National Institute for Health and Care Excellence

Health Technology Evaluation

Cipaglucosidase alfa with miglustat for treating Pompe disease [ID3771]

Response to consultee and commentator comments on the draft remit and draft scope

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Comment 1: the draft remit

Section	Consultee/ Commentator	Comments [sic]	Action
Appropriateness	Amicus Therapeutics	Amicus believe it is highly appropriate for this topic to be referred to NICE for appraisal. However, further to NICE's recommendation that this topic should be considered as part of a Single Technology Appraisal (STA), Amicus strongly believes that this topic should be referred to NICE for preparation of a Highly Specialised Technology (HST) appraisal. In particular, Amicus would like to provide feedback on the decision by NICE that the HST criterion *"The condition is chronic and severely disabling"* has not been fully met. • **Pompe disease is a chronically debilitating condition** where patients experience progressive loss of muscle causing severely disabling symptoms including worsening pulmonary function, respiratory failure, limb weakness, fatigue, pain and, ultimately, premature death.[1, 2] In a study presented at the World Muscle Society 2021, most adult UK Pompe patients felt that the disease severely affected their lives with impacts on their lifestyle, daily activities, social	Comment noted. Following the consultation on this proposed appraisal was decided that this topic will proceed within the NICE work programme as a technology appraisal (TA) in line with recent topic selection decisions for other topics for treating pompe disease.

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		life, ability to continue working and family relationships.[3] People living with Pompe disease, their caregivers, families and healthcare providers continue to express this urgent need for additional improved treatment options.[4-6] • Whilst the benefits of alglucosidase alfa treatment are well-known, there is a lack of long-term data available. Of the findings published, several have shown a **lack of sustained benefit of alglucosidase alfa over time**, with patients reaching a therapeutic plateau within just a few years.[7] Therefore, the evidence base cannot support the fact that alglucosidase alfa, as the only treatment currently available, is a sufficient treatment option to mitigate the severe morbidity and mortality of the disease. This was recognised both through the approval of the Early Access to Medicines Scheme (EAMS) for cipaglucosidase alfa with miglustat [redacted]. • The innovative design of cipaglucosidase alfa with miglustat is a step change that optimises glycosylation necessary for enhanced targeting and uptake in muscle cells, whilst the addition of the small molecular enzyme stabiliser (miglustat) enhances the ability of cipaglucosidase to reduce accumulated glycogen.[8] This combination allows recombinant human acid α-glucosidase (rhGAA) to be fully processed by the body to maximise cellular and muscular uptake, thereby enabling the **change in efficacy outcomes** observed compared with alglucosidase alfa.[8, 9] • Amicus therefore believe that routing cipaglucosidase alfa with miglustat through the STA programme would result in **inequality in patient access to the technology** as well as further delays in the advancement of a next generation therapy, despite being keenly anticipated by rare disease communities**.**	

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		Further detail is provided in our response to the HST Criteria Company Proforma (ID3771).	
	Association for Glycogen Storage Disease-UK and Metabolic Support UK joint submission	It is highly appropriate to refer this topic for appraisal given there is currently only one other medical treatment option and improved treatments are urgently needed to prevent deterioration in this severe, degenerative condition. Cipaglucosidase alfa with miglustat is an improvement on the only current ERT available -alglucosidase alfa. Following the advent of the first new treatment over ten years ago, earlier diagnosis with Pompe disease has resulted from awareness raising by patient organisations, improved medical training, better access to testing and the impact of the Highly Specialised Metabolic Centres. Increasing numbers of people identified earlier in their disease progression could therefore benefit from the potential of this new treatment to prevent health decline.	Comment noted. No action required.
	Pompe Support Network	Yes	Comment noted. No action required.
	Gene People	Yes we believe that this is an appropriate topic for NICE to appraise. Gene People is uncertain as to the rationale for the route to be the STA rather than the HST route given the patient population in England who are affected by Pompe disease. Our understanding is that there are approximately 200 patients with the condition across the whole of the UK and would ask that the rationale for this route is revisited and published.	Comment noted. Following the consultation on this proposed appraisal it was decided that it will proceed within the NICE work programme as a technology appraisal (TA) in line with recent topic

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			selection decisions for other topics for treating pompe disease.
	NHS England	It would be appropriate to refer this to NICE. These are high cost drugs administered through highly specialised services and require objective evaluation of cost effectiveness.	Comment noted. No action required.
Wording	Amicus Therapeutics	The wording of the remit appropriately reflects the clinical and cost-effectiveness issues that NICE should consider.	Comment noted. No action required.
	Association for Glycogen Storage Disease-UK and Metabolic Support UK joint submission	The wording is appropriate, though in evaluating cost-effectiveness consideration should also be given to the potential cost-savings derived from maintaining functionality in patients who are in the early stages of deterioration.	Comment noted. No action required.
	Pompe Support Network	Yes	Thank you for your comment. No action required.
	NHS England	Yes	Thank you for your comment. No action required.
Timing Issues	Amicus Therapeutics	There is a high degree of urgency for NICE to issue a technology appraisal on this topic. Pompe disease is a serious, debilitating, and ultimately life-threatening disease associated with high morbidity and mortality.[1, 2] The disease is	Comment noted. No action required.

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		progressive in nature, gradually impairing mobility and respiratory function. A study in adults with Pompe disease found that 10–15 years after diagnosis, 50% of patients were either wheelchair-bound or ventilator dependent, and patients requiring wheelchair or respiratory support had a shorter life expectancy at any age than those who did not.[1, 7] Pompe disease will continue to progress over time in most patients treated with the standard of care enzyme replacement therapy (ERT).[2] There is strong evidence from long-term real world studies that the initial functional efficacy of alglucosidase alfa diminishes leading to noticable declines within 6 months for motor function measures and within 2.2 years for the 6-minute walk distance (6MWD).[7] Adults with Pompe disease, caregivers, patient organisation representatives, and clinicians have expressed a need for newer and better treatment options as soon as possible, as there is a proportion of patients who continue to deteriorate significantly despite therapy with current standard of care which underpins the urgent remaining unmet need.[10, 11] Furthermore, the urgency of this appraisal has been echoed through feedback from NHS representatives as well as through the positive demand that has been seen with the EAMS for cipaglucosidase alfa with miglustat. The innovative design of cipaglucosidase alfa with miglustat enables the change in efficacy outcomes compared with standard of care ERT,[12] and provides an opportunity to address current areas of unmet need. Ongoing absence of a NICE appraisal for this indication would therefore significantly contribute to the ongoing unmet need in patients with Pompe disease. The marketing authorisation (MA) for cipaglucosidase alfa with miglustat is expected to be granted in [redacted]	

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	Association for Glycogen Storage Disease-UK and Metabolic Support UK joint submission	Starting treatment for Pompe disease with the best available therapy as early as possible is vital to prevent deterioration in health and quality of life.	Comment noted. No action required.
	Genetic Alliance UK	Starting treatment as early as possible is vital in order to prevent deterioration in health.	Comment noted. No action required.
	Pompe Support Network	MHRA have awarded EAMS approval for this treatment, assessing that it fulfils a high unmet need. Registration for EAMS closes in June 2022 after which patients who may benefit from the treatment will no longer have access to it.	Comment noted. No action required.
	NHS England	Ideally this should align with the end of the EAMS scheme for this drug. There is only one commissioned treatment for patients with Pompe disease and that drug has never been appraised by NICE.	Comment noted.
Additional comments on the draft remit	Amicus Therapeutics	No further comments.	N/A
	Pompe Support Network	We are very surprised that Cipaglucosidase is being assessed through STA and not the HTA process. We are very concerned that this would jeopardise the outcome of the appraisal. All conditions for an HST appraisal would seem to be met by this treatment and the disease, so we would urge NICE to reconsider the chosen route.	Following the consultation on this proposed appraisal it was decided that this topic will proceed within

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			the NICE work programme as a technology appraisal (TA) in line with recent topic selection decisions for other topics for treating Pompe disease.
	Gene People	For the benefit of the reader the following comments explains Gene People's interest in this consultation. Gene People (formerly Genetic Disorders UK) is a registered charity that provides direct support to those affected by genetic conditions and their families through our unique genetic counsellor-led helpline and web resources and hosts a growing Partnership Network of over 130 condition-specific support organisations. We are not limited to rare genetic conditions, although the majority of our Partnership Network members represent rare and very rare conditions. Gene People is responding to the consultation on the scope because the AGSD UK - Association for Glycogen Storage Disease is a member of our Partnership Network and Pompe is a genetic condition. Please note: the Partnership Network is free for condition-specific support groups to join, and Gene People does not benefit financially from AGSD UK's membership.	Comment noted. No action required.

Comment 2: the draft scope

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Background information	Amicus Therapeutics	Currently, Amicus feels that the background section does not sufficiently capture the severity of the condition. Therefore please could the following symptoms also be added: • **Gastrointestinal issues** including abdominal discomfort, chronic diarrhoea or constipation, and poor weight gain.[13] • Deterioration of the diaphragm and other muscles involved in respiration leading to **difficulties in feeding and swallowing**.[2] • Progressive loss of muscle function in patients leading to **organ failure** and the need for **ventilatory and ambulatory support**.[13] • **Cerebrovascular abnormalities**, including dolichoectasia of the basilar artery, white matter lesions, microbleeds and aneurysms.[14,15] In addition, Amicus does not feel that the epidemiological evidence presented in the background section accurately reflects the anticipated number of adults with Pompe disease in the UK. Based on clinical expert input, Amicus believe that there are [redacted] treated adult Pompe disease patients in England who could be eligible for treatment with cipaglucosidase alfa/miglustat.[10]	Comments noted. The background section of the scope is intended to give a brief overview of the condition. No changes to the scope required.
	Association for Glycogen Storage Disease-UK and Metabolic Support UK joint submission	• The progressive symptoms of Pompe have a profound effect on every aspect of daily life for people affected. In addition to the increasingly debilitating impact on respiration and movement, which often result in dependency on wheelchairs and mechanical respiration in adult patients, symptoms such as fatigue, pain, impaired sleep, problems with temperature regulation, continence and gastrointestinal issues significantly impinge on quality of life. Relationships, family life, employment, financial wellbeing and social participation are all affected, with a significant additional impact on family, friends and carers.	Comments noted. The background section of the scope is intended to give a brief overview of the condition. The committee will consider the quality of life impact of the condition and the new technology in this appraisal. The NICE methods guide states

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		• Mental health is greatly affected by living with this degenerative and currently incurable neuromuscular condition, though cognitive function is not seriously impaired. Depression and anxiety weigh heavily on patients and those close to them. Clinical psychology is an important aspect of supportive treatment. • Along with the physical symptoms listed we would like to see the addition of the psychosocial impact of Pompe on patients and caregivers. Whilst making this evaluation the committee should consider the wider health, economic and societal benefits of this treatment.	that impact on carer quality of life can be considered when relevant. No changes to the draft scope required.
	Genetic Alliance UK	We defer to condition specific organisations on these points however, Pompe disease is a progressive lifelong condition that has a profound impact on quality of life for patients and those close to them.	Comment noted. No action required.
	Pompe Support Network	Second paragraph states “Late-onset can present from 1 year of age” I would reword as “Late-onset can present at any time after birth” The Late-Onset prevalence is a worldwide estimate made in 2018. Applied to the UK population would suggest 2000 patients; however less than 250 are known to the NHS. Conversely the figures emerging from the newborn screening programmes in the USA, Taiwan and Italy suggest that prevalence could be double that quoted. So clearly the estimates (and diagnostics) require much improvement.	Comments noted. The background section has been updated to address this comment.
	Gene People	The background information is brief but we cannot see any inaccuracies.	Comment noted. The background section of the scope is intended to give a brief overview of

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			the condition No action required.
The technology/ intervention	Amicus Therapeutics	We can confirm that the description of the technology is correct and have no further comments.	Comment noted. No action required.
	Association for Glycogen Storage Disease-UK and Metabolic Support UK joint submission	Dosing is an issue to be monitored.	Comment noted. No action required.
	Pompe Support Network	We believe so	Comment noted. No action required.
	Gene People	We cannot comment on the description of the technology as we are not the company.	Comment noted. No action required.
Population	Amicus Therapeutics	We can confirm that the wording describing the population and relevant subgroups for consideration is appropriate. [redacted]	Comments noted. NICE will appraise the technology within its marketing authorisation.
	Association for Glycogen Storage Disease-UK and Metabolic	Young people with LOPD could be considered separately to adults with LOPD.	Comments noted. NICE will appraise the technology within its marketing authorisation

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	Support UK joint submission		
	Pompe Support Network	We would prefer to see the age range of patients specified. The formulation for Miglustat will, no doubt, differ for very young children.	Comments noted. NICE will appraise the technology within its marketing authorisation
	Gene People	Our understanding is that there are approximately 200 people with Pompe disease in the UK as a whole. The studies for this treatment have included groups of adults and children who have received the existing ERT and those who have not. We have not had sight of the studies to be able to comment further.	Comments noted. NICE will appraise the technology within its marketing authorisation
Comparators	Amicus Therapeutics	Alglucosidase alfa is the only therapy licensed in the UK for this indication and is considered to be established clinical practice in the NHS for treating Pompe disease. We therefore can confirm that alglucosidase alfa would constitute the appropriate comparator in this appraisal.	Comment noted. No action required.
	Association for Glycogen Storage Disease-UK and Metabolic Support UK joint submission	Current treatment options are either supportive non-medical therapies alone or alglucosidase alfa with supportive therapies. Neither is the best alternative compared to Cipaglucosidase alfa with miglustat and supportive therapies.	Comment noted. No action required.
	Genetic Alliance UK	Current treatment for Pompe disease consists of supportive therapies and/or alglucosidase alfa however, some patients cannot tolerate alglucosidase alfa therefore there is an urgent need for a treatment for these individuals.	Comment noted. No action required.

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		We have been informed by condition specific patient organisations that patients have reported a plateauing in the effectiveness of current treatment on disease progression. This emphasises the urgency and need for alternative treatment options in order to prevent further deterioration. Cipaglucosidase alfa with miglustat is considered amongst the community to be a significant improvement for the potential of disease management.	
	Pompe Support Network	yes	Comment noted. No action required.
	NHS England	This is the appropriate comparator	Comment noted. No action required.
Outcomes	Amicus Therapeutics	We can confirm that the listed outcome measures reflect those assessed in the key PROPEL trial.[16] As previously mentioned, Pompe disease is a serious and debilitating disease associated with high morbidity.[1, 2] The disease is progressive in nature, gradually impairing mobility, requiring assisted respiration, and ultimately leading to premature death.[7, 17, 18] As such, the company submission will focus on the severity of the disease and how this is reflected in the outcome measures. Mortality was not assessed as part of the Phase III PROPEL study, due to the one-year timeframe associated with collection of these data.	Comment noted. No action required.
	Association for Glycogen Storage Disease-UK and Metabolic	Outcome measurement can vary based on the degree of severity of the condition Outcome measures could include mental health self-report. The psychosocial aspects within the health related quality of life measures should be explicitly reviewed.	Comment noted. The appraisal committee will consider all relevant evidence. No changes to the scope required.

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	Support UK joint submission		
	Pompe Support Network	In essence yes but would also like to consider any changes to GI issues or muscle pain. It would also be interesting to examine how all outcomes vary across the 14 days between treatment.	Comments noted. The outcomes section of the scope is not intended to be exhaustive. The appraisal committee will consider relevant outcomes.
	NHS England	Carer and patient related quality of life should be considered Participation in activities of daily living Pain Fatigue	Comments noted. The NICE methods guide states that impact on carer quality of life can be considered when relevant. The outcomes section of the scope is not intended to be exhaustive. The appraisal committee will consider relevant outcomes.
Economic analysis	Amicus Therapeutics	We are happy with the suggestion to follow the reference case and confirm that the economic analysis will be appropriate. However, please note that a non-reference case discount rate is anticipated to be used.	Comment noted. No action required.

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	Association for Glycogen Storage Disease-UK and Metabolic Support UK joint submission	Whilst outside the scope of the economic analysis, employability and ability to work is severely affected by Pompe and the condition has an additional impact on family and carers.	Comment noted. No action required.
	Pompe Support Network	Cost per QALY is not an appropriate measure for such ultra-rare diseases, given the development and manufacturing costs for such a small patient population. It would be more sensible to compare the cost effectiveness in comparison with the current standard of care. As this will be an STA process, the QALY threshold is much too low for such a rare condition. When considering similar treatments for other rare diseases, we strongly feel that the higher HST threshold will be required, together with a QALY rating, for the treatment to be commercially viable. Experience of managed access agreements in other rare disease has not been good. We would prefer not to impose such procedures on patients, families, or treating clinicians.	Comment noted. Following the consultation on this proposed appraisal it was decided that that this topic will proceed within the NICE work programme as a technology appraisal (TA) in line with recent topic selection decisions for other topics for treating pompe disease. The committee will consider if there are health impacts which are not captured by the QALY. No changes required.

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Equalities	Amicus Therapeutics	In light of NICE's decision to route this topic through the STA process, we would like to highlight the inequity to adults with Pompe: • Cipaglucosidase alfa with miglustat would be subject to the lower willingness-to-pay threshold compared with the HST programme. • This 'traditional' threshold would not take into account that cipaglucosidase alfa with miglustat is an **innovative product** offering **considerable health benefits** in the treatment of adult Pompe disease, [redacted] • In addition, as with many rare diseases, not least Pompe disease, it is widely acknowledged that the small number of patients necessitates a relatively high cost per patient. Based on clinical expert input, Amicus believe that there are [redacted] treated adult patients with Pompe disease in England who could be eligible for treatment with cipaglucosidase alfa and miglustat.[10] It would therefore be less likely that a product such as this would be found cost-effective against the lower STA willingness-to-pay threshold. Therefore, we have concerns that routing a product for a very rare condition – with a significant unmet need and severity – through the STA programme, would result in **inequality in the potential for its access**, when compared to products for conditions with a much higher prevalence. We also have concerns that this decision will result in further delays in the advancement of a next generation therapy, despite these technologies being keenly anticipated by rare disease communities**.**	Comment noted. Following the consultation on this proposed appraisal, it was decided that this topic will proceed within the NICE work programme as a technology appraisal (TA) in line with recent topic selection decisions for other topics for treating pompe disease. The committee will consider any relevant equality issues.
	Association for Glycogen Storage Disease-UK and Metabolic	Consider BAME groups. This is a genetic, recessive condition with higher prevalence in communities where consanguineous marriage is more prevalent.	Comment noted. The appraisal committee will consider any potential equalities issues. No

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	Support UK joint submission		changes to the scope required.
	Pompe Support Network	Ftra	Comments noted. The summary of product characteristics will provide additional information for the treatment. No changes to the draft scope required.
	Gene People	Gene People is concerned that the routing of this treatment through STA rather than HST will put those with Pompe disease at a disadvantage, as it may mean that this decision makes it harder for them to access the technology.	Comment noted. Following the consultation on this proposed appraisal it was decided that this topic will proceed within the NICE work programme as a technology appraisal (TA) in line with recent topic selection decisions for other topics for treating Pompe diseaseThe committee will consider any relevant equality issues.

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Other considerations	Amicus Therapeutics	Amicus would like to re-iterate that Pompe disease is a very rare disease, and that cipaglucosidase alfa fulfils the HST criteria: • Pompe disease is managed in 5 **specialist centres** in England, and would be used exclusively as part of a highly specialised service.[19] • Pompe disease in adult patients is **very rare**; Amicus believe that there are only [redacted] treated adult patients with Pompe disease in England who could be eligible for treatment with cipaglucosidase alfa and miglustat.[10] • Pompe disease in adults is **clinically distinct** as a patient population. • Pompe disease is a **chronic debilitating condition** where patients experience progressive loss of muscle causing severely disabling symptoms including worsening pulmonary function, respiratory failure, limb weakness, fatigue, pain and, ultimately, premature death.[7, 17, 18] • Pompe disease **treatment is required throughout patients' lives** in order to enable the breakdown of glycogen and prevent the abnormal build-up of glycogen in cells. Cipaglucosidase alfa therefore has the potential for lifelong use.[1, 17, 20, 21] • With a well-established decline in effectiveness for the current standard of care treatment alglucosidase alfa,[7] there is a substantial unmet need for effective treatments for adults with Pompe disease, which has been recognised through the approval of the EAMS for cipaglucosidase alfa with miglustat. As is usually the case for rare diseases, there are limited clinical and comparative data available. We would like to highlight our major concerns regarding the challenges of assessing a product of this nature via the STA process, particularly considering the severely disabling impact and increased mortality associated with Pompe disease in adults.	Comment noted. Following the consultation on this proposed appraisal it was decided that this topic will proceed within the NICE work programme as a technology appraisal (TA) in line with recent topic selection decisions for other topics for treating pompe disease.

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	Association for Glycogen Storage Disease-UK and Metabolic Support UK joint submission	Not all current patients tolerate or respond consistently to the only existing treatment so there is a need for an effective alternative. Plateauing in the effectiveness of the current treatment on disease progression is reported among patients, who stress the urgency of gaining access to more effective treatments as early as possible in the course of their condition. Patients with Pompe disease value and benefit from the highly specialised care they receive in Highly Specialist Centres but these are often at some distance from home. Given the need for fortnightly therapy with Cipaglucosidase alfa with miglustat, consideration will need to be given to appropriate care pathways that can support community administration under close supervision of specialist centres, once patients are safely established on the therapy.	Comment noted. The appraisal committee will consider all relevant evidence. No changes to the scope required.
Innovation	Amicus Therapeutics	The innovative protein structure and design of cipaglucosidase alfa, [redacted] allows rhGAA to be fully processed like endogenous GAA upon uptake into cells which is critical to attain the most active form of the enzyme GAA.[8] It is also co-administered with an enzyme stabiliser (miglustat) that prevents denaturation of the recombinant enzyme in the blood.[8] This enables the change in efficacy outcomes compared with alglucosidase alfa,[12] and provides an opportunity to address areas of unmet need which are not currently being addressed. The potential for cipaglucosidase alfa to improve outcomes in the treatment of adult Pompe disease patients is reflected by the Priority Innovative Medicines (PIM) designation, awarded by the MHRA in 2020.[22] PIM designations are only awarded to treatments that could offer a major advantage for patients, for conditions with a high unmet need (for example, where existing methods of treatment have serious limitations).[23] The PIM designation was awarded	Comment noted. The innovative nature of the technology will be considered by the appraisal committee based on evidence presented to it. No action required.

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		following the potential showed by cipaglucosidase alfa with miglustat in Phase I/II data. Cipaglucosidase alfa with miglustat is also expected to demonstrate a range of societal benefits. A burden of illness study has shown that Pompe disease is associated with substantial medical costs.[24] Adults with Pompe disease typically received 8 hours of home care and 19 hours of informal care per week, whilst both patients and their caregivers experienced productivity losses due to the disease. In light of the efficacy improvements anticipated with use of cipaglucosidase alfa with miglustat, it is anticipated that these will translate into societal benefits for patients and caregivers.[9]	
	Association for Glycogen Storage Disease-UK and Metabolic Support UK joint submission	AGSD UK consultation with members representing those with Pompe disease considers this to be a 'step-change'. It provides significant and substantial potential for improvement in disease management and an alternate option for treatment.	Comment noted. The innovative nature of the technology will be considered by the appraisal committee based on evidence presented to it. No action required.
	Pompe Support Network	Yes we do. We have followed the development of second-generation enzyme replacement therapies and have taken advice from international KOLs on the benefits of new technologies. We were disappointed by the clinical study results which we believe highlighted the problems of short study timescales and the size and selection of treatment and placebo cohorts. Papers such as that cited below indicate that important improvements in cell metabolism are introduced by this therapy, although we believe that the effects may take a few years to show the full benefit to patients, by slowing the progression of the disease.	Comment noted. The innovative nature of the technology will be considered by the appraisal committee based on evidence presented to it. No action required.

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		Meena NK, Ralston E, Raben N, Puertollano R. Enzyme Replacement Therapy Can Reverse Pathogenic Cascade in Pompe Disease. *Mol Ther Methods Clin Dev*. 2020;18:199-214. Published 2020 Jun 10. doi:10.1016/j.omtm.2020.05.026	
	NHS England	Yes this drug does have the potential to add to the range of treatment options available to patients with Pompe disease	Comment noted. The innovative nature of the technology will be considered by the appraisal committee based on evidence presented to it. No action required.
Questions for consultation	Amicus Therapeutics	**Do treatment options differ if people have been previously treated with enzyme replacement therapy with alglucosidase alfa?** Cipaglucosidase alfa with miglustat would give an alternative treatment option to both ERT-experienced and naïve patients. As discussed previously, both of these patient populations experience high levels of unmet need and require urgent treatment in order to avoid further deterioration of their condition.[3, 17, 18] [redacted]	Comments noted. No changes to the scope required.
	Genetic Alliance UK	We are not aware as to which of the HST criteria has ruled this treatment out, therefore routing it through STA. This technology meets all of the criteria for the HST and due to the small population size, we believe this technology would be disadvantaged by the standard appraisal process. It therefore would fit NICE's stated objectives for the HST programme: 'The objective and intent of the HST programme is to provide fair and equitable access to treatments	Following the consultation on this proposed appraisal it as decided that this topic will proceed within the NICE work programme

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		for patients with serious and severe ultra-rare conditions where there is vulnerability, substantial unmet needs, or very limited, not very effective treatment options, who would be disadvantaged by an appraisal undertaken via the standard appraisal process.' We are aware that a precedent has been set with a previous treatment for Pompe disease that was routed through the STA process however we dispute that decision and do not want this treatment to follow suit.	as a technology appraisal (TA) in line with recent topic selection decisions for other topics for treating pompe disease.
	Pompe Support Network	All relevant comparators are included. Treatment options may differ if a patient had a severe adverse reaction to the standard of care.	Comment noted. No action required.
	NHS England	The majority of the cohort will have been treated with alglucosidase alfa so the question on treatment options for previously treated patients may be hard to answer.	Comment noted. No action required.
Additional comments on the draft scope	Amicus Therapeutics	We re-iterate our earlier comments in this response document that we strongly believe that it would be more appropriate for this topic to be referred to NICE for an HST appraisal as opposed to the STA process, given that cipaglucosidase alfa with miglustat meets both the current and revised HST criteria as part of the latest NICE Process and Methods Review.[25] We believe that routing cipaglucosidase alfa with miglustat through the STA programme will ultimately result in inequality in patient access to this innovative technology.	Following the consultation on this proposed appraisal it was decided that this topic will proceed within the NICE work programme as a technology appraisal (TA) in line with recent topic selection decisions for other topics for treating Pompe disease.

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	Association for Glycogen Storage Disease-UK and Metabolic Support UK joint submission	We are unclear why this treatment is being taken through the Single Technology Assessment process rather than the Highly Specialised Technology Assessment process specifically designed for rare conditions. This technology clearly meets all the criteria for the HST programme. In particular we would highlight the severity and complexity of this chronic, degenerative condition, with its far reaching physical and psychosocial impact and distinct clinical needs. Treatment for the approximately 250 people diagnosed with Pompe in the UK is commissioned nationally and concentrated in highly specialised centres. We consider this treatment with potential for lifelong use would represent a step change in management of the condition, given reports of plateauing in the impact of the only established treatment among some patients and the proportion of those affected in whom it is poorly tolerated or less effective. We are concerned about the implications for future therapies for severe rare conditions of the choice of assessment route for this treatment. This may have a negative impact on addressing the urgent need for access to improved therapies for people with severe, degenerative, life limiting conditions, including Pompe and other glycogen storage disorders.	Following the consultation on this proposed appraisal it was decided that this topic will proceed within the NICE work programme as a technology appraisal (TA) in line with recent topic selection decisions for other topics for treating Pompe disease.
	Pompe Support Network	Experience with the current standard of care highlighted that the standard dose of 20mg/kg/eow is not sufficient to fully protect all growing children or severely affected adults. If recommended, we would favour a label that gives the treating physician as much flexibility as possible to adjust the dosage, without the need for off-label prescribing.	Comments noted. No changes to the scope required.