NHS ENGLAND SPECIALISED SERVICES

CLINICAL PANEL REPORT

Date: January 2022

Intervention: Alglucosidase alfa

Indication: infantile onset Pompe disease (all ages)

URN: 2107

Gateway: 2, Round 1

Programme: Women and Children

CRG: Metabolic Disorders

Information provided to the Panel

Evidence Review completed by NICE

Policy Proposition

Blueteq™ Form

Patient Pathway

Evidence to Decision Making Summary

Patient Impact Report

Equality and Health Inequalities Assessment (EHIA) Report

Clinical Priorities Advisory Group (CPAG) Summary report

Policy Working Group Appendix

This Policy Proposition recommends the routine commissioning of alglucosidase alfa for patients with infantile-onset Pompe disease for all ages. This is recommending an off label use of the medicine which has a marketing authorisation for this condition. IOPD is characterised by progressive hypertrophic cardiomyopathy and skeletal muscle weakness causing hypotonia, mobility problems and subsequently respiratory failure. Untreated patients with IOPD have a life expectancy of less than 2 years.

Clinical Panel noted that NICE is in the process of conducting a Technology Appraisal (TA) on Avalglucosidase alfa for treating Pompe disease [3737], currently listed for publication in August 2022. In this TA, Avalglucosidase alfa is compared to the licensed dose of Alglucosidase alfa (20mg once every two weeks) rather than the current standard treatment dose of Alglucosidase alfa (20mg/kg once weekly for three months followed by 20mg/kg once every two weeks).

Clinical Panel members were presented with the evidence base supporting this proposition. One paper was identified for inclusion. The study (n=18) was a prospective observational before and after study using standardised assessments. It compared outcomes in babies and infants newly diagnosed with IOPD who started treatment with the licensed dosage of alglucosidase alfa between 2003 and 2009 (n=6) with those who started treatment with alglucosidase alfa 40 mg/kg once weekly from 2009 (n=12). No studies were identified comparing alglucosidase alfa 40 mg/kg once weekly with current standard treatment. Also, no studies were identified comparing alglucosidase alfa 20 mg/kg once weekly with the licensed dosage or current standard treatment.

The evidence levels indicated low to very low certainty based on GRADE methodology. The members heard that the evidence demonstrates a higher proportion of patients using alglucosidase alfa 40 mg/kg once weekly demonstrated improved overall survival (92% vs 67%) and ventilation-free survival (92% vs 50%) and achieved walking outcomes compared with patients using the licensed dosage. However, the difference between the groups was statistically significant only for the ability to walk at 3 years of age (92% vs 33%, p=0.02).

No evidence was identified for quality of life or cost-effectiveness.

The Clinical Panel examined the proposition. There was concern expressed amongst members whether increasing the dosage and frequency of administration as was being recommended was a safe thing to do, particularly as babies' clearance of medicine is immature, and if there was wider pharmacy expert support for this. There are no pharmaco-kinetic dosing studies to support this change.

The proposition stated multidisciplinary team (MDT) review and decision regarding treatment and any increase in dosage but there is no reference to the criteria or decision-making framework they would use to determine this.

Regarding reassessment, it suggests that cardiac function assessment stops at 24 weeks. This should be checked and the proposition amended if this is ongoing.

Clinical Panel members considered that the proposition was written reflective of the evidence base.

EHIA – no additional comments received.

Patient Impact Report – no additional comments received.

Recommendation

Clinical Panel recommends that this proposition progresses as proposed, with the amendments requested, and once the further information requested has been considered by the Clinical Panel Chair and they are assured.

Why the panel made these recommendations

The Panel considered that the evidence base supported the proposition, albeit very low certainty as the study population was small due to the rarity of the condition.

Documentation amendments required

Policy Proposition:

- How many patients would actually benefit from the higher dosage? Not clear in the proposition.
- MDT review and decision-making - need to be clearer what would trigger the higher dose, what framework of questions would be used to determine eligibility.
- Cardiac Reassessment - it suggests that cardiac function assessment stops at 24 weeks. This should be checked and the proposition amended if this is ongoing. Also, antibody levels that are being monitored are not stated.
- Reassessment list reads like a specification and the stopping criteria very brief. Consider whether some or all of the reassessment points are required and use more discrete criteria for continuation and dose increase. Need to modify this section or take out

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Declarations of Interest of Panel Members: None

Panel Chair: James Palmer, National Director, Specialised Services

Post panel notes

Response to queries raised

Policy Proposition:

- How many patients would actually benefit from the higher dosage? Not clear in the proposition. Up to *20 would receive treatment in year one, 17 patients who are current patients and 3 new patients that it is expected will present annually.*
- Seek pharmacy expert opinion on the safety of the increased dosing and increased frequency of administration. *A subgroup of metabolic pharmacists reviewed the safety concerns and agreed that that the use of the drug, as set out in this policy proposition, was acceptable from a safety perspective.*
- Table on page 3 – suggests patients would immediately start on 20mg/kg but MDT reference suggests otherwise. Need to make clearer. *This has been clarified and the MDT section now states that the starting dose is 20mg/kg.*
- MDT review and decision-making - need to be clearer what would trigger the higher dose, what framework of questions would be used to determine eligibility. *The criteria have been clarified*
- Cardiac Reassessment - it suggests that cardiac function assessment stops at 24 weeks. This should be checked, and the proposition amended if this is ongoing. *This has been done*. Also, antibody levels that are being monitored are not stated. *This has been removed.*
- Reassessment list reads like a specification and the stopping criteria very brief. Consider whether some or all of the reassessment points are required and use more discrete criteria for continuation and dose increase. Need to modify this section or take out. *This section has been removed. The policy refers to the regular monitoring of patients and that their condition is assessed during these appointments as an ongoing process.*