NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Avalglucosidase alfa for treating Pompe disease

Final Scope

Final remit/appraisal objective

To appraise the clinical and cost effectiveness of avalglucosidase alfa within its marketing authorisation for treating Pompe disease.

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. Other symptoms include pain, mental fatigue and an impact on mental health.

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]

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]

© National Institute for Health and Care Excellence 2021. All rights reserved.

The technology

Avalglucosidase alfa (Nexviadyme, 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.

Avalglucosidase 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. It has also been studied in a single-arm trial in adults with late-onset Pompe disease who have and have not previously had treatment with ERT.

Intervention(s)	Avalglucosidase alfa
Population(s)	Children and adults with Pompe disease
Comparators	• Alglucosidase 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).
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.

© National Institute for Health and Care Excellence 2021. All rights reserved.

Other considerations	If the evidence allows the following subgroups will be considered: • people with infantile onset Pompe disease • people with late onset Pompe disease 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) 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)

References

1. Xu S, Lun Y, Frascella M, Garcia A, Soska R, Nair A, et al. Improved efficacy of a next-generation ERT in murine Pompe disease. JCI Insight. 2019 Mar 7;4(5). Available from: https://www.ncbi.nlm.nih.gov/pubmed/30843882 10.1172/jci.insight.125358
2. Lim JA, Sun B, Puertollano R, Raben N. Therapeutic Benefit of Autophagy Modulation in Pompe Disease. Mol Ther. 2018 Jul 5;26(7):1783-96. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29804932
3. National Health Service - Cambridge University Hospitals. Pompe. Available from: https://www.cuh.nhs.uk/addenbrookes-hospital/services/lysosomal-disorders/disorders/pompe Accessed February 2020

© National Institute for Health and Care Excellence 2021. All rights reserved.

4. Van der Ploeg AT, Reuser AJ. Pompe's disease. Lancet. 2008 Oct 11;372(9646):1342-53. Available from: https://www.ncbi.nlm.nih.gov/pubmed/18929906
5. European Medicines Agency (EMA). Miglustat for the treatment of glycogen storage disease type II (Pompe's disease). Available from: https://www.ema.europa.eu/en/documents/orphan-designation/eu/3/18/2129-public-summary-opinion-orphan-designation-miglustat-treatment-glycogen-storage-disease-type-ii_en.pdf
6. Orphanet – Prevalence and incidence of rare diseases: Bibliographic data. Available from https://www.orpha.net/orphacom/cahiers/docs/GB/Prevalence_of_rare_diseases_by_diseases.pdf Accessed April 2020
7. Association for glyocogen storage disease (AGSD) UK. Available from: https://agsd.org.uk/all-about-gsd/gsd-variants/pompe-disease-gsd2/ Accessed February 2020
8. Van der Ploeg AT, Kruijshaar ME, Toscano A, Laforet P, Angelini C, Lachmann RH, et al. European consensus for starting and stopping enzyme replacement therapy in adult patients with Pompe disease: a 10-year experience. Eur J Neurol. 2017 Jun;24(6):768-e31. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28477382

© National Institute for Health and Care Excellence 2021. All rights reserved.