cerliponase alfa (Brineura®)

Policy # 00595
Original Effective Date: 12/20/2017
Current Effective Date: 01/08/2024

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider cerliponase alfa (Brineura®)‡ to slow the loss of ambulation in symptomatic pediatric patients with late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency, to be **eligible for coverage.****

Patient Selection Criteria
Coverage eligibility for cerliponase alfa (Brineura) will be considered when the following criteria are met:

Initial (6 months):

- Patient has a diagnosis of late infantile neuronal CLN2 [also known as TPP1 deficiency] as confirmed by one of the following diagnostic testing results:
  - Deficient TPP1 activity in leukocytyes; OR
  - Pathogenic variants/mutations in each allele of the TPP1/CLN2 gene (includes single gene sequencing, gene panels, or whole exome sequencing); AND
- Patient is 3 years of age or older; AND
- Patient has a score of AT LEAST "3" on the CLN2 Clinical Rating Scale (with AT LEAST a "1" in each of the Motor and Language Domains); AND
  *(Note: This specific patient criterion, based on clinical trials, is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

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- Patient is symptomatic (e.g., seizures, loss of language, motor abilities, delay of language development, unsteady gait, visual failure, etc.); AND
- Underlying neurological disorders that may have caused the patient's seizures or cognitive decline have been ruled out; AND
  *(Note: This specific patient criterion, based on clinical trials, is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient does NOT have a contraindication for neurosurgery (e.g., congenital heart disease or severe respiratory impairment); AND
- Patient does NOT have an underlying condition that would make the patient prone to complications from using an intraventricular shunt (e.g., hydrocephalus or ventricular shunts); AND
- Patient has NOT had generalized motor status epilepticus or severe infections within 4 weeks before the first scheduled dose of Brineura; AND
  *(Note: This specific patient criterion, based on clinical trials, is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Brineura is dosed at 300 mg given every other week as an intraventricular infusion followed by infusion of intraventricular electrolytes.

Continuation (1 year)

- Initial criteria were met; AND
- Patient is responding to Brineura therapy: e.g., Patient DOES NOT have an unreversed 2 point (or greater) decline from baseline in the Motor Domain of the CLN2 Clinical Rating Scale OR patient DOES NOT have a score of 0 in the Motor Domain of the CLN2 Clinical Rating Scale.
  *(Note: This specific patient criterion, based on clinical trials, is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

Note that the CLN2 Clinical Rating Scale is located in the Background section of this policy. The baseline CLN2 Clinical Rating Scale Score (broken down by domain) MUST be provided when requesting the drug.

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When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of cerliponase alfa (Brineura) when any of the following patient selection criteria are not met to be **not medically necessary**:**

- For Initial:
  - Patient has a score of AT LEAST "3" on the CLN2 Clinical Rating Scale (with AT LEAST a "1" in each of the Motor and Language Domains).
  - Underlying neurological disorders that may have caused the patient's seizures or cognitive decline have been ruled out.
  - Patient has NOT had generalized motor status epilepticus or severe infections within 4 weeks before the first scheduled dose of Brineura.
- For Continuation:
  - Patient is responding to Brineura therapy: e.g., Patient DOES NOT have an unreversed 2 point (or greater) decline from baseline in the Motor Domain of the CLN2 Clinical Rating Scale OR patient DOES NOT have a score of 0 in the Motor Domain of the CLN2 Clinical Rating Scale.

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of cerliponase alfa (Brineura) when patient selection criteria are not met (with the exception of those denoted as **not medically necessary****) to be **investigational.***

Background/Overview

Brineura is a hydrolytic lysosomal N-terminal tripeptidyl peptidase indicated to slow the loss of ambulation in symptomatic pediatric patients 3 years of age and older with late infantile CLN2, also known as TPP1 deficiency. Deficiency in TPP1 activity results in the accumulation of lysosomal storage materials normally metabolized by this enzyme in the central nervous system (CNS), leading to progressive decline in motor function. Brineura, or cerliponase alfa (rhTTP1), a proenzyme, is taken up by target cells in the CNS and is translocated to the lysosomes through the Cation Independent Mannose-6-Phosphate Receptor (CI-MPR, also known as M6P/IGF2 receptor).

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Brineura is activated in the lysosome and the activated proteolytic form of rhTPP1 cleaves tripeptides from the N-terminus of proteins. Brineura is essentially an enzyme replacement for this condition.

CLN2 is a rare condition (0.5 to 1 cases per 100,000 live births). As mentioned earlier, this disease results in progressive neurodegeneration. The onset of CLN2 typically occurs between 2 and 3 years of age. Loss of ambulation is usually around 6 years of age while progressive vision loss and death occur between 6 and 16 years of age. The rating scale used in clinical trials for Brineura is listed below:

CLN2 Clinical Rating Scale:

Domain	Score	CLN2 Scale
Motor	3	Grossly normal gait
	2	Abnormal gait, independent ≥10 steps, frequent falls, obvious clumsiness
	1	No unaided walking or crawling only; cannot walk 10 unassisted steps
	0	Immobile, mostly bedridden
Language	3	Grossly normal (age appropriate)
	2	Has become recognizably abnormal (worse than the individual maximum)
	1	Hardly understandable
	0	Unintelligible or no language

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Brineura was approved in 2017 to slow the loss of ambulation in symptomatic pediatric patients 3 years of age and older with late infantile CLN2, also known as TPP1 deficiency.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA approval status, nationally

accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The safety and efficacy of Brineura was assessed over 96 weeks in a non-randomized single-arm dose escalation study with extension in patients with late infantile CLN2 disease, as confirmed by TPP1 deficiency. The Brineura treated patients were compared to untreated patients from a natural history cohort. Brineura treated patients had a Motor-Language CLN2 Clinical Rating Scale score of ≥3 prior to enrollment. Twenty-four patients were enrolled. Patients were assessed for decline in the Motor Domain of the CLN2 Clinical Rating Scale at 48, 72, and 96 weeks. Per the package insert, "due to the inability to establish comparability for the CLN2 Language domain ratings between the clinical study with extension and the natural history cohort, efficacy of Brineura for the Language domain cannot be established." In this study, of the 22 patients treated with Brineura, 95% were responders (e.g., absence of a 2 point decline in the Motor Domain of the CLN2 Clinical Rating Scale score or absence of a score of 0 in the Motor Domain of the CLN2 Clinical Rating Scale) at week 96 as compared to 50% in the natural history cohort.

References

1. Brineura [package insert]. Biomarin Pharmaceutical, Inc. Novato, California.
2. Brineura Drug Evaluation. Express Scripts. Updated June 2017.

Policy History

Original Effective Date: 12/20/2017
Current Effective Date: 01/08/2024

12/07/2017	Medical Policy Committee review
12/20/2017	Medical Policy Implementation Committee approval. New policy.
02/06/2018	Coding update
12/06/2018	Medical Policy Committee review
12/19/2018	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2019	Coding update
12/05/2019	Medical Policy Committee review

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12/11/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/03/2020	Medical Policy Committee review
12/09/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/02/2021	Medical Policy Committee review
12/08/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/01/2022	Medical Policy Committee review
12/14/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/07/2023	Medical Policy Committee review
12/13/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 12/2024

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2022 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which

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contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.
Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J0567 Delete effective 01/01/2024: J3490, J3590
ICD-10 Diagnosis	All related Diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment,

would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.