NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Highly Specialised Technology Evaluation

Cerliponase alfa for treating neuronal ceroid lipofuscinosis type 2

Final scope

Remit/evaluation objective

To evaluate the benefits and costs of cerliponase alfa within its licensed indication for treating neuronal ceroid lipofuscinosis type 2 for national commissioning by NHS England.

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
Comparators	Established clinical management without cerliponase alfa (including a multidisciplinary and multiagency approach to manage 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 (including quantitative measure such as the Hamburg scale, CLN2 rating scale, and the Weill Cornell LINCL score) • 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)
Nature of the condition	• disease morbidity and patient clinical disability with current standard of care • impact of the disease on carer's quality of life

	• extent and nature of current treatment options
Impact of the new technology	• overall magnitude of health benefits to patients and, when relevant, carers • heterogeneity of health benefits within the population • robustness of the current evidence and the contribution the guidance might make to strengthen it • treatment continuation rules (if relevant)
Value for Money	• cost effectiveness using incremental cost per quality-adjusted life year • patient access schemes and other commercial agreements • the nature and extent of the resources needed to enable the new technology to be used
Impact of the technology beyond direct health benefits	• whether there are significant benefits other than health • whether a substantial proportion of the costs (savings) or benefits are incurred outside of the NHS and personal and social services • the potential for long-term benefits to the NHS of research and innovation • the impact of the technology on the overall delivery of the specialised service • staffing and infrastructure requirements, including training and planning for expertise.
Other considerations	If appropriate, the evaluation should include consideration of the costs and implications of changes in service delivery for CLN2, but will not make recommendations on service provisions. If the evidence allows, the following subgroup should be considered: • based on disease progression • pre-symptomatic siblings with confirmed CLN2 • asymptomatic siblings with confirmed CLN2 Guidance will only be issued in accordance with the marketing authorisation.

	Guidance will take into account any Managed Access Arrangements.
Related NICE recommendations and NICE Pathways	None
Related National Policy	NHS England Manual for prescribed specialised services, service 71: lysosomal storage disorder service (adults and children), November 2012. http://www.england.nhs.uk/wp-content/uploads/2012/12/pss-manual.pdf NHS England Standard Contract for Lysosomal Storage Disorders Service (Children), 2013. http://www.england.nhs.uk/wp-content/uploads/2013/06/e06-lyso-stor-dis-child.pdf

References

1. CLN2 disease, late infantile. Batten Disease Family Association. Accessed September 2016.
2. Neuronal Ceroid Lipofuscinosis. Orphanet. Accessed September 2016.