NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Cipaglucosidase alfa with miglustat for treating Pompe disease

Final Scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of cipaglucosidase alfa with miglustat 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 and the late onset. The late onset usually presents from 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] While acid alpha-glucosidase activity is typically absent or nearly absent in infantile onset Pompe disease, there is still some residual activity present in those with late onset Pompe disease.[5]

In 2019 in the EU, Pompe disease was estimated to affect approximately 0.3 in 10,000 people.[6] 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.[7]

Current clinical management includes 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

Cipaglucosidase alfa (brand name unknown, Amicus Therapeutics Europe Ltd) with miglustat (Accord Healthcare, Piramal Critical Care and Janssen-Cilag) does not currently have a marketing authorisation in the UK for treating Pompe disease. Cipaglucosidase alfa in combination with miglustat has been studied in clinical trials compared with alglucosidase alfa in adults with late-onset Pompe disease. It has been studied in adults who have received enzyme replacement therapy with alglucosidase alfa and also in adults who have not. It has also been studied in children with late onset Pompe disease who have received enzyme replacement therapy with alglucosidase alfa and also in children who have not.

Intervention	Cipaglucosidase alfa with miglustat
Population	People with Pompe disease
Subgroups	If the evidence allows the following subgroups will be considered: • people who have received prior treatment with alglucosidase alfa • people who have not received prior treatment with alglucosidase alfa
Comparators	• Alglucosidase alfa • Avalglucosidase alfa (subject to ongoing NICE appraisal)
Outcomes	The outcome measures to be considered include: • change in respiratory function • change in motor function • change in muscular function • mortality • immunogenicity response • adverse effects of treatment • health-related quality of life
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 availability of any managed access arrangement for the intervention will be taken into account. The availability and cost of biosimilar and generic products should be taken into account.
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	**Appraisals in development** Avalglucosidase alfa for treating Pompe disease (2022). NICE technology appraisal guidance 3737. Publication expected August 2022.
Related National Policy	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

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