EFFECTIVE DATE:08|01|2017
POLICY LAST UPDATED: 7|18|2017

Cerliponase Alfa (Brineura)

OVERVIEW

Cerliponase alfa 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 neuronal ceroid lipofuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency

MEDICAL CRITERIA

BlueCHiP for Medicare and Commercial

Cerliponase Alfa (Brineura)is medically necessary when ALL of the following are met:

1. The patient is a pediatric patient at least the minimal age noted in the FDA labeled indication (i.e., ≥3 years old to <18 years old)
   AND
2. ONE of the following:
   a. The prescriber is a specialist in the area of the patient's diagnosis (e.g., pediatric neurologist, geneticist)
      OR
   b. The prescriber has consulted with a specialist in the area of the patient's diagnosis
   AND
3. The patient is symptomatic (e.g., new-onset of unprovoked seizures, early language delay, ataxia, developmental delay)
   AND
4. The patient has a diagnosis of neuronal ceroid lipofuscinosis type 2 (CLN2) disease/ tripeptidyl peptidase 1 (TPP1) deficiency evidenced by at least ONE of the following:
   a. BOTH of the following:
      i. Deficient TPP1 enzyme activity in leukocytes, fibroblasts, or dried blood spots
         AND
      ii. Normal activity of ≥1 appropriate control enzyme (e.g., PPT1 and/or â-galactosidase)
   OR
   b. Identification of 2 pathogenic variants/mutations in *trans* (i.e. separate parental alleles) in the TPP1/CLN2 gene
   AND
2. The patient specifically has late infantile onset neuronal ceroid lipofuscinosis type 2 (CLN2)/tripeptidyl peptidase 1 (TPP1) deficiency (roughly defined as onset at 2-4 years old)
   AND
3. The patient is ambulatory
   AND
4. The patient does not have any FDA labeled contraindication(s) to therapy with the requested agent

Length of Approval: 12 months

Renewal Criteria
Cerliponase Alfa (Brineura) is medically necessary after the initial 12 month approval when all of the following criteria are met:

1. The patient has been previously approved for therapy with the requested drug
   AND
2. The prescriber indicates that the patient is a pediatric patient (i.e., patient must not be ≥18 years old)
   AND
3. ONE of the following:
   a. The prescriber is a specialist in the area of the patient's diagnosis (e.g., pediatric neurologist, geneticist)
      OR
   b. The prescriber has consulted with a specialist in the area of the patient's diagnosis
   AND
4. The patient is ambulatory
   AND
5. The prescriber indicates that the patient has shown clinical benefit from the requested agent
   AND
6. The patient does NOT have any FDA labeled contraindications to therapy with the requested agent

Length of Approval: 12 months

PRIOR AUTHORIZATION
Prior authorization is required for BlueCHiP for Medicare and recommended for Commerical Products

POLICY STATEMENT
BlueCHiP for Medicare and Commercial
Cerliponase Alfa (Brineura) is medically necessary when the above criteria have been met.

COVERAGE
Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage or Subscriber Agreement for applicable physician administered drug benefits/coverage.

BACKGROUND
The neuronal ceroid lipofuscinoses, collectively referred to as Batten disease, are a family of autosomal recessive neurodegenerative disorders that annually affect 1:100,000 live births worldwide. This family of diseases results from mutations in one of 14 different genes that share common clinical and pathological etiologies. Clinically, the diseases are subcategorized into infantile, late infantile, juvenile and adult forms based on their age of onset. CLN2 disease is a late infantile-onset lysosomal storage disorder caused by deficient activity of the enzyme tripeptidyl peptidase 1 (TPP1). TPP1 catabolizes polypeptides in the central nervous system. Deficient TPP1 activity leads to intralysosomal accumulation of autofluorescent storage material and is associated with neuronal and retinal cell loss.

In the late infantile form of the disease, signs and symptoms typically begin between ages 2 and 4 and include language delay, seizures, ataxia, movement disorders, motor deterioration, dementia, blindness, and early death. Affected children most commonly present with an unprovoked seizure, although febrile seizures have also been reported. Other initial symptoms include prominent truncal and peripheral ataxia, behavioral disturbances, and other developmental delays. Seizures may be polymorphic (e.g., generalized tonic-clonic, myoclonic, atonic) and often become drug-resistant. Following the onset of seizures, a rapid deterioration in cognitive and motor functions ensues over two to three years, leading to loss of speech and loss of voluntary movement by the age of six years. Visual impairment may begin as early as 4 years of age, but is not usually apparent until severe deterioration is evident. Children will eventually become blind between the ages of 7-10. Death usually occurs by mid-adolescence.

Early diagnosis is critical to optimize clinical care and improve outcomes for the patient and family; however, delays in the diagnosis of CLN2 are common due to low disease awareness, nonspecific clinical presentation, and limited access to diagnostic testing in some areas. Once clinical suspicion of CLN2 disease has been established, the patient should undergo biochemical testing. The gold standard for diagnosis is the demonstration of deficient TPP1 enzyme activity (in leukocytes, fibroblasts, or dried blood spots), together with the detection of pathogenic mutations in each allele of the TPP1 gene (also known as the CLN2 gene). However, when it is not feasible to perform both analyses, either deficient TPP1 enzyme activity in leukocytes or fibroblasts or the detection of two pathogenic mutations in *trans* alone can be diagnostic for CLN2 disease. A palmitoyl-protein thioesterase 1 (PPT1) enzyme activity assay should also be performed to rule out CLN1 disease.

The management of CLN2 disease is complex. No management guidelines exist and there is a paucity of published disease-specific evidence to inform clinical practice, which currently draws upon experience from the field of childhood neurodisability. Historically, treatment has been limited to symptomatic and supportive care. Multidisciplinary care is necessary due to the high symptom load and the rapid rate of functional decline. Patients will need management of seizures and movement disorders, as well as ophthalmologic, respiratory, and gastrointestinal therapies. Cerliponase alfa is the first FDA approved treatment for CLN2 disease, used to slow loss of walking ability in symptomatic pediatric patients aged 3 years and older. Cerliponase alfa is an enzyme replacement therapy and is a recombinant form of human TPP1. Cerliponase alfa is taken up by target cells in the central nervous system and is translocated to the lysosomes through the Cation Independent Mannose-6-Phosphate Receptor (CI-MPR, also known as M6P/IGF2 receptor). Cerliponase alfa is activated in the lysosome and the activated proteolytic form cleaves tripeptides from the N-terminus of proteins.

CODING

There is no specific HCPCS code at this time, claims must be filed with an unlisted code such as J3490 and the NDC number

RELATED POLICIES

None

PUBLISHED

September 2017

REFERENCES:

1. Brineura (cerliponase alfa) prescribing information. BioMarin Pharmaceutical Inc. 4/2017.
2. Williams, Ruth et al. Management Strategies for CLN2 Disease. Pediatric Neurology 69;2017:102-112.
3. Food and Drug Administration (FDA). Brineura (cerliponase alfa) BLA Approval Letter. 4/27/2017.