Washington State Health Care Authority

Endocrine and Metobolic Agents : Metobolic Modifiers – Tripeptidyl Peptidase 1 Deficiency Agents cerliponase alfa (Brineura)

Medical policy no. 30.90.90-1 Effective Date: July 1, 2019

Background:

Late infantile neuronal ceroid lipofuscinosis type 2 (CLN2) is a nervous system disorder that is caused by insufficient activity of the tripeptidyl peptidase 1 (TPP1) enzyme. Decreased TPP1 activity leads to progressive loss of motor function and other symptoms such as delayed speech development, loss of developmental milestones, visual impairment, cerebral atrophy, and seizures.

Brineura (cerliponase alfa) is the first FDA-approved treatment to slow the loss of ability to walk or crawl in symptomatic patients 3 years of age or older with CLN2. Cerliponase alfa is a proenzyme that is taken up by target cells and activated in the lysosomes to act as the TPP1 enzyme.

Medical necessity

Drug	Medical Necessity
cerliponase alfa (Brineura)	Brineura may be considered medically necessary when it is used 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.

Clinical policy:

Drug	Clinical Criteria (Initial Approval)
cerliponase alfa (Brineura)	1. Patient is 3 years of age or older; **AND** 2. Patient has documented diagnosis of late infantile neuronal ceroid lipofuscinosis type 2 (CLN2) confirmed by TPP1 deficiency and genetic testing to show mutation of the TPP1 gene on chromosome 11p15; **AND** 3. Medication is prescribed by or in consultation with a specialist with expertise in the treatment of CLN2 (e.g. pediatric neurologist, pediatric epileptologist, or geneticist); **AND** 4. Patient is ambulatory; **AND** 5. Documentation of baseline CLN2 Clinical Rating Scale score with score at least 1 in motor domain and at least 1 in language domain; **AND**

	6. Documentation of no acute intraventricular access device-related complications (for example, leakage, device failure, or device-related infection) or ventriculoperitoneal shunt. If ALL criteria are met, the request will be approved for 6 month
	Criteria (Reauthorization) 1. Documentation of positive clinical improvement (e.g., no decline in the CLN2 Clinical Rating Scale with score at least 1 in motor domain and at least 1 in language domain); **AND** 2. Medication is prescribed by or in consultation with a specialist with expertise in the treatment of CLN2 (e.g. pediatric neurologist, pediatric epileptologist, or geneticist);; **AND** 3. Patient is ambulatory; **AND** 4. Documentation of no acute intraventricular access device-related complications (for example, leakage, device failure, or device-related infection) or ventriculoperitoneal shunt. If ALL criteria are met, the request will be approved for 12 months

Dosage and quantity limits

Drug Name	Dose and Quantity Limits
Brineura™	300 mg IV every other week

Coding:

HCPCS Code	Description
J0567	Injection, cerliponase alfa, 1 mg

Definitions

Term	Description
CLN2 Clinical Rating Scale	Scale used to calculate patient's degree of disease severity

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

Evidence review

An open-label clinical trial assessed the effect of cerliponase alfa dosed every 2 weeks in pediatric patients with CLN2. The treatment group was compared to a group using the historical standard of care treatments. The treatment group had a smaller reduction in the motor-language score on the CLN2 clinical rating scale compared to the control group (0.27 vs 2.12) over 48 weeks of treatment ($p<0.001$). The median time for a 2 point reduction in the motor-language score was not significantly different between the groups.

An open-label dose escalation study was conducted to demonstrate a safe dosing range for CLN2 patients. A dosing range of 30 to 300 mg every 2 weeks was administered to pediatric patients. Twenty four patients were given the escalating doses, and 23 completed the study. The response rate was about 87% in the treated patients at week 48.

References

1) Cherukuri A, Cahan H, de Hart G, et al. Immunogenicity to cerliponase alfa intracerebroventricular enzyme replacement therapy for CLN2 disease: results from a Phase 1/2 study. Clin Immunol. 2018; 197:68-76.
2) Geraets RD, Koh SY, Hastings ML, et al. Moving towards effective therapeutic strategies for Neuronal Ceroid Lipofuscinosis. Orphanet J Rare Dis. 2016; 11:40.
3) Schulz A, Ajayi T, Specchio N, et al. Study of intraventricular cerliponase alfa for CLN2 disease. N Engl J Med. 2018; 378(20):1898-1907.
4) Worgall S, Kekatpure MV, Heier L, et al. Neurological deterioration in late infantile neuronal ceroid lipofuscinosis. Neurology. 2007; 69(6):521-535.
5) https://rarediseases.info.nih.gov/diseases/3045/neuronal-ceroid-lipofuscinosis-2
6) Brineura™ [Product Information], San Rafael, CA. Biomarin, April 2017.

History

Date	Action and Summary of Changes
05.06.2019	New Policy