NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Highly Specialised Technologies Evaluation

Velmanase alfa for treating alpha-mannosidosis

Final scope

Remit/evaluation objective

To evaluate the benefits and costs of velmanase alfa within its licensed indication for treating alpha-mannosidosis for national commissioning by NHS England.

Background

Alpha-mannosidosis is a rare genetic disease caused by the deficiency of an enzyme called alpha-mannosidase. It is inherited as an autosomal recessive disorder, which means that both chromosome copies carry mutations in the alpha-mannosidase gene MAN2B1, and both parents may be unaffected carriers. Alpha-mannosidase breaks down oligosaccharides and in the absence of this, oligosaccharides accumulate inside cells, resulting in damage of tissues and organs and leading to cell death. This is characterised by skeletal changes, deterioration of bones and joints, muscle weakness, hearing loss, recurring infections and developmental impairment.

Alpha-mannosidosis can present at infancy, childhood or early adolescence. The onset and severity of symptoms varies widely across a broad spectrum. The most severe forms of alpha-mannosidosis manifest during infancy and are typically characterised by enlargement of the liver, severe infections and poor survival rates. More moderate disease is associated with slow progression but the characteristics of alpha-mannosidosis are evident and have a substantial impact on physical and mental wellbeing. These characteristics may be absent in people with mild disease.[1]

The exact prevalence of alpha-mannosidosis is not known, but has been estimated to be approximately 1 in 500,000.[2] The MPS Society has identified 30 people with alpha-mannosidosis in the UK, although it is expected that there may be more patients whose disease has not been diagnosed.[3]

There are currently no pharmacological treatments for alpha-mannosidosis. Treatment options are aimed at managing symptoms, delaying progression and improving quality of life. Allogeneic haematopoietic stem cell transplant (HSCT) from a family member or unrelated donor is a treatment option for some patients when clinically indicated, although there are significant risks associated with allogeneic HSCT.

The technology

Velmanase alfa (Lamzede, Chiesi) is a long-term enzyme replacement therapy for people with alpha-mannosidosis. It is administered by intravenous infusion.

Velmanase alfa does not currently have a marketing authorisation in the UK for alpha-mannosidosis. It has been studied in clinical trials, compared with placebo, in people with a confirmed diagnosis of alpha-mannosidosis as defined by alpha-mannosidase activity less than 10% of normal activity.

Intervention(s)	Velmanase alfa
Population(s)	People with mild to moderate alpha-mannosidosis
Comparators	Established clinical management without velmanase alfa (including, where clinically indicated, allogeneic haematopoietic stem cell transplant)
Outcomes	The outcome measures to be considered include: • mobility and motor function • hearing and language • cognition • lung function • rates of infection • mortality • adverse effects of treatment (including immune response) • health-related quality of life (for patients and carers).
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	• clinical effectiveness of the 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, and on the delivery of the specialised services	• 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	• Guidance will only be issued in accordance with the marketing authorisation. • Guidance will take into account any Managed Access Arrangements • Where evidence allows consideration may be given to clinical characteristics (such as, age of onset and severity of disease)
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. Beck, M. et al. (2013). Natural history of alpha mannosidosis a longitudinal study. Orphanet Journal of Rare Disease 8:88.

2. Malm, D. (2008). Alpha-mannosidosis. Orphanet Journal of Rare Disease 3:21.

3. The MPS society. What is Mannosidosis? http://www.mpssociety.org.uk/diseases/related-diseases/mannosidosis/ Accessed October 2017