**National Institute for Health and Care Excellence**

**Health Technology Evaluation**

# Givinostat for treating Duchenne muscular dystrophy in people 6 years and over [ID6323]

## Response to stakeholder organisation comments on the draft remit and draft scope

**Please note:** Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

### Comment 1: the draft remit and proposed process

| Section | Stakeholder | Comments [sic] | Action |
|---|---|---|---|
| Appropriateness of an evaluation and proposed evaluation route | ITF Pharma UK Ltd | ITF Pharma UK (ITF) believe that the evaluation by NICE of givinostat for Duchenne muscular dystrophy (DMD) for people aged 6 years and over is appropriate due to the substantial unmet need of people with DMD as outlined below. There is a lack of data describing the prevalence of DMD by age in the literature. Given that an estimated 1,500 people aged 6 years and over are living with DMD in England, of whom ITF anticipate 1,000 would be eligible for givinostat, ITF agree that a single technology appraisal is an appropriate route for evaluation. However, ITF note that DMD meets two of the criteria for highly specialised technologies, in that it (1) significantly shortens life and severely impairs quality of life, and (2) that there are no other satisfactory treatment options available, and the technology is likely to offer significant additional benefit over existing treatment options. | Thank you for your comment. |

| Section | Stakeholder | Comments [sic] | Action |
|---|---|---|---|
| | Association of British Neurologists | Appropriate. | Thank you for your comment. |
| | British Society of Paediatric Endocrinology and Diabetes | Appropriate as another option or alternative disease modifying therapies are needed, and in particular those with good safety profile. | Thank you for your comment. |
| | Muscle interest group BPNA | I think this is the appropriate route. | Thank you for your comment. |
| | Neonatal and Paediatric Pharmacy Group | [No comment]. | - |
| | Action Duchenne | Evaluating the clinical and cost effectiveness of givinostat for Duchenne muscular dystrophy (DMD) through a single technology appraisal (STA) seems appropriate given the significance of the condition and the potential impact of the treatment on patient outcomes and healthcare resources. Given the lack of widely accepted standard treatments for DMD beyond Translarna, which is also under review, it's crucial to evaluate the efficacy and cost-effectiveness of emerging therapies like givinostat. An STA would provide a structured framework for assessing the evidence and making recommendations for its use within the NHS. Additionally, when looking at long-term effects and optimal dosing regimen, NICE should carefully assess caregiver opinions on quality of life benefits quantitatively. | Thank you for your comment. The scope has been updated to include quality of life outcome for caregivers. |

| Section | Stakeholder | Comments [sic] | Action |
|---|---|---|---|
| | | Duchenne muscular dystrophy (DMD) is a rare condition with a profound impact on quality of life, and it's crucial to ensure that the evaluation isn't hindered by the limited evidence from smaller population numbers. | |
| | Duchenne UK | We believe that a complex disease like DMD should be considered through the Highly Specialised Technology (HST) route to be fairly assessed.<br><br>Duchenne muscular dystrophy (DMD) is a rare disease, with approximately 2500 people in the UK affected by the condition. While routing criteria 1 and 2 may exclude givinostat from HST, NICE is explicitly allowed flexibility in both criteria.<br><br>The complex and paediatric nature of DMD means that there are many uncertainties and inevitable gaps in the data which have to handled flexibly, and HST has a better ability to tackle those uncertainties than STA, which is the standard route that treatments for adults and the general population are considered through. | Thank you for your comment. After consideration, NICE concluded that givinostat does not meet the criteria for evaluation through the highly specialised technologies programme. This evaluation has been scheduled into the single technology appraisal work programme. |
| | Genetic Alliance UK | Duchenne muscular dystrophy (DMD) is a rare condition that can have a significant impact on quality of life. As this technology has been routed through an STA rather than an HST pathway, it’s important that the appraisal is not disadvantaged by the evidence constraints of smaller population numbers. | Thank you for your comment. If appropriate, the committee may take into account relevant considerations regarding the population size in its deliberations. |

| Section | Stakeholder | Comments [sic] | Action |
|---|---|---|---|
| | Muscular Dystrophy UK | We think that this is an appropriate topic to evaluate and given the number of likely patients who could access the technology, the single technology appraisal route is appropriate. | Thank you for your comment. |
| Wording | ITF Pharma UK Ltd | ITF agree that the wording of the remit reflects the clinical and cost-effectiveness of givinostat for the treatment of DMD in people aged 6 years and over. | Thank you for your comment. |
| | Association of British Neurologists | Appropriate wording for lay person understanding. More information may be helpful to appreciate the burden of care associated with loss of independence in DMD in late adolescence and adulthood. | Thank you for your comment. The scope is intended to be a brief overview of the condition. The background has been updated to include a description of the impact of Duchenne muscular dystrophy on caregivers. |
| | British Society of Paediatric Endocrinology and Diabetes | Appropriate. | Thank you for your comment. |
| | Muscle interest group BPNA | Yes. | Thank you for your comment. |
| | Neonatal and Paediatric | [No comment]. | - |

| Section | Stakeholder | Comments [sic] | Action |
|---|---|---|---|
| | Pharmacy Group | | |
| | Action Duchenne | The wording of the remit appropriately reflects the issues of clinical and cost effectiveness that NICE should consider regarding givinostat for DMD. | Thank you for your comment. |
| | Duchenne UK | The wording is appropriate. | Thank you for your comment. |
| | Genetic Alliance UK | [No comment]. | - |
| | Muscular Dystrophy UK | The wording is appropriate. | Thank you for your comment. |
| Timing | ITF Pharma UK Ltd | DMD is a rare, progressive, lethal genetic neuromuscular disorder caused by the lack of dystrophin protein.[1,2] The lack of dystrophin leads to a series of pathological events, including muscle fibre injury, the activation of chronic inflammatory pathways, the impairment of muscle regeneration mechanisms, fibrogenesis and adipogenesis.[3–5]<br>DMD is associated with significant disease-related burden for patients, families and caregivers in terms of physical, health demands, logistical, emotional, psychological, and financial burden.[6–16] Given that DMD symptoms can present from two years old, from early childhood, children with DMD live their whole life with gradually increasing physical impairment and dependency on other people.[17] In the early stages, DMD symptoms include difficulty climbing stairs, walking and standing, resulting in frequent falls and a considerably greater risk of bone fractures.<br>Ultimately, the characteristic early progressive muscle injury results in loss of ambulation and impaired then lost upper limb function.[18–21] The physical burden of DMD is particularly substantial in non-ambulant patients due to a | Thank you for your comment. |

| Section | Stakeholder | Comments [sic] | Action |
|---|---|---|---|
| | | general lack of strength and fatigue. As individuals lose ambulation, their bones become weaker, further increasing the risk of fractures.[22,23] Muscle weakness can hamper chewing and swallowing, while cognitive impairment can lead to speech delay, problems with word finding and difficulty in fluent language production.[16] Once an individual has lost ambulation they will require mobility aids such as a scooter or specialist wheelchair that need to be accommodated in the home and school, and have to be adapted over time to the child's growth. At the point of wheelchair dependency, people with DMD experience a drastic decrease in independence, a reduction in normal daily living and an increased risk of additional comorbidities. These comorbidities include the more rapid progression of muscular contractures and scoliosis. Scoliosis specifically leads to the development of an asymmetry between a patient's hip and shoulder, detrimentally impacting their chest cavity size and positioning and ultimately leading to respiratory issues requiring surgery.[26] Independently, muscle weakening leads to impaired respiratory function, with an increased need for cough and ventilatory support. Life expectancy for people with DMD is in the order of 22–25 years.[27–29]<br><br>DMD progression significantly impacts a patient's quality of life and imposes a substantial financial burden on the healthcare system.[30–33] Lower levels of strength and slower rates of functional performance correlate with participation in fewer physical and social activities, which have a significant negative impact on quality of life.[30–32]<br><br>Most DMD patients are cared for on a day-to-day, long-term basis by a combination of informal caregivers (i.e., non-professional, paid or unpaid), family members and formal caregivers (paid). This includes emotional and social support and assistance with basic and instrumental activities of daily living (e.g., transfers to the wheelchair, preparing meals, cleaning, dressing, eating, and toileting).[13] | |

| Section | Stakeholder | Comments [sic] | Action |
|---|---|---|---|
| | | Caring for a person with DMD is time-consuming and has a severe negative impact on several aspects of daily living, requiring attendance at regular medical and related appointments and the associated travel, home adjustments, impact on parents' productivity, and processes to obtain reimbursement for various aspects of the child's care.[13,34] The burden for caregivers increases with disease progression, significantly impacting caregivers' overall quality of life, physical, emotional and mental well-being, as well as their employment status.[6,13,35] Caregivers report depression, stress, anxiety and feelings of isolation and exhaustion frequently.[36,37] Caregivers who work have a mean loss in work time and productivity, corresponding to more than 1 day of a 5-day working week.[35] Informal care and indirect costs together account for approximately 47% of the total costs of illness in the UK.[35]<br>While parental burden is high in DMD, the growing burden of disease progression on the family means that even siblings may be required to contribute to caregiving duties. This can lead to practical and psychological difficulties for the sibling, involving a negative impact on their social life (such as school performance and involvement in leisure activities) as well as a negative impact on their emotional wellbeing (such as being fearful, aggressive or withdrawn).[38]<br>In the absence of any disease-modifying treatment, there is an urgent unmet need for a new and effective therapy that demonstrates clinically meaningful improvements in outcomes for people with DMD compared with current established clinical management. | |
| | Association of British Neurologists | This drug represents access to disease modifying therapy in a broad group of patients with DMD who do not currently qualify for gene-specific therapies. In a disabling and life-threatening disease any option to improve outcome across the breath of the genotype is an urgent unmet need. | Thank you for your comment. |

| Section | Stakeholder | Comments [sic] | Action |
|---|---|---|---|
| | British Society of Paediatric Endocrinology and Diabetes | Urgently needed. | Thank you for your comment. |
| | Muscle interest group BPNA | It is of utmost urgency as we currently still do not have any effective treatments for DMD and this is a severe muscle wasting and life limiting condition. This drug is non-mutation specific so has good reach for many children with this condition and would need careful monitoring for safety and effectiveness. It would therefore need to be done in a neuromuscular specialist centre/northstar centre and appropriate resources for monitoring outcome measures and safety bloods. | Thank you for your comment. |
| | Neonatal and Paediatric Pharmacy Group | [No comment]. | - |
| | Action Duchenne | The relative urgency of this evaluation to the NHS is significant, given the severity and progressive nature of DMD and the limited treatment options currently available. Individuals with DMD face significant challenges in managing the condition, and there is an unmet need for effective therapies that can slow disease progression and improve outcomes. Therefore, expediting the evaluation process to provide timely guidance on the use of givinostat within the NHS would be beneficial for patients, caregivers, and healthcare providers alike. | Thank you for your comment. |
| | Duchenne UK | DMD is a disease which progresses quickly, with severe health and life impacts resulting from muscle wasting – such as the loss of ambulation and independent breathing. Any treatment which can slow this progression must | Thank you for your comment. |

| Section | Stakeholder | Comments [sic] | Action |
|---|---|---|---|
| | | be approved as quickly as possible, so patients can retain their muscle function before it is lost. | |
| | Genetic Alliance UK | Given the progressive nature of DMD, there may be families currently with no alternative treatment options therefore it would be beneficial to proceed with this appraisal without delay to potentially benefit as many families as possible. | Thank you for your comment. |
| | Muscular Dystrophy UK | There is an urgency to this evaluation, to ensure that givinostat can be accessed by patients as soon as possible given the progressive nature of the condition. There are currently no other non-steroidal technologies available for people living with DMD regardless of their genetic variant. | Thank you for your comment. |
| Additional comments on the draft remit | ITF Pharma UK Ltd | None. | Thank you for your comment. |
| | Association of British Neurologists | [No comment]. | - |
| | British Society of Paediatric Endocrinology and Diabetes | [No comment]. | - |
| | Muscle interest group BPNA | [No comment]. | - |
| | Neonatal and Paediatric | [No comment]. | - |

| Section | Stakeholder | Comments [sic] | Action |
|---|---|---|---|
| | Pharmacy Group | | |
| | Action Duchenne | [No comment]. | - |
| | Duchenne UK | We welcome the age bracket of this draft remit (ages 6 and over), as we believe that is a fair and accurate range, and note that it is the label approved by the FDA. | Thank you for your comment. |
| | Genetic Alliance UK | [No comment]. | - |
| | Muscular Dystrophy UK | [No comment]. | - |

**Comment 2: the draft scope**

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| Background information | ITF Pharma UK Ltd | ITF broadly agree that the background information is accurate and is complete in its description of the symptoms and consequences of disease progression faced by people with DMD. However, the background currently fails to recognise the significant burden faced by caregivers of people with DMD previously described.<br>Children usually present with DMD at approximately 3 years old, become non-ambulatory in their early teens and typically die before 30 years of age.[39–41] Therefore, unlike caregivers of children without DMD, caregivers of people with DMD face additional constraints and hidden costs that impact their health and financial well-being, extending long beyond the usual period of childhood | Thank you for your comment. The scope is intended to be a brief overview of the condition. The background has been updated to include a description of the impact of Duchenne |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | | dependency. As a result, caregivers of people with DMD have reported worse mental health, difficulty paying bills, and more hours missed from work than parents without a child diagnosed with DMD.[42] Providing caregiving support to people with DMD during their teenage years is considered to be the most challenging. DMD caregivers describe having to curtail their educational and professional ambitions and modify their homes to accommodate the disability associated with DMD.[42] As described above, the burden for caregivers increases with DMD progression, significantly impacting caregivers' overall quality of life, physical, emotional and mental well-being, as well as their employment status.[6,13,35]<br>The impact of DMD on families reaches beyond caregivers to siblings, the wider family and their local community as well. In addition to having to help with DMD caregiving, many siblings give up time with friends, sports or extracurricular activities and/or travel.[42] Support networks of extended family and trusted community members are essential in giving caregivers time to rest and recharge.[43,44] Attendance at school is important for children with DMD to enable them to make friends and learn important skills for their future. However, the most significant changes in a child's physical ability will occur during their primary school years, and the presence of additional learning needs and behavioural difficulties is common in children with DMD. Therefore, specialist support and adaptations or modifications to the classroom environment will be required to ensure children with DMD can reach their potential.[45,46]<br>In recognition of the significant wider societal burden of DMD, ITF request that text describing the burden on caregivers be added to the background. | muscular dystrophy on caregivers. |
| | Association of British Neurologists | Additional information on current survival in DMD in the UK with numbers receiving supportive and current standard of care would be desirable. Additional detail about the associated disability and burden of care and | Thank you for your comment. The background section is intended to give a brief |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | | support required for a highly disabled patient in adolescence and adulthood with this condition would alsobe appropriate. | overview of the condition and treatment pathway. |
| | British Society of Paediatric Endocrinology and Diabetes | Corticosteroid as disease modifying therapy is standard of care and used in the majority of young people with DMD. This is not mentioned. | Thank you for your comment. The scope states: “Interventions may include the use of steroids (associated with several side effects)…” |
| | Muscle interest group BPNA | Yes. | Thank you for your comment. |
| | Neonatal and Paediatric Pharmacy Group | [No comment]. | - |
| | Action Duchenne | The background information provided appears to be comprehensive and accurate. | Thank you for your comment. |
| | Duchenne UK | We have comments on a few areas of the background information:<br><br>1) "Initial symptoms of DMD usually present between the ages of 1 and 3 years”: there are symptoms of DMD from birth, but they usually only present to caregivers in subsequent years. Importantly, DMD can be diagnosed at birth by newborn screening. | Thank you for your comments. The background section has been updated to clarify that DMD symptoms can be diagnosed at birth. The background section is intended to |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | | 2) “After the age of 12 most children will need to use a wheelchair as their muscles weaken and they lose the ability to walk.”: Patients may become entirely dependent by the age of 12, but most boys use wheelchairs to some extent by 6-7 years of age.<br>3) “Most other treatment options do not treat the underlying cause”, to our knowledge, there are no approved treatments which treat the underlying cause. Only one treatment is approved in the UK (ataluren) and that is under review by the MHRA.<br>4) the treatments and support described are not available to all patients due to how care is managed differently across the UK. The difference in care management across the UK leads to different health outcomes for patients and their families. | give a brief overview of the condition and treatment pathway.<br>If appropriate, the committee may consider how care is managed across the NHS in its deliberations. |
| | Genetic Alliance UK | [No comment]. | - |
| | Muscular Dystrophy UK | The wording is appropriate. | Thank you for your comment. |
| Population | ITF Pharma UK Ltd | Yes, ITF agree that the description of the eligible population is defined appropriately. | Thank you for your comment. |
| | Association of British Neurologists | Yes – in accordance to the published evidence for this medication. | Thank you for your comment. |
| | British Society of Paediatric | Need comment from the neuromuscular clinicians and professional groups and patient organizations. | Thank you for your comment. |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | Endocrinology and Diabetes | | |
| | Muscle interest group BPNA | The DMD population is defined, this drug is essentially eligible for all mutation types. | Thank you for your comment. |
| | Neonatal and Paediatric Pharmacy Group | [No comment]. | - |
| | Action Duchenne | The population is appropriately defined as individuals with Duchenne muscular dystrophy (DMD) aged 6 years and older, consistent with the specified target population for givinostat outlined in the draft scope. However, it is suggested to encompass both ambulant and non-ambulant populations,and include upper muscle strength as a targeted area. | Thank you for your comment. The appraisal population includes both ambulant and non-ambulant people with Duchenne muscular dystrophy. |
| | Duchenne UK | Yes. | Thank you for your comment. |
| | Genetic Alliance UK | [No comment]. | - |
| | Muscular Dystrophy UK | The population is appropriate. | Thank you for your comment. |
| Subgroups | ITF Pharma UK Ltd | No, ITF does not believe that there are subgroups that should be considered separately. The appraisal population includes both people with DMD who are | Thank you for your comment. |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | | ambulant and non-ambulant. Data describing the efficacy of givinostat in ambulant boys is from EPIDYS. As described in Question 5 below, [redacted] boys were non-ambulant at baseline in Study 51. A new data cut of Study 51 has been performed ([redacted]) and is currently being analysed. Preliminary results from this data cut indicate that a [redacted] these data may provide further information on the efficacy of givinostat [redacted]. The manufacturer will provide outcomes for these patients in the submission. | |
| | Association of British Neurologists | The point of difference of this medication compared to the comparators listed is primarily that Ginivostat is not a genotype specific therapy and therefore should be applicable across the full spectrum of the disease, rather than niche populations. It therefore will apply widely but particularly for those not eligible for genotype-specific therapies.<br><br>However, there are limitations in that a significant proportion of patients with DMD cannot tolerate corticosteroid (standard care) and/or are difficult to include in clinical trials because of learning disbility/difficulties. This group often have worse functional, respiratory and cardiac outcomes. There is no evidence for potential benefit of this drug in this high-need subgroup because of their lack of involvement in trials and may be predicted to benefit equally or possibly more (because of their inability to tolerate corticosteroids). | Thank you for your comment. |
| | British Society of Paediatric Endocrinology and Diabetes | Subgroups have not been suggested but perhaps this should be clarified.<br>Is this to be considered as an addition to corticosteroid therapy or those who are not treated with corticosteroid or both groups? Need comment from neuromuscular clinicians and the relevant professional groups; and patient organizations. | Thank you for your comment. The technology will be evaluated in line with its marketing authorisation. |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | Muscle interest group BPNA | There may be more emphasis on the ambulant, younger boys as they will potentially have more benefit, but if it can prevent or slow down upper limb and arm function deterioration in non-ambulant boys then this also improves independence and ultimately quality of life. | Thank you for your comment. |
| | Neonatal and Paediatric Pharmacy Group | [No comment]. | - |
| | Action Duchenne | While the draft scope mentions specific age groups (e.g., children aged 4 to 7 years who can walk), it does not explicitly identify other potential subgroups within the population - older boys with Duchenne. However, considering the heterogeneity of DMD presentation and progression, further exploration of potential subgroups based on factors such as disease severity, genotype, or ambulatory status may be warranted. | Thank you for your comment. The background section of the scope is intended to provide a broad overview of the condition. If evidence allows, consideration may be given to relevant subgroups. |
| | Duchenne UK | The population (people with DMD) is defined appropriately. | Thank you for your comment. |
| | Genetic Alliance UK | [No comment]. | - |
| | Muscular Dystrophy UK | We do not consider that there are subgroups in which the technology is expected to be more clinically or cost effective. | Thank you for your comment. |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| Comparators | ITF Pharma UK Ltd | ITF agree that established clinical management (typically glucocorticosteroids and best support care) is the most appropriate comparator to givinostat for the treatment of DMD in people aged 6 years and over.<br>ITF note that the European Medicines Agency (EMA) confirmed the Committee on Medicinal Products for Human Use (CHMP) recommendation for non-renewal of the conditional marketing authorisation for ataluren for DMD in January 2024.[47] The CHMP made this recommendation after re-examination of data from a study carried out after its conditional approval identified that treatment with ataluren "failed to show the medicine was effective in patients with a progressive decline in their ability to walk."[47] ITF is not aware of any information in the public domain about a reappraisal of ataluren by the Medicines and Healthcare Regulatory Agency (MHRA) but considers that the use of ataluren as part of routine NHS clinical practice for the treatment of DMD may become uncertain during the course of the appraisal of givinostat.<br>ITF would, however, like to request the removal of delandistrogene moxeparvovec as a comparator for the following reasons.<br>• The NICE methods guidance stipulates that the identified comparators are established practice in the NHS.[48] However, delandistrogene moxeparvovec does not yet have a GB marketing authorisation and is not an established therapy in NHS practice for the treatment of DMD.<br>• Further, while the wording of any potential GB marketing authorisation for delandistrogene moxeparvovec for the treatment of DMD is unknown, ITF consider the US label wording to be a useful proxy for any future GB indication. The current FDA label for delandistrogene moxeparvovec restricts its use to children aged 4 to 5 years of age,[49] which is not consistent with the population specified in the givinostat scope (for children 6 years of age and older). Therefore, the age group in which delandistrogene moxeparvovec is anticipated to be approved for use does | Thank you for your comment. The scope has been updated to remove delandistrogene moxeparvovec as a comparator because its publication date is to be confirmed. |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | | not overlap with the expected indication for givinostat in DMD based on the inclusion criteria for the EPIDYS study.<br>Consequently, ITF does not believe that delandistrogene moxeparvovec is a relevant comparator and requests that NICE considers its removal from the appraisal scope. | |
| | Association of British Neurologists | No, not fully. It is important to include a non-corticosteroid comparator group as up to 30% of DMD patients cannot tolerate corticosteroids for bone health, endocrine or behavioural/ psychiatric reasons.<br>Standard of care subsets should include:<br>• Supportive care only<br>• Supportive care plus corticosteroids<br>This would better represent real life clinical practice in the UK and NHS. | Thank you for your comment. The comparators listed in the scope aim to be inclusive. The rationale for excluding any comparators from the evidence submission will be considered by the appraisal committee. |
| | British Society of Paediatric Endocrinology and Diabetes | Ataluren is only used in those with nonsense mutation (only about 10% of those with DMD).<br>Comparator need to be better defined; as mentioned a large proportion are treated with corticosteroids. | Thank you for your comment. The comparators listed in the scope aim to be inclusive. The rationale for excluding any comparators from the evidence submission will be considered by the appraisal committee. |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | Muscle interest group BPNA | Yes, comparators are listed but as Atalaren is only for a subset of DMD it is unfortunately not a true comparator.<br>Apart from steroids there is no drug used as per standard of care that compares with Givinostat. | Thank you for your comment. The comparators listed in the scope aim to be inclusive. The rationale for excluding any comparators from the evidence submission will be considered by the appraisal committee. |
| | Neonatal and Paediatric Pharmacy Group | Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.<br><br>Response:<br>*For givinostat we are only aware of the Epidys study which was a comparison against placebo in ambulant patient >6 years of age, and also a study vs placebo in non-ambulant patients 9 -18 years ago.*<br>*This makes assessment difficult when in practice, a patient may well be on other medications*. | Thank you for your comment. |
| | Action Duchenne | The comparators mentioned in the draft scope are Translarna and gene therapy. Gene therapy, which targets the underlying genetic cause of a condition, is not yet approved in the UK and is undergoing the drug appraisal process. Given that Duchenne muscular dystrophy (DMD) lacks widely accepted standard treatments beyond Translarna, which is also under review by the MHRA, it's crucial to ensure that the comparators listed in the appraisal process accurately reflect the available options for managing the condition. | Thank you for your comment. The scope has been updated to remove delandistrogene moxeparvovec as a comparator because its publication date is to be confirmed. The |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | | This comprehensive approach will enable an accurate assessment of givinostat's efficacy and provide valuable insights for clinical decision-making.<br>Access to multiple treatments in Duchenne muscular dystrophy (DMD) is of paramount importance due to the complex nature of the condition and the significant variability in symptoms and disease progression among patients. With DMD being a rare and progressive genetic disorder, having a range of treatment options available is crucial for addressing the diverse needs of individuals affected by the disease. | comparators listed in the scope aim to be inclusive. The rationale for excluding any comparators from the evidence submission will be considered by the appraisal committee. |
| | Duchenne UK | We have concerns over the use of ataluren/Translarna as a comparator. Ataluren has been recently withdrawn from the EU by the EMA, and is currently under review by the MHRA. In addition,<br><br>Similarly, delandistrogene moxeparvovec has not yet been assessed by NICE, and is not widely available.<br><br>The ability for the committee to fairly compare givinostat to these two treatments is restricted, and we believe that the comparator the committee use should be best standard of care with corticosteroids. | Thank you for your comment. The scope has been updated to remove delandistrogene moxeparvovec as a comparator because its publication date is to be confirmed. The comparators listed in the scope aim to be inclusive. The rationale for excluding any comparators from the evidence submission will be considered by the appraisal committee. |
| | Genetic Alliance UK | One of the comparators stated in the draft scope is subject to a NICE evaluation, it is therefore not widely available and as far as we understand, the definition of a comparator is a technology that is routinely used in the | Thank you for your comment. The scope |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | | NHS, therefore we have concerns that this comparator appears to be outside of the usual definition of a comparator. In addition, this comparator is a gene therapy that is used to address the underlying cause of a specific subgroup of DMD whereas Givinostat aims to manage some of the symptoms, therefore it is not a direct comparator.<br><br>We understand that there may be circumstances that are appropriate to use technologies that are currently being assessed by NICE as a comparator but we would appreciate an overview of how decisions about expanding the definition of a comparator are made, and a discussion with the patient community as to the potential risks and benefits of using comparators outside of the definition and when it may be appropriate to do so. Otherwise, we fear this may lead to an inconsistency and inequality between appraisals.<br><br>Ataluren is another comparator listed in the draft scope. It is important to note that Ataluren is only suitable for a small subgroup of people with DMD whereas Givinostat would be available to a broader group of people as it's more inclusive of younger age groups.<br><br>Additionally, having multiple treatment options for the same condition improves patient care and outcomes. Our current understanding as to why some people respond better to some medications than others is still developing therefore having multiple options means that patients can find the best treatment option for them. | has been updated to remove delandistrogene moxeparvovec as a comparator because its publication date is to be confirmed. The comparators listed in the scope aim to be inclusive. The rationale for excluding any comparators from the evidence submission will be considered by the appraisal committee. |
| | Muscular Dystrophy UK | The current standard of care with corticosteroids is an appropriate comparator. | Thank you for your comment. The scope has been updated to remove delandistrogene |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | | However, we are not convinced that other technologies would be appropriate comparators as they are addressing different aspects of the condition and are not 'like for like' treatments. For example, Delandistrogene moxeparvovec (subject to NICE evaluation) would not be a suitable standalone comparator as this technology aims to deliver a shortened version of the DMD gene to muscle cells. As we understand it, the technology is not designed to target any existing pathology.<br><br>For the same reasons outlined above, we are not convinced that ataluren (for boys with a nonsense mutation) is an appropriate comparator. It should also be noted that only around 10 per cent of people with DMD have a nonsense mutation.<br><br>It is our experience that in other appraisals, technologies that have not received positive NICE guidance have not been included as comparators. | moxeparvovec as a comparator because its publication date is to be confirmed. The comparators listed in the scope aim to be inclusive. The rationale for excluding any comparators from the evidence submission will be considered by the appraisal committee. |
| Outcomes | ITF Pharma UK Ltd | ITF agree that the outcomes listed are appropriate and will capture the most important health-related benefits and harms of givinostat. However, ITF would like to ask that NICE expands the health-related quality of life outcome to specify "in patients and carers" as per previous and ongoing NICE technology appraisals in DMD.[50–53] | Thank you for your comment. The scope has been updated. |
| | Association of British Neurologists | The outcome listed are generally appropriate but disease specific scores as used in clinical trial setting should be included:<br>• Four step climb<br>• TTCLIMB<br>• NSAA<br>• TTSTAND | Thank you for your comment. The scope has been updated. |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | | • Time to rise<br>• 6minute walk<br>• MRC sum score | |
| | British Society of Paediatric Endocrinology and Diabetes | Appropriate but should define what is meant by endocrine function- in regards to endocrine function these could include growth (height), weight gain, fractures (long bone and vertebral fractures); in particular if Givinostat could reduce the use of corticosteroids information on hospital use (including hospital admission) for complications of corticosteroids could be useful to review but may not be available as yet and will depend on the scope of the approval sought. | Thank you for your comment. |
| | Muscle interest group BPNA | These are the main outcomes that we generally capture in clinic apart from QoL regularly and this should possibly be looked at to get more information. | Thank you for your comment. |
| | Neonatal and Paediatric Pharmacy Group | [No comment]. | - |
| | Action Duchenne | The outcomes listed encompass a broad range of measures relevant to the assessment of givinostat's clinical and cost effectiveness in treating DMD. These outcomes include parameters such as walking ability, muscle function, cardiac function, adverse effects, and health-related quality of life. Overall, the outcome measures appear appropriate and comprehensive in capturing the most important health-related benefits and harms associated with the technology. | Thank you for your comment. |
| | Duchenne UK | We agree with the existing list of comparators, though we would like two more areas to be considered: | Thank you for your comment. Although the EQ-5D measure captures elements of |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | | 1) we would like to see the inclusion of aspects of mental health for patients and carers included<br>2) care and care quality of life is excluded from the list of outcomes. This is an important area which should not be neglected by the committee, even if it is currently difficult to quantify. | mental health within its quality-of-life evaluations, we encourage stakeholders to provide further evidence regarding mental health outcomes and the effects on carers in their submissions. This supplementary information enhances understanding of the broader effects of the treatment on both people with Duchenne muscular dystrophy and their carers, ensuring a comprehensive evaluation of quality-of-life benefits.<br>The scope has been updated to include quality of life outcome for caregivers. |
| | Genetic Alliance UK | [No comment]. | - |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | Muscular Dystrophy UK | The outcomes are broadly OK although we were concerned to see that the health-related quality of life outcome did not specifically mention carers.<br><br>It is essential to include a quantitative evaluation of carer utility values in relation to Quality-of-Life benefits. We recognise that it is challenging to accurately capture the carer perspective in QoL measures. However, this is a vital aspect that must be accounted for as is the fact that there is often more than one carer affected by the condition in families who have children with DMD.<br><br>It is important to ensure that the mental health aspects within the health-related quality of life (for patients and carers) outcomes are explicitly reviewed. | Thank you for your comment. The scope has been updated to include quality of life outcome for carers.<br><br>Although the EQ-5D measure captures elements of mental health within its quality-of-life evaluations, we encourage the company to provide further evidence regarding mental health outcomes and the effects on carers in their submission. This supplementary information enhances our understanding of the broader effects of the treatment on both people with Duchenne muscular dystrophy and their carers, ensuring a comprehensive evaluation of quality-of-life benefits. |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| Equality | ITF Pharma UK Ltd | ITF is unaware of any potential impacts of the draft remit and scope on the equality of opportunity or discrimination against people with protected characteristics. | Thank you for your comment. |
| | Association of British Neurologists | Please see comments below regarding significant proportion of patient with DMD and learning or behavioural difficulties and their associated poor outcomes, limited access to comprehensive study and inclusion in novel therapeutic RCTs and impact on equity of care. | Thank you for your comment. The committee will consider any relevant equality issues when it makes its recommendations. |
| | British Society of Paediatric Endocrinology and Diabetes | [No comment]. | - |
| | Muscle interest group BPNA | [No comment]. | - |
| | Neonatal and Paediatric Pharmacy Group | [No comment]. | - |
| | Action Duchenne | It's crucial to highlight that the Duchenne population in the UK is very small due to the rare nature of the disease. Given this context, it's commendable that NICE is actively seeking feedback to ensure equality and inclusion in their evaluation process. | Thank you for your comment. |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | Duchenne UK | It is important to ensure that no patient has to travel excessive distances to receive the treatment given the level of disability that many will face. | Thank you for your comment. The committee will consider any relevant equality issues when it makes its recommendations. |
| | Genetic Alliance UK | [No comment]. | - |
| | Muscular Dystrophy UK | It is important to ensure that no patient has to travel excessive distances to receive the treatment bearing in mind that children with DMD experience varying levels of disability. | Thank you for your comment. The committee will consider any relevant equality issues when it makes its recommendations. |
| Other considerations | ITF Pharma UK Ltd | Beyond ITF's request for the significant caregiver burden of DMD to be reflected in the background information, there are no other considerations that ITF would like to raise at this time. | Thank you for your comment. The scope has been included to include a brief overview on the impact on caregivers. |
| | Association of British Neurologists | [No comment]. | - |
| | British Society of Paediatric | [No comment]. | - |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | Endocrinology and Diabetes | | |
| | Muscle interest group BPNA | [No comment]. | - |
| | Neonatal and Paediatric Pharmacy Group | [No comment]. | - |
| | Action Duchenne | N/A. | - |
| | Duchenne UK | [No comment]. | - |
| | Genetic Alliance UK | [No comment]. | - |
| | Muscular Dystrophy UK | We feel that a managed access programme should not be ruled out. | Thank you for your comment. The company can submit a managed access proposal. The committee will consider whether managed access is appropriate in line with the principles of the innovative medicines fund. |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| Questions for consultation | ITF Pharma UK Ltd | **1. Where do you consider givinostat will fit into the existing care pathway for DMD?**<br>Givinostat is intended as an add-on treatment to established clinical management (glucocorticosteroids and best supportive care) in boys aged 6 years and over, irrespective of the presence of a DMD genetic mutation.<br>As detailed in the section discussing comparators, ITF believe the inclusion of ataluren in routine clinical management may be at risk following any regulatory reappraisal by the MHRA. However, were it to remain a part of routine clinical care, ITF consider that givinostat would displace ataluren in boys aged 6 years and over with DMD who have a nonsense mutation in the dystrophin gene.<br><br>**2. Please select from the following, will givinostat be:**<br>A. Prescribed in primary care with routine follow-up in primary care<br>B. Prescribed in secondary care with routine following in primary care<br>**C. Prescribed in secondary care with routine follow-up in secondary care**<br>D. Other (please give details)<br>ITF consider that givinostat will be both prescribed and followed-up in secondary care as per option C.<br><br>**3. For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention**<br>ITF do not anticipate any difference in the setting for prescribing and routine follow-up for givinostat versus its comparators.<br><br>**4. Are there any subgroups that are appropriate to consider?** | Thank you for your comments. |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | | ITF do not consider there to be any subgroups that should be considered in the appraisal of givinostat.<br><br>**5. Would givinostat be a candidate for managed access?**<br>ITF anticipate that the evidence for givinostat from the completed Phase III EPIDYS trial and the ongoing open-label extension Study 51 in ambulant boys with DMD will enable NICE to recommend givinostat funding via routine commissioning.[54] In Study 51, [redacted] boys were non-ambulant at baseline. A new data cut of Study 51 has been performed ([redacted]) and is currently being analysed. Preliminary results from this data cut indicate that a [redacted] these data may provide further information on the efficacy of givinostat [redacted]. Outcomes for these boys will be detailed in the manufacturer's submission.<br>To further support the efficacy of givinostat in non-ambulant children with DMD, data generation is ongoing in the ULYSSES study.[54] Initial trial read-out for ULYSSES is anticipated in [redacted], beyond the timelines for this appraisal. While ITF will present some evidence from non-ambulant children in its evidence submission, it is anticipated to be associated with uncertainty around comparative clinical effectiveness due to low patient numbers. In this circumstance, ITF would look to explore with NICE whether givinostat would be a candidate for managed access via the Innovative Medicines Fund (IMF) in non-ambulant children.<br><br>**6. Do you consider that the use of givinostat can result in any potential substantial health related benefits that are unlikely to be captured in the QALY calculation? Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.** | |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | | ITF believe that givinostat can result in substantial qualitative benefits that extend beyond people with DMD and their caregivers to include siblings, the wider family, and their local community e.g., their school setting. ITF consider that these positive impacts are unlikely to be captured in the QALY calculation.<br><br>**7. NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:**<br>• **could exclude from full consideration any people with protected by the equality legislation who fall within the patient population for which givinostat will be licensed**<br>• **could lead to a recommendation that have a different impact on people protected by equality legislation than on the wider population, e.g., by making it more difficult in practice for a specific group to access the technology**<br>• **could have an adverse impact on people with particular disability or disabilities**<br>**Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.**<br>As described above, ITF is unaware of any potential impacts of the draft remit and scope on the equality of opportunity or discrimination against people with protected characteristics. | |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | Association of British Neurologists | Where do you consider givinostat will fit into the existing care pathway for Duchenne muscular dystrophy?<br><br>Please select from the following, will givinostat be:<br>A. Prescribed in primary care with routine follow-up in primary care<br>B. Prescribed in secondary care with routine follow-up in primary care<br>C. **Prescribed in secondary care with routine follow-up in secondary care**<br>D. Other (please give details):<br>For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.<br>**The diagnosis and management of patients with DMD should take part in a secondary care setting with appropriately skilled clinicians and AHP support. Any intervention in this setting requires appropriate clinical follow up and should involve similar and <u>disease appropriate outcome measures</u> including:**<br>• **NSAA: North Star Ambulatory assessment**<br>• **Time to stand**<br>• **Time to climb/ time to rise**<br>• **6min walk test (where applicable)**<br>• **Cardiac and respiratory function (as per standard of care)**<br>• **Tolerance, compliance and safety observations should accompany efficacy follow-up in a similar manner to comparators**<br><br>Are there any subgroups that are appropriate to consider?<br>**Although Ginivostat does not limit access to treatment according to specific dystrophin genetic states (as per Ataluran: dystrophin missense mutations and Delandistrogene moxepavovec: exon 8 or 9 deletions), the RCT restricted its use to patients already on standard of care corticosteroid therapy. As significant proportions of DMD patients** | Thank you for your comments. The committee will consider any relevant equality issues when it makes its recommendations. |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | | **do not tolerate corticosteroids because of behavioural issues intrinsic to the disease itself it is unfortunate that this important subgroup of patients may not have access to this ginivostat if approval is granted entirely related to the confines of the trial.**<br>Would givinostat be a candidate for managed access?<br>**Yes. There is an urgent unmet clinical need to treat or at least modify progression of this disabling and lethal disease. In particular in those who do not meet genetic criteria for Ataluran or (potentially) mini-dystrophin therapies under consideration currently.**<br>Do you consider that the use of givinostat can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?<br>**In the RCT (Mercuri et al., Lancet Neurol., 2024) a significant STE (Standardised trial effect) was found in four step climb, NSAA, cumulative loss of function scores suggesting some impact on function and mobility at 72 weeks compared to the placebo group. It is not clear whether these changes will be detectable as substantial health-related benefits in the QALY calculation. Actual changes were small, potentially difficult to detect over the course of a year in a slowly progressive condition with variable phenotypes.**<br>**Of note, objective measurements such as time to rise, KE and EF muscle strengths did not show a significant STE over the time period of the phase 2/3 study.**<br>**It is likely that longer term follow up will be required to appreciate impact on time to loss of ambulation, time to loss of independent upper limb function, time to ventilatory support and overall survival.** | |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | | Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.<br><br>**Best available data providing information on natural history of DMD is available via international databases: CINRG Cooperative International Neuromuscular Research Group Duchenne Natural History Study (DNHS) or the North Star Project: UK North Star Clinical Network and Muscular Dystrophy UK for NHS relevant data.**<br><br>**This will need to be compared with OLE data from the Ginivostat trial, extrapolation from short term outcome data is unlikely to be accurate.**<br><br>NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:<br>• could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which givinostat will be licensed;<br><br>• could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;<br><br>• could have any adverse impact on people with a particular disability or disabilities. | |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | | **Careful consideration should be given to the significant proportion of patients with DMD who have learning difficulties, ADHD, autism and pre-existing psychiatric difficulties which make up around 30% of the adult/ adolescent population. These individuals are unlikely to tolerate standard of care corticosteroid treatment in whom there are worse cardiac outcomes and earlier, greater ventilatory needs (Pietrusz et al., 2023, Neuromuscular Disorders. Vol 33, Supp 1, pS106-107). Since the evidence for Ginivostat is based on its addition to standard of care corticosteroid therapy, this cohort will be excluded from access to this drug based on NICE evaluation requirements. This group of patients are particularly difficult to include in comprehensive studies because of cognitive and behavioural impairments which increases their inequality of access to care (L. Nart et al., Neuromuscular Disorders 2024; 35:13-18).**<br><br>Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.<br><br>**Real life clinical data on health care practice in DMD patients from UK specialist centres will provide information on proportions of patients who qualify for and tolerate existing disease modifying therapies (gene specific therapy and standard of care with corticosteroids) and the discrepancy in learning needs in the subsets with impact on functional, motor, cardiac and respiratory outcomes and survival.** | |
| | British Society of Paediatric Endocrinology and Diabetes | [No comment]. | - |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | Muscle interest group BPNA | [No comment]. | - |
| | Neonatal and Paediatric Pharmacy Group | Where do you consider givinostat will fit into the existing care pathway for Duchenne muscular dystrophy?<br>Please select from the following, will givinostat be:<br>A. Prescribed in primary care with routine follow-up in primary care<br>B. Prescribed in secondary care with routine follow-up in primary care<br>C. Prescribed in secondary care with routine follow-up in secondary care<br><br>Response:<br>Prescribed in secondary care with routine follow-up in secondary care –<br>*This would be appropriate with prescribing under a specialist service via homecare, ideally as patients may be geographically distanced from the specialist centre.*<br><br>Would givinostat be a candidate for managed access*?*<br><br>Response:<br>*Yes – this would allow further assessment of efficacy, potential medium term side effect profile and place in therapy. Resource costs for staff to collect relevant data on Northstar database should be included in evaluation of a managed access scheme. Place in therapy needs to be considered – would patients with nonsense mutation and on Alaluren stop their Ataluren or would this be added to treatment. Need to consider where delandistrogene moxeparvovec fits into the pathway (? 4-7 years of age) which is currently under NICE review.* | Thank you for your comments. |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | | Do you consider that the use of givinostat can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?<br><br>Response:<br>*Outcomes being assessed are appropriate.* | |
| | Action Duchenne | N/A. | - |
| | Duchenne UK | **Please select from the following, will givinostat be:**<br>**A. Prescribed in primary care with routine follow-up in primary care**<br>**B. Prescribed in secondary care with routine follow-up in primary care**<br>**C. Prescribed in secondary care with routine follow-up in secondary care**<br>**D. Other (please give details):**<br><br>From our understanding, B & C could apply to givinostat. We believe that once started, blood platelet count needs to be monitored for the first 12 weeks.<br><br>**For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.** | Thank you for your comments. |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | | Givinostat is an oral suspension taken twice a day. Therefore the proposed comparator delandistrogene moxeparvovec would be very different for prescribing and follow up. However, the proposed comparator ataluren is also taken orally, and could be more similar, but we detail the problems with using ataluren as a comparator above. | |
| | Genetic Alliance UK | [No comment]. | - |
| | Muscular Dystrophy UK | No additional comments to make here. | Thank you for your comment. |
| Additional comments on the draft scope | ITF Pharma UK Ltd | **Provisional stakeholder list:**<br>ITF agree with the provisional stakeholder list suggested by NICE and have no additions to recommend.<br>In recognition of the rarity of DMD and the necessary transition of care from paediatric to adult services over the life course of people with DMD, ITF would like to request that the NICE committee includes both clinicians who provide care to adults with DMD as well as those who provide care to children. Ideally, clinicians should have prior experience using givinostat. Further, as physiotherapy is essential to the management of DMD, ITF would like to request that a physiotherapist with experience in caring for children and/or adults with DMD should also be included in the NICE committee.<br>**Remit:**<br>Yes, ITF agree that the wording of the remit reflects the proposed marketing authorisation. | Thank you for your comments. Consultees are invited to nominate experts, who can provide written evidence, clarify issues about the evidence base and participate in committee meetings. |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | | **Current or proposed marketing authorisation**:<br><br>N/A. Givinostat is not approved in any other indication in the UK.<br><br>The proposed MHRA label is: [redacted]<br><br>Regulatory process: [redacted]<br><br>Target date for regulatory submission: [redacted]<br><br>Anticipated date of CHMP positive opinion (if applicable): [redacted]<br><br>Anticipated date of EU regulatory approval: [redacted]<br><br>Anticipated date of UK regulatory approval if different to Europe: [redacted]<br><br>Anticipated date of UK launch: [redacted]<br><br>[redacted]<br><br>[redacted]<br><br>**Economic model software:**<br><br>ITF will submit the cost-effectiveness and budget impact analysis in Microsoft Excel. | |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | Association of British Neurologists | Comments on the provisional stakeholder list:<br>In the consultee box, the stakeholders are appropriate except for the list of Others: these represent individual hospitals/ trusts or departments who should already be represented via the national organisations such as the Association of British Neurologists via it's neuromuscular advisory group. Therefore the listing of the following is superfluous.<br>• Alder Hey Children's Hospital NHS Foundation Trust, Liverpool<br>• Bristol Royal Hospital for Children, Bristol<br>• Department of Health and Social Care<br>• Dubowitz Neuromuscular Centre (DNC)<br>• MD UK Oxford Neuromuscular Centre, Oxford<br>• MRC Centre for Neuromuscular Diseases<br>• NHS England<br>• Queen Square Centre for Neuromuscular Diseases UCL<br>• Robert Jones and Agnes Hunt Orthopaedic Hospital, Oswestry<br>• Royal Manchester Children's Hospital NHS Foundation Trust, Manchester<br>• Ryegate Centre, Sheffield Children's NHS Foundation Trust, Sheffield<br>• The Addenbrooke's Neuromuscular Service, Cambridge<br>• The John Walton Muscular Dystrophy Research Centre, Newcastle<br>• The National Hospital for Neurology and Neurosurgery, London<br>• The Walton Centre, Liverpool<br>• Wessex Neurological Centre, Southampton General Hospital, Southampton | Thank you for your comment. The stakeholder list is intended to be broad and inclusive of all possible stakeholders. |
| | British Society of Paediatric Endocrinology and Diabetes | [No comment]. | - |

| Section | Consultee/ Commentator | Comments [sic] | Action |
|---|---|---|---|
| | Muscle interest group BPNA | Givinostat would be a drug that could be offered to patients with DMD non-mutation specific. It would be appropriate for this to be prescribed and monitored in specialist neuromuscular centres and part of a managed access agreement or similar to capture data in the real world out of a trial setting. | Thank you for your comment. |
| | Neonatal and Paediatric Pharmacy Group | [No comment]. | - |
| | Action Duchenne | N/A.<br>The provisional stakeholder list reflects NICE's commitment to inclusivity and transparency in stakeholder engagement. | Thank you for your comment. |
| | Duchenne UK | [No comment]. | - |
| | Genetic Alliance UK | [No comment]. | - |
| | Muscular Dystrophy UK | [No comment]. | - |

**The following stakeholders indicated that they had no comments on the draft remit and/or the draft scope**

N/A