

REFERENCES:

The following scientific references were utilized in the formulation of this medical policy. SWHP will continue to review clinical evidence related to this policy and may modify it at a later date 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 SWHP 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. BioMarin Pharmaceutical Inc. Prescribing Information. Brineura™ (cerliponase alfa). Available at http://brineura.com
3. 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

INTERNAL USE ONLY

Hayes:

Brineura is a recombinant human TPP1 replacement enzyme that is infused into the cerebrospinal fluid (CSF) via an intracerebroventricular access device implanted in the patient's head. The recommended dose of Brineura in pediatric patients 3 years of age and older is 300 mg administered once every other week

The FDA approved Brineura on April 27, 2017, to slow loss of walking ability in symptomatic pediatric patients aged 3 years and older with CLN2 disease. The FDA approval was based on results of a phase I/II open-label dose-escalation study of intracerebroventricular Brineura in patients aged 3 to 8 years with CLN2 disease. The FDA evaluated efficacy data in 22 patients and safety data in 24 patients.

Hayes: There is insufficient published evidence to draw firm conclusions regarding the safety and efficacy of Brineura for the treatment of CLN2 disease.

Cost: (List) about $700k per year **0.15 – 9.0 per 100,000 births**