NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Highly Specialised Technologies Evaluation

Avalglucosidase alfa for treating Pompe disease

Draft scope

Draft remit/evaluation objective

To evaluate the benefits and costs of avalglucosidase alfa within its marketing authorisation for treating Pompe disease for national commissioning by NHS England.

Background

Pompe disease, also known as glycogen storage disease type II or acid maltase deficiency is a rare inherited genetic disorder caused by the mutation of the GAA gene which makes an enzyme called acid alpha-glucosidase, resulting in the deficiency of this enzyme.[1] This leads to the progressive accumulation of glycogen, a sugar usually stored in multiple tissues including around the heart, skeletal muscles, respiratory muscles, vascular, gastrointestinal and nervous systems.[1,2] The signs and symptoms of Pompe disease are directly related to the muscles affected. The respiratory, skeletal and cardiac muscles are most profoundly affected.

Pompe disease is classified in two subtypes. The infantile onset which presents within the first months of life and is the most severe form of the disease with rapid progressive cardiomegaly, hepatomegaly, weakness and hypotonia. If untreated, this form is fatal by 1 to 2 years of age. The late onset presents after 1 year of age and is characterised by a progressive myopathy (with little or no cardiac involvement) which can lead to severe morbidity, respiratory failure and early mortality.[3,4]

In 2019 in the EU, Pompe disease was estimated to affect approximately 0.3 in 10,000 people.[5] In 2018 in the EU, the reported birth prevalence was 0.8 per 100,000 people for the infantile onset form and 1.75 per 100,000 for the late-onset form according to European Orphanet data.[6] The incidence in the UK is about 1 in 40,000 according to the association for glycogen storage disease (AGSD).[7]

Current clinical management include enzyme replacement therapy (ERT) with alglucosidase alfa which aims to replace the missing or malfunctioning enzyme. The decision to start treatment is usually based on a set of criteria including confirmed diagnosis and the patient should be symptomatic, have residual skeletal and respiratory muscle function and not have another advanced stage life-threatening condition.[8] Supportive treatment is also needed and can include physiotherapist, occupational therapist, speech therapist and dietetician.[3]

The technology

Avalglucosidase alfa (brand name unknown, Sanofi Genzyme) is a second-generation, glycoengineered recombinant acid alpha glucosidase replacement therapy. It has increased bismannose-6-phosphate-tetra-mannose glycan (bis-M6P) levels compared with alglucosidase alfa. It is administered by intravenous infusion.

Avalgulcosidase alfa does not currently have a marketing authorisation in the UK for Pompe disease. It has been studied in clinical trials compared with alglucosidase alfa in children and adults with late-onset Pompe disease who have not previously had treatment with ERT and in children and adolescents with infantile onset Pompe disease who have had previous ERT.

Intervention(s)	Avalglucosidase alfa
Population(s)	Children and adults with Pompe disease
Comparators	• Alglucosidase alfa • Established clinical management without avalglucosidase alfa
Outcomes	The outcome measures to be considered include: • change in respiratory function • change in cardiac function • change in motor function • change in muscular function • mortality • immunogenicity response • adverse effects of treatment • 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
Clinical Effectiveness	• 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	• 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 (2019) The NHS long term plan NHS England (2018) Highly specialised services 2018 (Lysosomal storage disorders service (children & adults) NHS England (2018) NHS England Funding and Resource 2018/19: Supporting 'Next Steps for the NHS Five Year Forward View' Manual for prescribed specialised services 2018/19, 71. Lysosomal storage disorder service (adults and children) NHS standard contract for metabolic disorders

	(children, 2013/2014) NHS standard contract for metabolic disorders (laboratory services, 2013/2014) Department of Health & Social Care (2019) The UK strategy for rare diseases: 2019 update to the Implementation Plan for England

Questions for consultation

Have all relevant comparators for avalglucosidase alfa been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for Pompe disease?

Would avalglucosidase alfa be given in addition to alglucosidase alfa, after treatment with alglucosidase alfa or replace alglucosidase alfa?

Is the treatment approach different between the infantile and late onset forms of Pompe disease?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom the technology is expected to provide greater clinical benefits or more value for money, or other groups that should be examined separately?

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 avalglucosidase alfa will be 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 Highly Specialised Technologies Evaluation Committee to identify and consider such impacts.

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

NICE intends to evaluate this technology through its Highly Specialised Technologies Programme. We welcome comments on the appropriateness of evaluating this topic through this process. (Information on the Institute's Highly Specialised Technologies interim methods and evaluation processes is available at: https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-highly-specialised-technologies-guidance/HST-interim-methods-process-guide-may-17.pdf.

References

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