NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Cerliponase alfa for treating neuronal ceroid lipofuscinosis type 2 (review of HST12) [ID6145]

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of cerliponase alfa within its marketing authorisation for treating neuronal ceroid lipofuscinosis type 2.

Background

Neuronal ceroid lipofuscinosis type 2 (CLN2) is a rare genetic disease caused by the deficiency of an enzyme called tripeptidyl peptidase1 (TPP1). CLN2 is one form of neuronal ceroid lipofuscinosis (NCL), also known as Batten disease. CLN2 disease is inherited as an autosomal recessive disorder, which means that both chromosome copies carry mutations in the CLN2 gene, and both parents are unaffected carriers.[1] A deficiency of TPP1 results in abnormal storage of proteins and lipids in neurons and other cells. Accumulation of these proteins and lipids prevent the cells from functioning as they should.

CLN2 is characterised clinically by a decline of mental and other capacities, epilepsy, and vision loss through retinal degeneration, and histopathologically by intracellular accumulation of ceroid lipofuscin in the neuronal cells of the brain and retina.[2] Symptoms in children with CLN2 start to arise in the second year of life and can then progress rapidly with the onset of seizures, decline in speech, loss of mobility, involuntary muscle spasms and later on, visual impairment leading to blindness. Ultimately the child will become totally dependent on families and carers for all of their needs. Life expectancy is around 6 to 13 years.

The exact prevalence and incidence of CLN2 is unknown. It is estimated that in the UK, around 3 to 6 children are diagnosed each year and currently around 30 to 50 children are living with the condition.[1]

Currently there is no cure or life extending options available. Current clinical management options focus on symptom control, monitoring and prevention of complications, and palliative care. Management aims to maintain function as long as possible and to improve quality of life. This involves a multidisciplinary and multiagency team to control symptoms and complications such as, malnutrition, gastroesophageal reflux, pneumonia, anxiety, Parkinsonian symptoms and dystonia, through medication and physical therapy. Children often receive multiple medications and clinicians need to balance symptom control with the adverse effects and treatment interactions.

The technology

Cerliponase alfa (Brineura, BioMarin) is a recombinant human tripeptidyl peptidase 1 which is an enzyme replacement therapy. It is administered by intracerebroventricular infusion every 2 weeks.

Cerliponase alfa has a marketing authorisation in the UK for, "the treatment of neuronal ceroid lipofuscinosis type 2 (CLN2) disease, also known as tripeptidyl peptidase 1 (TPP1) deficiency". It has been studied in patients with a confirmed diagnosis of CLN2, with a 2-domain score of 3 to 6 on motor and language domains of the Hamburg Scale and a score of at least 1 in each of these domains.

Intervention(s)	Cerliponase alfa
Population(s)	People with a confirmed diagnosis of CLN2
Subgroups	If the evidence allows, the following subgroup should be considered: • IVT patients • Age at treatment initiation
Comparators	Established clinical management without cerliponase alfa (including managing the symptoms and complications associated with CLN2)

Outcomes	The outcome measures to be considered include:
	• Clinical outcomes
	  ○ CLN2 Clinical Rating Scale (reported as 4-domain scale and combined score of the motor and language domains)
	  ○ Weill Cornell LINCL Scale (4-domain scale)
	• Neurodevelopmental outcomes including Bayley Scales of Infant Development III, Wechsler PreSchool and Primary Scale of Intelligence (WPPSI-IV), Vineland Adaptive Behaviour Scale, and WISC-V
	• Safety outcomes including missed infusions, electrocardiogram, 12-lead, electroencephalogram, assessment for epileptiform activity, frequency slowing (focal vs generalised), brain MRI, electroretinogram, visual Evoked Potentials, and Optical Coherence Tomography
	• Patient reported outcomes including PedsQL, EQ-5D, and CLN2-QoL

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The use of cerliponase alfa is conditional on the presence of CLN2. The economic modelling should include the costs associated with diagnostic testing for CLN2 in people with CLN2 disease who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related highly specialised technology appraisals:** Cerliponase alfa for treating neuronal ceroid lipofuscinosis type 2 (2019) NICE highly specialised technology guidance 12.
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2018) NHS manual for prescribed specialist services (2018/2019) NHS England (2023) NHS England Manual for prescribed specialised services, service 71: lysosomal storage disorder service (adults and children) NHS England (2013) NHS England Standard Contract for Lysosomal Storage Disorders Service (Children)

Questions for consultation

Where do you consider cerliponase alfa will fit into the existing care pathway for neuronal ceroid lipofuscinosis type 2?

Do you consider that the use of cerliponase alfa can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

Do you think that costs and treatments should be analysed separately for existing and new patients? Should this be done by age?

Should any outcomes currently listed under "safety outcomes" be instead listed under clinical outcomes?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which cerliponase alfa is licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Highly Specialised Technologies Evaluation Programme. We welcome comments on the appropriateness of evaluating this topic through this process. (Information on NICE's health technology evaluation processes is available at: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).

References

1. CLN2 disease, late infantile. Batten Disease Family Association. Accessed August 2023.
2. Neuronal Ceroid Lipofuscinosis. Orphanet. Accessed August 2023.