

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Appraisal consultation document

# Nusinersen for treating spinal muscular atrophy

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

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

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

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- 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, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

**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 appraisal committee will meet again to consider the evidence, this appraisal 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 appraisal document.
- Subject to any appeal by consultees, the final appraisal document may be used as the basis for NICE's guidance on using nusinersen in the NHS in England.

For further details, see NICE's [guide to the processes of technology appraisal](#).

**The key dates for this appraisal are:**

Closing date for comments: 5 September 2018

Second appraisal committee meeting: 23 October 2018

Details of membership of the appraisal committee are given in section 5.

## 1 Recommendations

- 1.1 Nusinersen is not recommended, within its marketing authorisation, for treating 5q spinal muscular atrophy.
- 1.2 This recommendation is not intended to affect treatment with nusinersen that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop. This decision should be made jointly by the clinician and the child or young person, and the child's or young person's parents or carers.

### Why the committee made these recommendations

Spinal muscular atrophy is a rare genetic condition, the most severe types of which affect babies and young children. Currently there is an unmet need for effective treatments that could slow disease progression.

Clinical trial evidence shows that nusinersen improves a range of outcomes that are important to patients. However, there is no long-term evidence, so the long-term benefits are highly uncertain.

There are also important limitations and uncertainties in the economic evidence. The most plausible cost-effectiveness estimates, based on the list price of nusinersen, are likely to be between £400,000 and £600,000 per quality-adjusted life year gained but may be higher.

The committee considered a wide range of important factors that affected its decision-making, in particular the rarity and severity of spinal muscular atrophy, the nature of the population, uncertainties, and whether the cost effectiveness of nusinersen should be considered according to that for end-of-life treatments.

Even taking these factors into account, and considering the proposed commercial arrangement; the cost of nusinersen is too high for it to be considered a cost-effective use of NHS resources. Because of this, nusinersen is not recommended.

## 2 Information about nusinersen

<b>Marketing authorisation indication</b>	Nusinersen (Spinraza, Biogen Idec) has a marketing authorisation for 'the treatment of 5q spinal muscular atrophy'.
<b>Dosage in the marketing authorisation</b>	12 mg, by intrathecal infusion, on days 0, 14, 28 and 63, then every 4 months.
<b>Price</b>	The list price is £75,000 per vial (excluding VAT; British National Formulary, accessed June 2018). At list price the total annual treatment cost is £450,000 for the first year and £225,000 for subsequent years. The company proposed a commercial arrangement which would apply if the technology had been recommended.

## 3 Committee discussion

The appraisal committee (section 5) considered evidence submitted by Biogen Idec and a review of this submission by the evidence review group (ERG). See the [committee papers](#) for full details of the evidence.

### *The condition*

#### **Spinal muscular atrophy is a neuromuscular disorder, the most severe types of which affect babies and young children**

- 3.1 Spinal muscular atrophy (SMA) is rare, progressive neuromuscular disease most commonly caused by a genetic mutation in the SMN1 gene on chromosome 5q. People with the condition have a range of symptoms, such as worsening physical disability, mobility loss and respiratory dysfunction. SMA can be grouped into 5 main types (type 0 to 4), based on the age of onset and the maximum motor function achieved by the person, which correlates with prognosis. Type 0 SMA, the most severe, affects babies before birth. Babies with type 0 SMA do not develop any

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motor skills and often survive for only a few weeks after birth. Babies with SMA type 1 have severe muscle weakness which affects movement, swallowing and breathing. In type 2 SMA, the onset of symptoms is between 7 and 18 months of age, and people with this condition are often severely disabled and unable to walk unaided. Type 3 SMA is a condition in which varying degrees of muscle weakness appear between age 18 months and 18 years; most people with type 3 SMA can walk or sit unaided at some point, but many lose mobility over time. Type 4 SMA, the least severe, affects adults. Adults with type 4 SMA may have only mild motor impairment and live a normal lifespan. The clinical experts suggested that of all diagnosed cases of SMA, around 60% are type 1 and around 40% are types 2 and 3; types 0 and 4 are rarely diagnosed. The patient experts commented that the classification system is useful but does not always reflect the full extent of the disease: boundaries between the different SMA classifications are blurred and can be subjective. The clinical experts accepted these limitations, but nevertheless acknowledged that the current classification system is the most accurate predictor of severity and prognosis available. The committee acknowledged the challenge in the current classification, but that this was all it could consider at this point. It concluded that the most severe types of SMA affects babies and young children.

### **Spinal muscular atrophy severely affects quality of life for patients, carers and their families**

3.2 The clinical and patient experts explained that people with SMA need constant support. This can include full-time care and attention, requiring physical effort (such as lifting and carrying) and causing loss of sleep, stress, and fear at loss of abilities. All of these factors have a major effect on family members' health-related quality of life. The committee heard from parents and carers that living with the condition involves daily care, exercises and constant vigilance (especially at night, when people with SMA need assistance in bed). SMA also causes anxiety, emotional distress and disruption to work and income, as well as straining

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relationships. The committee concluded that SMA has a substantial effect on the quality of life of patients, carers and their families.

## ***Current treatments***

### **There is an unmet need for an effective treatment**

3.3 There are no disease-modifying therapies for SMA. Current treatments are based on symptom control and aim to maintain movement and function for as long as possible and to improve quality of life. This involves a multidisciplinary approach including respiratory, gastroenterology and orthopaedic care, as well as nutritional support, physiotherapy, assistive technologies, occupational therapy and social care. However, the clinical and patient experts emphasised that current treatments do not affect disease progression, so people with SMA will ultimately become totally dependent on their families and carers. The committee recognised that treatment options are limited and there is an unmet need for patients with SMA.

## ***The technology***

### **Nusinersen has a marketing authorisation for all types of SMA but the company only presented evidence for types 1 to 3**

3.4 Nusinersen has a marketing authorisation for all types of SMA. The clinical experts agreed that nusinersen may benefit patients with any type of SMA. However, they considered that it may have a relatively greater benefit for those with more severe types of SMA (although using nusinersen to treat type 0 SMA might be futile because of the degree of established damage at the time treatment could be started). The committee heard that the presence of SMN2 can compensate for the SMN1 deletion to some degree as it is a similar gene, and that the number of SMN2 gene copies is inversely related to the severity of SMA and can be used to predict the course of the disease. However, the clinical experts stated that gene testing may lead to delays in starting

treatment. Moreover, they considered the correlation between copy number and disease severity is much less reliable than the clinical classification system in identifying the likely course of SMA. The committee acknowledged that nusinersen should be considered within its marketing authorisation (that is, for all types of SMA) but the company had not presented evidence for type 0 and type 4 SMA.

### ***Clinical trial evidence***

#### **Evidence from the clinical trials, including ENDEAR and CHERISH, is uncertain but relevant for decision-making**

3.5 The main clinical-effectiveness evidence for nusinersen came from 2 clinical trials:

- ENDEAR, a randomised, double-blind, multicentre (including the UK), phase III, sham procedure-controlled trial. The trial recruited 122 children who developed SMA symptoms between the ages of 2 weeks and 6 months, which corresponds to type 1 SMA (described by the company as 'early-onset' SMA).
- CHERISH, a randomised, double-blind, multicentre, phase III, sham procedure-controlled trial. The trial recruited 126 patients who developed SMA symptoms between the age of 6 months and 12 years and who were able to sit independently but never had the ability to walk independently. This corresponds with type 2 SMA and the more severe presentations of type 3 SMA (described by the company as 'later-onset' SMA).

There are also 3 ongoing studies: NURTURE, a phase II, single-arm study for pre-symptomatic infants genetically diagnosed with SMA; SHINE which is a continuation of ENDEAR and CHERISH; and EMBRACE, for patients with SMA who are not eligible to participate in the clinical studies ENDEAR and CHERISH. The ERG considered that there were limitations in the clinical evidence. In particular, in ENDEAR the nusinersen population had a poorer baseline prognosis than the control group and in

CHERISH the strict entry criteria resulted in a population that is more homogeneous than would be expected in clinical practice. The ERG also explained that the dose regimen in CHERISH was not consistent with nusinersen's marketing authorisation, because the maintenance doses were less frequent. Follow-up periods were relatively short for both ENDEAR and CHERISH, so the long-term benefits of nusinersen are unknown. The committee concluded that although the evidence had uncertainties, it was suitable for decision-making.

### **Nusinersen improves survival for people with early-onset spinal muscular atrophy**

3.6 Results from ENDEAR show that compared with sham, nusinersen statistically significantly improved event-free survival, overall survival and motor function in patients with type 1 SMA:

- The hazard ratio for event-free survival (defined as time to death or permanent ventilation) was 0.53 (95% confidence interval 0.32 to 0.89;  $p=0.005$ ).
- The hazard ratio for overall survival was 0.37 (95% confidence interval 0.18 to 0.77;  $p= 0.004$ ).
- In terms of motor function, 51% of patients in the nusinersen group achieved motor milestone responses compared with none in the control group (as measured by HINE-2 [Module 2 of the Hammersmith Infant Neurological Examination]).

Based on the strength of the survival benefit shown, the ENDEAR was stopped early. The committee agreed that the trial showed a substantial benefit for nusinersen compared with sham.

### **Other health benefits of nusinersen for early-onset spinal muscular atrophy are less certain**

3.7 ENDEAR measured other important outcomes including respiratory function, time on ventilator and hospitalisations. The results cannot be reported here because they are academic in confidence, but the

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committee noted that these outcomes did not show a substantial benefit with nusinersen. The committee considered it counterintuitive that an observed substantial survival benefit (section 3.6) was not associated with a substantial benefit in other outcomes. However, the clinical experts explained that although nusinersen would likely improve respiratory function, any improvements in motor function may in turn place greater stress on the respiratory system. The patient experts emphasised that the benefits of nusinersen seen in the trials and in clinical practice were valuable to patients and their families. They emphasised the importance of any stabilisation and even small improvement in symptoms, especially any improvement in motor function. The committee recognised that any improvements would be highly valued by patients and that nusinersen provides important health benefits for patients with early-onset SMA but concluded that the size of these benefits, and if there were any benefits in some outcomes, remained uncertain.

### **Nusinersen substantially improves motor function for people with later-onset spinal muscular atrophy**

3.8 Results from CHERISH show that compared with sham, nusinersen statistically significantly improved motor function of children with later-onset SMA. Motor function as measured by HFMSE (Hammersmith Functional Motor Scale-Expanded) had a least squares mean change difference (that is, a difference in differences of means) of 4.9 (95% confidence interval 3.1 to 6.7;  $p < 0.0000001$ ). The committee agreed that nusinersen provides important health benefits for people with later-onset SMA, but it was unclear how this affects survival because there were no deaths during the CHERISH trial.

### **Long-term benefits with nusinersen are uncertain**

3.9 The committee noted that both ENDEAR and CHERISH had short follow-up periods; ENDEAR had a follow-up of only 13 months, and only 16% of people having nusinersen and 39% of those having sham died, whereas CHERISH had a follow-up of only 15 months, and there were no deaths. It

heard from the clinical experts that there was considerable uncertainty surrounding the long-term benefits of nusinersen. It was possible that some patients may not achieve motor function milestones despite having nusinersen. The ERG considered that this was a source of substantial uncertainty in the clinical evidence base. The committee concluded that although nusinersen would likely provide long-term benefits, the size and nature of these benefits were uncertain.

### ***The company's economic model***

#### **The company's economic models have limitations but are suitable for decision-making**

3.10 The company presented 2 separate models: an early-onset model, for type 1 SMA (from 5.58 months) and a later-onset model, for types 2 and 3 SMA (from 43.71 months). Both models compared nusinersen with standard care, and transitions through health states were based on assessments of motor milestones using HINE-2 for early onset and HFMSE and WHO criteria for later onset. Although the model structure was based solely on motor milestones, the ERG explained that motor function was not the only factor affecting health-related quality of life; factors such as participating in activities, respiratory function, pain and physical impairment were also important. The committee acknowledged that the model structure was consistent with the main outcomes of the clinical trials. It concluded that the models had limitations but were nevertheless suitable for decision-making.

#### **The company's transition probabilities are optimistic and do not reflect clinical practice**

3.11 The transition probabilities used in the models assume that in the long term (that is, after the trial follow-up), SMA treated with nusinersen could not get worse but SMA treated with best supportive care could not get better. The ERG noted this was not consistent with the observed trial data, in which a small proportion of people who had sham therapy had

improvements in symptoms over almost all time periods. The clinical experts stated that it is plausible that, if left untreated, early-onset SMA would progressively worsen with no observable improvement. However, they considered it implausible that SMA treated with nusinersen could not get worse, and this did not reflect their experience using nusinersen in clinical practice, where taking nusinersen would improve some SMA whereas for others SMA would worsen. The committee concluded that the assumptions for long-term disease progression in the model were optimistic. It considered that the ERG's exploratory scenarios analyses in which 5% to 10% of people having nusinersen lose a milestone each cycle were more suitable for decision-making.

**The modelled long-term overall survival benefit is based on optimistic assumptions and is highly uncertain**

3.12 In both models, after the trial period the company applied a mortality adjustment to the best health states (informed by external study sources and general population mortality risk), such that patients had a similar mortality risk to patients with less severe types of SMA. The ERG highlighted that the overall survival benefit of nusinersen was driven mainly by this mortality adjustment. However, the ERG noted expert advice that this assumption was optimistic. The committee recalled the overall survival gain with nusinersen seen in clinical trials, and heard that this gain had also been seen in clinical practice. The clinical expert explained that nusinersen may help to preserve respiratory muscle function, so it would be reasonable to predict a longer-term survival benefit. The committee recalled that the long-term benefits of nusinersen were highly uncertain (section 3.9). It acknowledged that nusinersen is likely to improve long-term survival but considered the adjustment assumed by the company to be implausibly large and concluded that the modelled long-term overall survival was likely to be optimistic.

### **Utility values in the economic model are highly uncertain**

3.13 The committee recognised that identifying robust utility values in babies and young children is exceptionally challenging. The ERG considered that the utility values used in the company's models had limited face validity, with high values in poor health states and limited range. The ERG was also concerned that the algorithm used to map PedsQL to EQ-5D was limited, because it was based on healthy schoolchildren who would have different responses to people with SMA, and had few responses for the worst health states. The ERG preferred instead to use a vignette study based on EQ-5D assessments by healthcare professionals. This addressed some of the limitations identified by the ERG, but also lacked face validity because it resulted in very low values for the worst health states. The committee considered that both the company's and the ERG's approaches had serious limitations. It concluded that, whilst the utility values were highly uncertain, it would use both approaches in its decision-making at this time.

### **Including carer-related disutilities introduces more uncertainty**

3.14 The company derived carer-related utilities using a single estimate from a cross-sectional study and adjusting it using the change in patient utility between the different health states. The ERG noted that this assumed an equal effect of achieving a particular milestone for both patients and carers. It explained that although some degree of correlation in utility values between patients and carers might be expected, carer burden would be driven by factors other than restricted motor function (for example, incidence of frequent infections, pain, loss of sleep and emotional burden). The ERG proposed that alternative carer disutilities measured by SMA type would be preferable. However, the committee considered that these also lacked face validity because the largest carer disutility was seen in the best health state. The committee recalled that SMA has a substantial effect on carers and families as well as patients

(section 3.2), but concluded that quantifying carer-related disutilities was extremely difficult.

### ***Results of the cost-effectiveness analysis***

**The ICER is uncertain. At list price it is likely to be in the range of £400,000 to £600,000 per QALY gained but may be higher**

3.15 The incremental cost-effectiveness ratios (ICERs) including the patient access scheme for nusinersen are commercial in confidence and cannot be reported here. Based on the list price, the company's base-case ICERs for nusinersen compared with standard care were £407,605 per quality-adjusted life year (QALY) gained for early-onset SMA and £1,252,991 per QALY gained for late onset SMA. Including carer-related disutilities decreased the ICERs to £402,361 and £898,164 per QALY gained. The ERG presented an analysis including its preferred assumptions, in which it amended the starting health state distributions, end-of-life costs and patient and carer utilities. This analysis produced ICERs for nusinersen compared with standard care of £421,303 per QALY gained for early-onset SMA and £408,769 per QALY gained for later-onset SMA. Including carer-related disutilities increased the ICERs to £631,583 and £632,850 per QALY gained respectively. The ERG emphasised that it considered the modelling of transition probabilities and long-term survival to be optimistic (section 3.12), but it could not address these concerns in its analyses; it noted that if these concerns were addressed, the ICER would increase. The committee recalled that the ERG's exploratory analyses in which 5% to 10% of patients having nusinersen lose a milestone each cycle were relevant (section 3.11), and noted that they increased the ICERs by up to £200,000 per QALY gained. It was mindful of the substantial uncertainty surrounding all the analyses, including the ERG's preferred analysis. The committee concluded that it would be reasonable to predict that the ICER, based on the list price, may be in the range of £400,000 to £600,000 per QALY gained but may be higher.

## ***Other factors***

### **If a managed access arrangement were to be pursued, further details would be needed to make an assessment**

3.16 The committee noted that the company intended to engage with NHS England, stakeholders and NICE to develop a managed access arrangement for nusinersen. It agreed that data from the use of nusinersen in clinical practice collected through a managed access arrangement may be useful to address uncertainties in the evidence. It also acknowledged the need to manage risks associated with the identified uncertainties. However, the committee considered that the details of the company's proposed managed access arrangement were vague and currently insufficient for it to assess whether it could be an option for nusinersen. The committee was aware that NICE has published a number of pieces of guidance that include 'managed access arrangements', and that if a managed access arrangement is to be developed for nusinersen elements from these arrangements should be incorporated into the proposal, and these elements would need to be described in detail before the committee could properly assess the proposal. Although the committee recognised that a managed access arrangement could reduce the risk to the NHS, the ICER for nusinersen would need to plausibly be within a range that could be considered cost effective, and it would require NHS England, patients, carers and clinicians to sign up to it.

### **Nusinersen is the first disease-modifying therapy for spinal muscular atrophy**

3.17 The committee considered whether nusinersen could be considered innovative. The company explained that nusinersen has been recognised in several countries as the first treatment to address the cause and natural history of motor neurone degeneration in SMA. The committee recognised that nusinersen is an innovative treatment and the first disease-modifying therapy for SMA. However, it was not presented with any data to show

distinct and substantial benefits relating to the innovative nature of nusinersen that have not been captured in the economic analyses.

**There are important uncaptured health benefits, but it is unclear to what extent this affects the cost effectiveness of nusinersen**

3.18 The committee considered whether there were any health-related benefits that were not captured in the analysis. The committee recalled that SMA severely affects quality of life for patients, carers and their families (section 3.2). It recalled that analyses had tried to incorporate carer-related disutilities, but these were highly uncertain (section 3.14). It was not presented with any data to show other distinct and substantial benefits of nusinersen that have not been captured in the economic analyses. It concluded that it was difficult to assess how these benefits may affect the cost-effectiveness estimates.

**The committee considered the nature of the eligible population and the disease in its decision-making**

3.19 The committee noted that the population for which nusinersen is indicated includes children and young people. It considered that the fact that children are affected by the condition is reflected in the clinical evidence, model and the committee's understanding of the nature of the condition. The committee was mindful of the need to consider whether any adjustments to its normal considerations were needed. It discussed the need to balance the importance of improving the lives of children and their families with fairness to people of all ages. It noted [NICE's social value judgements: principles for the development of NICE guidance](#), which emphasise the importance of considering the distribution of health resources fairly within society as a whole, as well as considering factors other than relative costs and benefits. The committee also heard that the population eligible for nusinersen includes people with disabilities. The committee acknowledged and considered the nature of the eligible population as part of its decision-making, in particular in considering the circumstances in which nusinersen could be recommended as a cost-

effectiveness treatment. It concluded that no further considerations or adjustments were needed.

- 3.20 Although nusinersen has a number of features that are commonly seen in the [highly specialised technologies programme](#), it was considered as a single technology appraisal. This is because the population covered by the marketing authorisation is larger than that which can be considered in highly specialised technologies evaluations, and SMA is not commissioned through a highly specialised service. The committee acknowledged the difficulty of appraising drugs for very rare conditions. When developing the social value judgements, the [Citizens Council](#) considered that rarity alone is not a mitigating factor for accepting high ICERs, but the committee should consider taking into account other factors such as disease severity in its decision-making. The committee was aware that SMA is both rare and a very serious condition. The committee also reflected on the benefits associated with nusinersen, and how they are highly valued by patients and families. The committee was mindful during its decision-making of the need to consider whether any adjustments to its normal considerations were needed to take into account the rarity and severity of the disease.

### ***End of life***

- 3.21 The committee considered the advice about life-extending treatments for people with a short life expectancy in NICE's [guide to the methods of technology appraisal](#). The company proposed that nusinersen met NICE's criteria for a life-extending treatment at the end of life in the early-onset SMA population, but did not make a case for its meeting the criteria in the later-onset. The committee accepted that nusinersen did not meet the end-of-life criteria in the later-onset because, although nusinersen may provide a survival benefit, life expectancy in children with later-onset SMA is likely to be well over 2 years. For early-onset SMA, the company noted that survival depends on the nature and extent of supportive care, which may vary by country, institution and physician and the preferences of

patients and families. The median age of death or permanent respiratory support in published natural history studies was 9 to 13 months, and the median event-free survival in the control group of ENDEAR was 22.6 weeks. The ERG commented that low survival rates may not reflect current practice; some patients with less severe early-onset SMA may survive to school age. The ERG also commented that mean survival for patients with early onset SMA in the model receiving standard care was 3.87 years. The committee recognised that the life expectancy was uncertain, but considered it reasonable to accept that nusinersen could meet the short life expectancy criterion for early-onset SMA.

3.22 The company's economic model estimated that the life years gained for nusinersen were 5.95 for early-onset SMA and 1.38 years for later-onset SMA. The committee concluded that nusinersen extends life by more than 3 months.

3.23 The committee noted that nusinersen for early-onset SMA could meet the end-of-life criteria, but later-onset SMA did not. The committee recalled that SMA type is defined based on the age of onset and the maximum motor function achieved, and that the boundaries between the different SMA classification levels are blurred and can be subjective (section 3.1). In that context, and given the nature of the population (including that it contained children; see section 3.19) and the rarity and severity of SMA (section 3.20), the committee concluded that it could be unreasonable to apply a different level at which nusinersen would be considered cost effective depending on the age of onset of SMA. Considering the very high incremental cost-effectiveness ratios, the committee did not conclude on this at this time.

## ***Conclusion***

### **The committee was willing to be flexible in its considerations related to uncertainty**

3.24 The committee considered the advice about the acceptability of the technology as an effective use of NHS resources and factors influencing cost effectiveness in the [guide to the methods of technology appraisal](#). Specifically, it considered:

- the degree of certainty around the ICER
- whether there are strong reasons to indicate there are substantial benefits not captured by the model
- the likelihood of decision error and its consequences
- whether the technology meets criteria for special consideration.

The committee recalled the substantial uncertainties in the clinical trial evidence, particularly concerning long-term benefits, and the consequence is that some assumptions in the model are highly uncertain resulting in a wide range of plausible ICERs (section 3.15). The very high cost of nusinersen means that there is a significant financial risk to the NHS if the committee were to recommend a technology for routine use that may not be cost effective. The committee noted that the risk to the NHS could be reduced through a managed access arrangement, but that such an agreement would have to carry the support of NHS England, patients, carers and clinicians, and that nusinersen would need to have the plausible potential to be cost-effective (section 3.16). It recalled that there were uncaptured benefits, but it was unclear how this affects the cost effectiveness of nusinersen (section 3.18). It also recalled that as part of the technology's special consideration its cost effectiveness could be considered according to that for end-of-life treatments (section 3.23). The committee was prepared to take into account a wide range of factors in its decision-making, including the nature of the population (including that it contained children; section 3.19) and the rarity and severity of the disease

(section 3.20). In that context, although nusinersen would need to plausibly be within a range that could be considered cost effective, the committee concluded that it was willing to be flexible in its considerations around uncertainty, particularly if access could be managed such that the risk to the NHS was reduced.

### **Nusinersen is not recommended for treating spinal muscular atrophy**

3.25 The committee recognised that the ICERs with the patient access scheme were very high. Even taking into account the other factors it considered important in its decision-making (sections 3.2, 3.5, 3.10, 3.19, 3.20, 3.23 and 3.24) as well as the cost-effectiveness estimates presented, the committee concluded that it could not recommend nusinersen for treating SMA.

## **4 Proposed date for review of guidance**

4.1 NICE proposes that the guidance on this technology is considered for review by the guidance executive 3 years after publication of the guidance. NICE welcomes comment on this proposed date. The guidance executive will decide whether the technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

Stephen O'Brien

Chair, appraisal committee

August 2018

## **5 Appraisal committee members and NICE project team**

### ***Appraisal committee members***

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by [committee C](#).

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

The [minutes](#) of each appraisal 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 technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

#### **Lulieth Torres**

Technical Lead

#### **Ian Watson and Thomas Strong**

Technical Advisers

#### **Joanne Ekeledo**

Project Manager

ISBN: **[to be added at publication]**