Clinical Commissioning Policy: Alglucosidase alfa for patients with infantile-onset Pompe disease (all ages) (2107) [221002P]

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Summary

Alglucosidase alfa is recommended as a not for routine commissioning treatment option for infantile-onset Pompe disease (IOPD) within the criteria set out in this document.

Committee discussion

Please see Clinical Panel reports for full details of Clinical Panel's discussion. The Clinical Priorities Advisory Group committee papers can be accessed here.

What we have decided

NHS England has carefully reviewed the evidence to treat infantile onset Pompe disease with alglucosidase alfa. NHS England recognises that the published evidence identifies that, at present, there is sufficient evidence to commission this treatment. However, following the relative prioritisation process undertaken in July 2022 for funding interventions in 2022/23, NHS England has concluded that, balanced against other relative priorities that were also considered during this process, alglucosidase alfa for pompe disease will not be funded at this time within the resources available.

The evidence review which informs this commissioning position can be accessed here.

Plain language summary

Pompe disease is a very rare disease which causes damage to muscles and can lead to mobility difficulty, breathing problems and death before two years in untreated patients. Infantile-onset Pompe disease is when the symptoms start in children under one year old and affects the heart muscle as well as the muscles of movement and breathing. Patients with infantile-onset Pompe disease can be treated with a medication called alglucosidase alfa, which replaces the enzyme that may be missing or not working properly.

Alglucosidase alfa is given as a regular injection into a vein. The proposed treatment is to use the same medication but at an increased frequency (once every week instead of once every two weeks) and/or at an increased dose.

About infantile onset Pompe disease

Pompe disease is a rare, multisystem, hereditary disease inherited in an autosomal recessive pattern caused by abnormalities in the GAA gene. The GAA gene contains the genetic information for the production of a protein called acid alpha-glucosidase. Reduced or absent activity of this enzyme inhibits the degradation of glycogen into glucose, which causes a build-up of glycogen, primarily in skeletal, smooth and cardiac muscles leading to damage to the muscles. IOPD is defined as symptom onset before one year of age and with hypertrophic cardiomyopathy.

IOPD is characterised by progressive hypertrophic cardiomyopathy, skeletal muscle weakness causing hypotonia and mobility problems and resulting in respiratory failure. Earlier onset is associated with more rapid progression of the disease. The most severely affected infants present within the first 3 months after birth with characteristic hypertrophic cardiomyopathy, respiratory problems and hypotonia. Untreated patients with IOPD have a life expectancy of less than 2 years.

Over 50% of patients with IOPD in the UK are requiring long-term ventilatory support and less than 30% are ambulatory compared to a ventilation rate of 5% in the Dutch population (Kishnani et al. 2007) and 0% of those treated in a Taiwanese population (Chien et al. 2020) with increased levels of enzyme replacement therapy.

About the current treatment

Patients with IOPD are treated with alglucosidase alfa, which has marketing authorisation for long-term enzyme replacement in patients with confirmed Pompe disease. The marketing authorisation is for the use of 20mg/kg administered intravenously once every two weeks. In England, patients with IOPD currently receive initial treatment of 20mg/kg weekly for the first three months at diagnosis followed by ongoing treatment of 20mg/kg once every two weeks.

The proposed treatment

The proposed treatment is alglucosidase alfa at an off-label dose or frequency as described in Table 1.

Table 1: dose of alglucosidase alfa in the different patient populations.

	Current treatment Dose	Proposed treatment Dose
Newly diagnosed treatment naïve IOPD patients.	20mg/kg once weekly for three months followed by 20mg/kg once every two weeks.	20mg/kg once weekly alglucosidase alfa
IOPD patients already on enzyme replacement therapy who are not invasively ventilated.	20mg/kg once weekly for three months followed by 20mg/kg once every two weeks.	20mg/kg once weekly alglucosidase alfa
Patients with discernible clinical decline[1], (for example deteriorating respiratory or cardiac function or worsening motor function) despite treatment with 20mg/kg once weekly.	20mg/kg once weekly for three months followed by 20mg/kg once every two weeks.	up to 40mg/kg once weekly alglucosidase alfa

Epidemiology and needs assessment

The incidence of Pompe disease appears to vary across different ethnic groups and geographic region from 1 in 14,000 (African American), 1:40,000 (Netherlands and USA), 1 in 145,000 (Australia) and 1 in 600,000 (Portugal) (Park 2021), though areas with newborn screening programmes tend to have a higher frequency. Estimates of IOPD are around 1 in 138,000 births (Elenga et al. 2018).

Evidence summary

An independent evidence review was conducted for the use of alglucosidase alfa in patients with IOPD.. The evidence review which informs this commissioning position can be accessed here:

Governance arrangements

This policy should be used in conjunction with E06/S(HSS)c Lysosomal Storage Disorders (Children) Service Specification.

[1] See starting criteria

Policy review date

This document will be reviewed when information is received which indicates that the policy requires revision. If a review is needed due to a new evidence base then a new Preliminary Policy Proposal needs to be submitted by contacting england.CET@nhs.net.

Our policies provide access on the basis that the prices of therapies will be at or below the prices and commercial terms submitted for consideration at the time evaluated. NHS England reserves the right to review policies where the supplier of an intervention is no longer willing to supply the treatment to the NHS at or below this price and to review policies where the supplier is unable or unwilling to match price reductions in alternative therapies.

Equality statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and

Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

Definitions

Autosomal recessive	One of several ways in which a disease can be passed down through families. It requires two copies of an abnormal gene to be present in an individual for the disease to develop.
Hypertrophic cardiomyopathy	A disease in which the heart muscles become abnormally thick. The thicker muscle can make it harder for the heart to pump blood effectively round the body.
Multidisciplinary team (MDT)	A group of health care workers who are members of different disciplines (may include pediatricians, specialist nurses, dieticians' physiotherapists, occupational therapists, play specialists, pediatric radiographers etc.) each providing specific services to the patient.

References

Chien YH, Tsai WH, Chang CL, Chiu PC, Chou YY, Tsai FJ, Wong SL, Lee NC, Hwu WL. Earlier and higher dosing of alglucosidase alfa improve outcomes in patients with infantile-onset Pompe disease: evidence from real-world experiences. Molecular Genetics and Metabolism Reports. 2018. 23:100591.

Elenga N, Verloes A, Mrsic Y, Basurko C, Schaub R, Cuadro-Alvarez E, Kom-Tchameni R, Carles G, Lambert V, Boukhari R, Fahrasmane A, Jolivet A, Nacher M, Benoist J-F. Incidence of infantile Pompe disease in the Maroon population of French Guiana. BMJ Paediatrics Open. 2018, 2(1):e000182.

Kishnani PS, Corzo D, Nicolino M, Byrne B, Mandel H, Hwu WL, Leslie N, Levine J, Spencer C, McDonald M, Li J, Dumontier J, Halberthal M, Chien YH, Hopkin R, Vijayaraghavan S, Gruskin D, Bartholomew D, van der Ploeg A, Clancy JP, Parini R, Morin G, Beck M, De la Gastine GS, Jokic M, Thurberg B, Richards S, Bali D, Davison M, Worden MA, Chen YT, Wraith JE. Recombinant human acid [alpha]-glucosidase: major clinical benefits in infantile-onset Pompe disease. Neurology. 2007. 68(2): 99-109.

Park KS. Carrier frequency and predicted genetic prevalence of Pompe disease based on a general population database. Molecular Genetics and Metabolism Reports. 2021, 27:100734.