NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

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

Final scope

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 typically start to arise in the second year of life and can then progress rapidly with the onset of seizures, sleep disturbance, 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 creating a large familial burden. Life expectancy is typically around 6 to 13 years but children with attenuated forms may live longer.

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, epilepsy, spasticity, 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 CLN2
Subgroups	If the evidence allows, the following subgroup should be considered: • Stage of progression of CLN2
Comparators	Established clinical management without cerliponase alfa (including managing the symptoms and complications associated with CLN2)

Outcomes	The outcome measures to be considered include:
	• Symptoms of CLN2 including visual function, seizures, myoclonus, dystonia, spasming, pain and feeding.
	• Disease progression
	  ○ 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)
	  ○ Hamburg scale
	• Neurological development which may informed by measures specified in the managed access agreement for HST12 including Bayley Scales of Infant Development III, Wechsler PreSchool and Primary Scale of Intelligence (WPPSI-IV), Vineland Adaptive Behaviour Scale, and WISC-V
	• Need for medical care (including hospitalisation, emergency care and primary and secondary care appointments, and concomitant medication)
	• Mortality
	• Adverse effects of treatment (including immune response and effects and complications related to treatment administration)
	• Health-related quality of life (for patients and carers, and including impact on families such as social and mental health and impact on siblings). This may be informed by quality-of-life measures including PedsQL, EQ-5D, and CLN2-QoL.Compliance/adherence to treatment

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)

References

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

Appendix B