NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Evaluation consultation document

Ataluren for treating Duchenne muscular dystrophy with a nonsense mutation in the dystrophin gene (review of HST3)

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using ataluren in the context of national commissioning by NHS England. The highly specialised technologies evaluation committee has considered the evidence submitted by the company and the views of non-company consultees and commentators, clinical experts, patient experts and NHS England.

This document has been prepared for consultation with the consultees. It summarises the evidence and views that have been considered, and sets out the draft recommendations made by the committee. NICE invites comments from the consultees and commentators for this evaluation and the public. This document should be read along with the evidence (see the committee papers).

The evaluation committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of the criteria considered by the committee, and the clinical and economic considerations reasonable interpretations of the evidence?
- Are the provisional recommendations sound and a suitable basis for guidance on the use of ataluren in the context of national commissioning by NHS England?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, sex, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

Issue date: September 2022

Note that this document is not NICE's final guidance on this technology. The recommendations in section 1 may change after consultation.

After consultation:

- The evaluation committee will meet again to consider the evidence, this evaluation consultation document and comments from the consultees.
- At that meeting, the committee will also consider comments made by people who are not consultees.
- After considering these comments, the committee will prepare the final evaluation document.
- Subject to any appeal by consultees, the final evaluation document may be used as the basis for NICE's guidance on using ataluren in the context of national commissioning by NHS England.

For further details, see the interim process and methods of the highly specialised technologies programme.

The key dates for this evaluation are:

Closing date for comments: 21st October 2022

Second evaluation committee meeting: 15th December 2022

Details of membership of the evaluation committee are given in section 5

1 Recommendations

1.1 Ataluren is not recommended, within its marketing authorisation, for treating Duchenne muscular dystrophy resulting from a nonsense mutation in the dystrophin gene in people 2 years and over who can walk.

1.2 This recommendation is not intended to affect treatment with ataluren that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue until they and their NHS clinician consider it appropriate to stop. This decision should be made jointly by the clinician, the child or young person, and their parents or carers.

Why the committee made these recommendations

This guidance reviews the evidence for ataluren for treating Duchenne muscular dystrophy with a nonsense mutation in the dystrophin gene. It includes new real-world evidence (evidence collected outside clinical trials) on ataluren and evidence collected as part of the managed access agreement for NICE highly specialised technologies guidance 3.

Duchenne muscular dystrophy, with a nonsense mutation in the dystrophic gene, is a rare and progressive condition. Over time it causes muscle weakness resulting in the loss of the ability to walk and reductions in respiratory ability, and it significantly reduces life expectancy. Current treatment options are limited.

The company used an indirect treatment comparison of ataluren compared with best supportive care based on 2 real-world evidence studies to estimate treatment benefits. The company did not use data from the managed access agreement in its economic model because it believed it did not provide the most appropriate outcome measures. The evidence provided, along with feedback from clinicians and patients, suggests that ataluren is likely to slow down disease progression and delay the time at which the ability to walk is lost.

Evidence for improvements in later stages of the disease and improved survival with ataluren is limited and highly uncertain but ataluren may also improve outcomes once the ability to walk has been lost.

The cost-effectiveness estimates are uncertain because of how treatment benefits were estimated and the limitations of the clinical effectiveness data. There is uncertainty around the estimated costs of ataluren in the company's model. The way that caregivers' quality of life was included in the model was not realistic so this was considered qualitatively. If the committee's preferred assumptions are used, the cost-effectiveness estimates for ataluren are substantially above the range that NICE considers acceptable for highly specialised technologies. Therefore, ataluren is not recommended.

2 Information about ataluren

Marketing authorisation indication

2.1 Ataluren (Translarna, PTC Therapeutics) has a conditional marketing authorisation for 'the treatment of Duchenne muscular dystrophy resulting from a nonsense mutation in the dystrophin gene, in ambulatory patients aged 2 years and older'.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics.

Price

2.3 The price for ataluren is £2,532 per box of thirty 125 mg sachets, £5,064 per box of thirty 250 mg sachets and £20,256 per box of thirty 1,000 mg sachets (excluding VAT; BNF online accessed September 2022).

The company has a commercial arrangement, which would have applied if the technology had been recommended.

3 Committee discussion

The evaluation committee considered evidence submitted by PTC Therapeutics, the views of people with the condition, those who represent them and clinical experts, NHS England and a review by the external assessment group (EAG). See the committee papers for full details of the evidence. In forming the recommendations, the committee took into account the full range of factors that might affect its decision, including in particular the nature of the condition, the clinical effectiveness, value for money and the impact beyond direct health benefits.

Nature of the condition

Duchenne muscular dystrophy with a nonsense mutation in the dystrophin gene

3.1 Duchenne muscular dystrophy (DMD) is a severe, progressive X-linked recessive disorder that mainly affects males. DMD with a nonsense mutation is caused by a single base variation in a person's DNA, which leads to incomplete dystrophin production in the skeletal, smooth and cardiac muscle fibres. Dystrophin production is usually affected from birth and symptoms of DMD often appear by age 3 years. The main symptom of DMD is motor dysfunction but, as the disease progresses, the gastrointestinal tract and vital organs such as the heart are affected. People with DMD have a decline in physical functioning, with subsequent respiratory and cardiac failure that leads to death, usually before the age of 30.

Impact of the condition on people with DMD and their families

3.2 The committee considered the submissions from patient organisations and patient experts. The patient experts explained that DMD significantly affected people with the condition and their caregivers. Their submissions outlined that the condition limits the types of activities people with DMD

can do, and puts strains on maintaining friendships. The patient experts highlighted the psychological impact of losing the ability to walk, and of the onset of respiratory symptoms. They said that ataluren provided hope to people with DMD and their caregivers because it slowed down disease progression and allowed caregivers more time to adjust to different stages of disease. They explained that people with DMD need assistance with everyday tasks, such as getting dressed and getting out of bed. They also described how caregiving becomes more challenging once someone stops being able to walk and the disease progresses. The patient experts said that delaying the loss of the ability to walk is very important to people with DMD and caregivers. Once this happens, maintaining upper limb function is valued highly because this means the person with DMD can still do some activities and tasks. And this reduces the impact on the caregiver to an extent. The committee concluded that DMD has a substantial impact on both patients and caregivers.

Clinical management

Managed access agreement

3.3 Ataluren has been available as a treatment option as part of a managed access agreement since the original NICE highly specialised technologies guidance for ataluren was published in 2016. The managed access agreement required data collection from people having treatment and their families. Before this, the only treatment option was best supportive care. Best supportive care for DMD includes treatment with corticosteroids, which is associated with a delay in the loss of walking but can have significant adverse effects. The clinical expert said that ataluren would not reduce the need for corticosteroids and would be given in addition. Other interventions include cardiac and respiratory monitoring and ventilation support, occasional inpatient orthopaedic intervention, spinal surgery and rehabilitation. Dietary advice (and, in some cases, gastric feeding), prevention and treatment of bone fragility, management of the

complications of long-term corticosteroid therapy, and psychosocial support may also be needed. Clinical care is provided by a range of healthcare professionals, depending on local services, including neurologists or paediatric neurologists and neuromuscular specialists, rehabilitation specialists, neurogeneticists, paediatricians and primary care physicians.

Clinical effectiveness

Data sources

3.4 The main evidence sources used by the company for this review came from 2 real-world studies: The Strategic Targeting of Registries and International Database of Excellence (STRIDE) study, which included people who had DMD caused by a nonsense mutation in the dystrophic gene, were aged 2 and over, and had received ataluren. This study was carried out mainly in Europe. The Cooperative International Neuromuscular Research Group (CINRG) study is designed to capture the natural history of the disease in people with DMD who had best supportive care, and was mainly carried out in North America. In the original highly specialised technologies guidance, 2 randomised controlled trials comparing ataluren with placebo over 48 weeks formed the main evidence base (Study 007 and Study 020). The primary outcome measure in these trials was the 6-minute walk distance (6MWD). The clinical expert said that the 6MWD is not routinely collected in clinical practice in England. The patient experts said 6MWD matters less to them than other outcomes, for example stamina in undertaking certain tasks. The company explained that it preferred to use the real-world evidence studies because it collected data on loss of the ability to walk and on other relevant disease timepoints, which it believed was a more relevant set of outcome measures than the 6MWD. It also noted that the real-world evidence sources provided longer-term data than the clinical trials. The committee was aware that ataluren has been available as a treatment

option as part of a managed access agreement and that at the time of the original guidance it had been expected that this data would inform the present review. The managed access agreement collected data from people having treatment and their caregivers. The company explained that it did not use data from the managed access agreement in its economic model because the primary outcome measure used was the NorthStar Ambulatory Assessment (NSAA). It outlined that the scores using this outcome measure generally improve up to 7 years of age in people with DMD because of usual child development, which made it difficult to show a significant treatment effect for ataluren for patients in the NHS. It also noted that the age at first symptom had not been collected. This is an important prognostic factor and its absence made matching with sources of natural history data difficult. The committee agreed to consider the data from STRIDE and CINRG for this review but also took into account the findings of the managed access agreement.

Indirect treatment comparison

3.5 The company used propensity score matching to indirectly compare the clinical effectiveness of ataluren with best supportive care because STRIDE and CINRG did not include a comparison of ataluren against best supportive care. In the company's base case, this involved matching patients in STRIDE to those in CINRG based on prognostic factors. The company used 4 prognostic factors in its matching (age at first symptoms, age at first corticosteroid use, duration of deflazacort, and other steroid use). The EAG said that it considered the company's matching methodology to be appropriate but noted some limitations. For example, there were some imbalances between the groups, which, along with methodological limitations, may have affected the results. It was also not clear if the different locations of the 2 studies might affect the results (see section 3.4). The EAG considered that these limitations added to the uncertainty of this comparison. The company's indirect comparison

showed that ataluren delayed the median time to the loss of the ability to walk by a median of 5.4 years compared with best supportive care (17.9 years compared with 12.5 years, p<0.0001). This comparison also estimated a delay in reaching a forced vital capacity (FVC) of less than 50%, but this result was not statistically significant. The company said that the STRIDE data was not mature enough to estimate outcomes at later disease time points of respiratory function or survival (see section 3.4). The company also provided 2 more indirect comparisons for ataluren compared with best supportive care. This included one that matched people in the managed access agreement data to those in the NorthStar registry (a natural history study of people with DMD having best supportive care in the UK). The company said this comparison was limited by the use of the NSAA outcome measure and because of difficulties in matching (see section 3.4). The company believed that this was why this indirect treatment comparison failed to show meaningful differences in outcomes. The company also provided an indirect comparison between Study 019 (a long-term follow-up study of people having ataluren) and CINRG, which the company provided to supplement its base case analysis. The EAG noted that the company's additional indirect comparisons provided less compelling evidence than the STRIDE and CINRG comparison, and said it had similar concerns over limitations in these 2 additional analyses. The committee acknowledged that ataluren is likely to slow down the progression of the disease, based on the results from the company's indirect treatment. The committee concluded that the STRIDE and CINRG indirect comparison was the most appropriate to use in decision making, but that its results were uncertain.

The company's economic model

Model based on ambulation status and FVC

3.6 In the previous evaluation of ataluren, the company developed a semi-Markov model. It had 6 health states, representing the progression of

DMD from the ambulatory phase (when the person can walk) to the non-ambulatory phases and death. In this previous model, transitions between health states used the results of the 6MWD from 2 randomised control trials of ataluren compared with placebo (Study 007 and Study 020). For the current review, the company presented a new economic model, which used partitioned survival models (see section 3.7) in each health state (ambulatory, non-ambulatory; FVC above 50%, below 50% and below 30%). The company explained that the health states in the new model corresponded to those defined in project HERCULES (a DMD natural history model) and better reflected the disease course than the model used in the original guidance. The company also said the model aligned well with outcomes included in the STRIDE and CINRG studies, which allowed use of longer-term data and avoided reliance on the 6MWD outcome (see section 3.4). The EAG noted that its clinical experts had said that in general the model structure was appropriate but that the model did not account for scoliosis, which had a substantial impact on quality of life. The committee agreed that the company's model structure was appropriate for decision making, but that data informing the model was limited, particularly at later disease stages. It also noted that scoliosis was not accounted for in the model structure.

Survival modelling

3.7 The company fitted standard parametric models to both STRIDE and CINRG data at each model timepoint (see section 3.6). The company in its original base case used log-logistic models to estimate the age at which people lose the ability to walk, and the age at which predicted FVC was less than 50%. It also applied a log-normal model to CINRG data to estimate the age at which predicted FVC was less than 30% for best supportive care. And it assumed a relative benefit for ataluren because there was no data available for this outcome in STRIDE (the amount of benefit is considered academic in confidence by the company and cannot

be shown here). The EAG assumed the same model selection for each health state as that in the company's original base case. However, it noted that the models selected did not appear to provide a good fit to the data for several of the modelled health states. The EAG also noted that the company had not considered more flexible models, which may have provided a better fit to the data. The company updated its base case after technical engagement to adopt a Weibull model for all health states, based on an EAG sensitivity analysis. The company considered that the cost-effectiveness analysis was relatively insensitive to the choice of standard parametric model, and therefore did not undertake analysis with a broader range of models. The committee considered that this was true for the company and EAG base case analyses but may not be the case if other assumptions in these analyses were changed. The EAG also highlighted that its clinical experts considered that the modelled health benefits (delays to loss of the ability to walk and in reaching respiratory milestones) estimated from the company's model appeared to be optimistic (the model also included additional benefits assumed to occur from starting treatment early; see section 3.8). The committee considered that the company's original base case model choices, as used in the EAG's base case analysis, were the most appropriate to use for decision making. However, it noted that the results were uncertain because of the poor fit of the models to the data.

Assumed additional early treatment benefits

3.8 The company assumed additional relative treatment benefits of ataluren compared with best supportive care because of the licence extension to allow use in people aged 2 years and over (previously this had been 5 years and over). The company based these assumptions on clinical expert input from a Delphi panel. It included the assumed additional benefits in the model by artificially shifting the ataluren survival curves to the right by an additional number of years. This increased the amount of

time spent in each health state (the number of additional years assumed in each health state is considered to be academic in confidence by the company and cannot be reported here). The company said that this was because earlier treatment would be associated with better outcomes compared with that estimated from the STRIDE and CINRG indirect comparison. The EAG noted that very few people had received ataluren in STRIDE before the age of 5 and that there was no other direct evidence to show that starting treatment early provided additional benefit. The committee was aware that the company's economic model assumed everyone would have treatment with ataluren at 2 years of age. They considered that this was inconsistent with published evidence and clinical expert opinion that most diagnoses of DMD in England are at around 4 years, and that there is currently no national screening programme for DMD. The committee therefore concluded that it would not include the additional assumed treatment benefits related to early treatment of ataluren in its preferred analysis.

Utility values

Treatment-dependent utilities

3.9 Health state utility values in the company and EAG base case analysis were assumed to depend on which treatment people were having. These values were taken from a DMD Delphi panel study (Landfeldt et al. 2020), which involved 6 Swedish neuromuscular experts who completed the Health Utility Index 3 (HUI3) questionnaire. Using this source resulted in utility values that were substantially higher for ataluren compared with best supportive care in each health state:

- ambulatory health state: ataluren 0.93, best supportive care 0.62
- non-ambulatory health states: ataluren 0.32, best supportive care 0.16.

The company said that it used treatment-dependent utility values

because they were supported by clinical experts and patient organisation submissions. It also explained that its economic model did not capture additional disease symptoms and benefits of ataluren. The committee noted that the Landfeldt et al. study was designed to ask experts to complete the HUI3 questionnaire for the ambulatory state based on 2 different descriptions of mobility (the 6MWD and assuming a mean age of 13), which reflected the trial results from Study 007 and Study 020 at 48 weeks. Therefore, the committee considered that the study did not reflect any utility benefits from ataluren in addition to those related to ambulation, but could simply reflect slowing of disease progression with ataluren. Study 007 and Study 020 showed a numerical increase in quality of life for people having ataluren compared with best supportive care at 48 weeks but these results were not statistically significant. The company said that this was likely because of the short duration of those trials and explained that changes in quality of life would take longer to show. The EAG noted that the company applied treatment-dependent utilities from the beginning of the model time horizon and applied them throughout the model, even when treatment with ataluren had been stopped. The EAG said its clinical experts had difficulty when commenting on the appropriateness of treatment-dependent utilities because of the limited evidence informing this. The EAG's clinical experts said that significant quality of life differences between treatments was unlikely in the ambulatory health state. One EAG expert said that ataluren may improve quality of life in non-ambulant health states because of a reduced risk of scoliosis. The clinical and patient experts said, in their response to technical engagement, that they believed it was appropriate to use treatment-dependent utilities because of the benefits of treatment with ataluren. The committee was aware that the company had not provided empirical evidence of quality of life differences from people having ataluren or best supportive care treatments. The clinical expert at the

committee meeting said that ataluren could reduce the risk of developing scoliosis and delay respiratory symptoms in non-ambulatory health states because it would allow muscle strength to be preserved for longer during puberty. The committee was aware that in the original guidance, the analysis did not include different utility values for ataluren compared with best supportive care within the same health state but did consider the impact of scoliosis on quality of life. The committee noted that the company's economic model for this review did not include the impact of scoliosis and therefore it is plausible that the health state utility may be higher in non-ambulatory health states for people having ataluren compared with best supportive care. The committee considered that the company had not provided robust evidence to support the use of treatment-dependent utility values in the ambulatory health state. The committee concluded that treatment-dependent utility values were not appropriate for the ambulatory health state but were plausible in the non-ambulatory health states.

Carer quality of life

3.10 The company assumed 2 caregivers in its analysis and used absolute values for caregivers' quality-adjusted life years (QALYs) from the Landfeldt et al. 2017 study. The company's approach estimated substantial incremental caregiver QALY gains for ataluren. The EAG highlighted that the approach taken by the company implicitly assumed that for caregivers, once the person they were caring for died, either the QALYs gained by caregivers were equal to zero, or these QALYs are not valued by society. The EAG therefore believed that this approach was inappropriate and in its base case used a carer disutility approach (which applied a disutility value to each health state). It said this was in line with methods used in previous highly specialised technologies evaluations in which caregivers' quality of life was included in the analysis. This included the previous evaluation of ataluren. The company noted that the EAG's

analysis resulted in a small reduction in QALYs for ataluren compared with best supportive care. This was because ataluren extended the time spent in each health state, which increased patient QALY values but also increased caregiver disutility over the lifetime of the company's model. The company believed that this was counterintuitive, because ataluren was estimated to provide a survival gain compared with best supportive care. The company updated its approach during technical engagement to apply caregiver QALYs until the median overall survival timepoint across both treatment groups in the model. It explained that this was an attempt to compensate for the potential overestimation of caregiver benefit in its original base case. The EAG considered that the company's updated approach was still inappropriate because it still did not value QALYs of caregivers once the person they were caring for had died. The committee acknowledged the testimonies of the patient experts, who outlined the benefits of ataluren treatment on caregivers (see section 3.2) and agreed that including caregiver quality of life within the economic model was challenging. The committee considered that the company's approach was not appropriate because it assumed that caregiver QALYs should equal zero in the economic model when the patient died. It also noted that there were apparent differences between the outcomes of the EAG approach and the testimonies of the patient experts in relation to QALY loss for caregivers. It therefore concluded that it would exclude estimated caregiver QALYs from its preferred analysis and instead would consider the impact on caregivers in its decision making in a qualitative way.

Stopping treatment

Rate of treatment discontinuation in the model

3.11 The company assumed that people would discontinue ataluren treatment by a constant rate based on data from STRIDE (the rate used is considered academic in confidence by the company and cannot be reported here). This rate was applied until the modelled formal treatment

stopping rule (see section 3.12). The EAG said the observed treatment discontinuation rate may have double counted the events that would be captured in the company's proposed stopping rule. It said that its clinical experts said that the rate used in the company's base case appeared implausibly high given the severity of the condition and lack of alternative treatment options. The EAG provided an analysis that reduced the discontinuation rate by 50% to explore the impact of this on cost effectiveness. It explained that changes to time on treatment only affected costs in the company's economic model and did not affect the estimated health outcomes. The committee concluded that the company's estimated discontinuation rate likely overestimated treatment discontinuation and therefore underestimated ataluren treatment costs. The committee preferred the EAG's scenario analysis, which reduced the discontinuation rate for decision making. But it noted that this reduction was arbitrary and added to the uncertainty.

Treatment stopping rule

3.12 In the managed access agreement, ataluren treatment was stopped no later than 6 months after the person with DMD was no longer able to walk. The committee was aware that wording had been removed from the summary of product characteristics for ataluren that said that there was no evidence ataluren had any efficacy once someone had lost the ability to walk. The company, in its base case, proposed extending the treatment stopping rule used in the managed access agreement to the point at which predicted FVC was less than 50%. It noted that this was the timepoint at which night-time ventilation was likely to be needed. However, the company and clinical experts highlighted that any stopping rule based on predicted FVC would be challenging because it was difficult to accurately measure the height (which is needed to assess FVC) of people with DMD who cannot walk. The EAG explained that STRIDE, which the company used to estimate ataluren's effectiveness (see section

3.4), did not impose a consistent stopping rule. Therefore, it was unclear how the treatment benefits estimated from STRIDE aligned with any stopping rule assumed in the company's economic model. The clinical expert said that clinicians would want to continue using ataluren after their patients lost the ability to walk because of the benefits in upper limb and respiratory function. The clinical and patient experts said that the decision to stop treatment should be taken after discussion between patients, caregivers and clinicians. The NHS England commissioning expert agreed with these experts' views. The committee noted that the company's economic model did not provide a scenario analysis for if there was no formal clinical stopping rule. It was also aware that changing the stopping rule scenarios in the company's economic model only affected total costs and did not change the estimated benefits. The committee agreed that it would not include a formal stopping rule in its preferred analysis, and that the decision to stop treatment would be taken after discussion between patients, caregivers, and clinicians. Because no scenario that reflected this situation was provided, for the purposes of cost-effectiveness modelling, the committee preferred to use the time when predicted FVC reached less than 30%. But it acknowledged that this may not align with how treatment is stopped in clinical practice.

QALY weighting

Criteria for applying a QALY weighting

3.13 The committee understood that NICE's interim process and methods of the highly specialised technologies programme (2017) specifies that a most plausible incremental cost-effectiveness ratio (ICER) of below £100,000 per QALY gained for a highly specialised technology is usually considered an effective use of NHS resources. For a most plausible ICER above £100,000 per QALY gained, judgements about the acceptability of the highly specialised technology as an effective use of NHS resources must take account of the size of the incremental therapeutic improvement.

This is shown by the number of additional QALYs gained and by applying a 'QALY weight'. The committee understood that a weight between 1 and 3 can be applied when the QALY gain is between 10 and 30 QALYs. It discussed the number of undiscounted QALYs in the analysis. It noted that these were 16.44 in the company's updated base case and 10.49 in the EAG's base case (11.65 when caregiver QALYs were excluded). The committee recalled that it considered treatment-dependent utility values were only appropriate for non-ambulatory states (see section 3.9). Using this assumption resulted in the estimated number of undiscounted QALYs being less than 10. The committee concluded that ataluren did not meet the criteria for applying a QALY weighting.

Cost-effectiveness estimates

Committee preferred assumptions

3.14 The company's base case analysis resulted in an ICER above £100,000 per QALY gained when applying the QALY weighting associated with the number of undiscounted QALYs (16.44) in the company's analysis (the exact ICER is considered confidential by the company and cannot be reported here). The committee recalled that this analysis did not account for its preferred assumptions:

- Assuming treatment-independent utility values for the ambulatory health state and treatment-dependent utility values for non-ambulatory health states (see section 3.9).
- Removing carer QALYs from the cost-effectiveness analysis and considering carer impacts qualitatively (see section 3.10 and 3.15).
- Removing early treatment effect benefits (see section 3.8).
- A lower treatment discontinuation rate for ataluren based on the EAG's sensitivity analysis (see section 3.11).
- Not imposing a defined treatment stopping rule; but for the cost-effectiveness analysis, costs in the model would be those if treatment is

stopped when predicted FVC is less than 30% (see section 3.12).

Taking these preferred assumptions into account resulted in an ICER substantially above £100,000 per QALY gained (the exact ICER is considered confidential by the company and cannot be reported here). The committee recalled that ataluren did not met the criteria for a QALY weighting (see section 3.13). It also noted the high levels of uncertainty in the evidence base for ataluren and in the economic modelling.

Impact of the technology beyond direct health benefits and on the delivery of the specialised service

Indirect benefits

3.15 The patient experts said that ataluren allowed people with DMD to have a more fulfilling life. They said it meant that education could be continued and friendships maintained. Patient expert submissions said that ataluren treatment might allow the parents of people with DMD to stay in employment for longer because it slows down disease progression and provides hope to carers and people with DMD. The committee had agreed to take a qualitative approach to considering the impact of ataluren treatment on caregivers. It also considered that it might be appropriate to view the benefits differently depending on the time in a child's life when they are gained, compared with best supportive care (that is, delaying loss of the ability to walk in childhood and adolescence). It noted that no empirical evidence was provided in relation to this aspect. The committee concluded that ataluren is likely to have a positive impact on people's lives beyond its direct health benefits.

Other factors

Equality issues

3.16 Some stakeholders said it was important that people with DMD did not have to travel excessive distances for treatment. The committee acknowledged that clinical expertise would usually be concentrated at a small number of centres. One stakeholder also said that the current managed access agreement stopping rules did not allow use in people who could not walk, and that this may discriminate against older DMD patients. The committee noted that it had not included a formal treatment stopping rule in its preferred assumptions. No other potential equality issues were identified by the committee.

Innovation

3.17 The clinical and patient experts said that ataluren is the first treatment licensed to treat DMD caused by a nonsense mutation in the dystrophin gene. They explained that ataluren's mechanism of action resulted in a step change in managing DMD caused by a mutation in the dystrophin gene. The committee concluded that ataluren was innovative.

Conclusion

Recommendation

3.18 The committee took into account its preferred assumptions (see section 3.14), indirect treatment benefits (see section 3.15), and other factors. It considered that the most plausible ICER was substantially above £100,000 per QALY gained (the exact ICER is considered confidential by the company and cannot be reported here). The committee concluded that ataluren was not cost effective compared with best supportive care, even when considering other factors such as the impact on caregivers' quality of life and the time in a child's life when benefits are gained. Therefore, it did not recommend ataluren for routine use in the NHS for

treating DMD resulting from a nonsense mutation in the dystrophin gene, in people 2 years and over who can walk.

Peter Jackson

Chair, highly specialised technologies evaluation committee

September 2022

4 Evaluation committee members and NICE project team

Evaluation committee members

The highly specialised technologies evaluation committee is a standing advisory committee of NICE.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered that there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of each evaluation committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each highly specialised technology evaluation is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the evaluation), a technical adviser and a project manager.

Alan Moore
Technical lead

Christian Griffiths
Technical adviser

Celia Mayers
Project manager

ISBN: [to be added at publication]