

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

	<p>Please read the checklist for submitting comments at the end of this form. We cannot accept forms that are not filled in correctly.</p> <p>The Appraisal Committee is interested in receiving comments on the following:</p> <ul style="list-style-type: none">• 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 provisional recommendations sound and a suitable basis for guidance to the NHS? <p>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 preliminary recommendations may need changing in order to meet these aims. In particular, please tell us if the preliminary recommendations:</p> <ul style="list-style-type: none">• could have a different impact on people protected by the equality legislation than on the wider population, for example by making it more difficult in practice for a specific group to access the technology;• could have any adverse impact on people with a particular disability or disabilities. <p>Please provide any relevant information or data you have regarding such impacts and how they could be avoided or reduced.</p>
<p>Organisation name – Stakeholder or respondent (if you are responding as an individual rather than a registered stakeholder please leave blank):</p>	<p>[Spinal Muscular Atrophy Support UK and The SMA Trust]</p>
<p>Disclosure Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry.</p>	<p>[None]</p>

Please return to: TACommE@nice.org.uk / NICE DOCS

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

Name of commentator person completing form:	[Liz Ryburn]
Comment number	Comments Insert each comment in a new row. Do not paste other tables into this table, because your comments could get lost – type directly into this table.
1	<p>Has all the relevant evidence been taken into account?</p> <p>NICE’s committee papers: evidence of population with SMA</p> <p>The evidence suggests that the committee’s estimation of the population that would access treatment is too high.</p> <p>We understand NICE is basing its discussions on the following statement in the summary slide ‘Disease Background’:</p> <p>‘It is estimated that about 100 people are born with SMA per year in the UK, and currently between 1,200 and 2,500 children and adults with SMA in the UK.</p> <p>We have been unable to ascertain how NICE has derived its prevalence and incidence data. We note that NICE’s figures are similar to estimates we were aware of in 2013 derived as follows:</p> <ul style="list-style-type: none">• At the 2013 SMARTnet /Patient Registry meeting, a lead clinician stated that there are some 1200 people affected by SMA in the UK at any one time – children and adults.• We asked another leading clinician that same year for their calculation which, based on the then estimated incidence of 100 children born with SMA per year, they gave as follows<ul style="list-style-type: none">• Type I: accounts for 50-60% of all SMA but median life expectancy is 1 year, so rough estimate is that there are about 25 children alive in the UK with Type I at any one time.• Type II: median life expectancy about 25 years, 25% of all SMA so prevalent

Please return to: TACommE@nice.org.uk / NICE DOCS

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

population is $25 \times 25 = 625$.

- **Type III:** by the same reasoning $25 \times 70 = 1750$.
- **TOTAL approx. 2,500**, but this is the upper limit and the **true figure is probably around 1,500-2,000**.

As there were no other figures available at this time, these figures and calculations became public.

We consider this to be incorrect based on evidence presented in these two recent studies:

- Verhaart I *et al.* (2017) **Prevalence, incidence and carrier frequency of 5q-linked spinal muscular atrophy –a literature review.** *Orphanet J Rare Dis* 12: 124.
- Verhaart I *et al.* (2017) **A multi-source approach to determine SMA incidence and research ready population.** *J Neurol* 264: 1465-1473

These conclude:

Incidence: approximately one in every 10,000 babies worldwide are born with a type of SMA. In England and Wales in 2017, there were 679,106 live births. This suggests that in that year approximately 68 babies were born with a type of 5q SMA.

Prevalence -between 1 and 2 people in every 100,000 worldwide have a type of SMA. In 2017, the population of England and Wales was approximately 58.4 million. Based on this, it is estimated that between 585 and 1170 people living in England and Wales have SMA.

We are aware these papers are based on global observations of incidence and prevalence but until we have an accurate UK wide register of those born with 5q SMA and those living with 5q SMA we ask NICE to use them to guide analysis and decision making.

Population that would seek treatment

From the perspective of NICE's decision making, it is not only important to know the actual population but also to be aware and take into consideration that:

- **Not everyone who has 5q SMA will want treatment.** Reasons cited are:
 - the invasive method of administration and necessary commitment to its long-term repetition
 - the unknown long-term outcomes
 - an awareness there are more treatments, such as gene therapy, on the horizon.

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

	<p>We remind NICE of our 2018 survey of parents/carers of children and young people with SMA and adults with SMA which we submitted in which:</p> <ul style="list-style-type: none">○ 18%. of people with SMA (total respondents 56) – most of whom would be adults - said they would not want nusinersen treatment○ 5% of parents/carers (total respondents 55) said they would not want nusinersen treatment for the child / young person they care for <p>The same observation applies to both groups in that those not interested in treatment may not have been engaging in the discussion let alone have responded to the survey – in which case the percentage who would not seek treatment may be higher.</p> <ul style="list-style-type: none">● The treatment may not be clinically safe for everyone with SMA● There has been no clinical evidence of the treatment for those with SMA Type 0 or 4. Although the number with these types of SMA are small, again this lowers the likely population that will seek treatment if it is funded by the NHS <p>In summary: when considering all with 5q SMA, we suggest that an appropriate population base is:</p> <ul style="list-style-type: none">○ Incidence: 1 in every 10,000 – approximately 68 babies born with 5q SMA each year in England and Wales.○ Prevalence: between 1 and 2 people in every 100,000 worldwide have a type of SMA - approximating to between 585 and 1170 people living in England and Wales having SMA <p>We further suggest that the population that would seek treatment is lower than the prevalent figure:</p> <ul style="list-style-type: none">○ Not everyone who has 5q SMA will want treatment○ The treatment may not be clinically safe for everyone with SMA○ There is no clinical evidence of the treatment for those with SMA Type 0 or 4. <p>We are concerned that an over estimation of the population who would seek and for whom this treatment would be clinically safe may lead to incorrect assumptions by NICE as to the total budget that would be required</p>
2	<p>Has all the relevant evidence been taken into account?</p> <p>Consultation Paper 3.5 NICE's Clinical Evidence</p> <p>We note that NICE only discusses evidence from the published results of the clinical trials ENDEAR and CHERISH. We understand that Biogen will be submitting further evidence</p>

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

published in 2018.

We would like to be assured that NICE has considered the additional recently published clinical evidence from ‘real world’ studies. Though the studies were not all conducted in the UK, all the clinical practice is guided by the 2017 internationally agreed Standards of Care for SMA (**Mercuri, E *et al.* (2017) Diagnosis and management of spinal muscular atrophy: Part 1: recommendations for diagnosis, rehabilitation, orthopedic and nutritional care.** *Neuromuscul Disord.* 2018 Feb;28(2):103-115. and **Finkel, R *et al* (2017), Diagnosis and management of spinal muscular atrophy: Part 2: Pulmonary and acute care; medications, supplements and immunizations; other organ systems; and ethics.** *Neuromuscul Disord.* 2018 Mar;28(3):197-207.)

We note that the real-world studies only review outcomes for children with SMA Type 1 for the first six months of treatment but consider ‘real world’ evidence critical to decision making. They all assist with confirming the certainty of evidence of effectiveness (see below). In particular we refer to:

Reviews of the Expanded Access Programme:

- **Europe** - 33 children aged from 8.3 to 113.1 months - December 2016 - May 2017.
Aragon-Gawinska, K *et al.* (2018) Nusinersen in spinal muscular atrophy type 1 patients older than 7 months. A cohort study *Neurology*[®] 2018;00:1-7. doi:10.1212/WNL.0000000000006281
- **Australia** – 16 patients aged 2.5 months to 35.7 years November 2016 – September 2017
Farrar, M *et al.* (2018) Nusinersen for SMA: expanded access programme *J Neurol Neurosurg Psychiatry* 2018;**89**:937–942. doi:10.1136/jnnp-2017-317412
- **England - Great Ormond Street Hospital** – 21 patients aged 8.3 – 113.1 months March – October 2017
Tillmann, A *et al.* (2018) Spinal Muscular Atrophy (SMA) type 1, a changing phenotype: Implications for motor function and physiotherapy management from the Nusinersen Expanded Access Program (EAP) *APCP Journal* Volume 9 Number 1
- **Germany** – 61 patients aged 1 – 93 months in seven neuromuscular centres November 2016 – June 2017
Pechmann, A *et al.* (2018) Evaluation of Children with SMA Type 1 Under Treatment with Nusinersen within the Expanded Access Program in Germany *Journal of Neuromuscular Diseases* 5 (2018) 135-143 DOI 10.3233/JND-180315

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

	<ul style="list-style-type: none">• Italy – 104 patients – aged 3 months – 19 years 9 months - first six months of EAP Pane, M <i>et al.</i> (2018) Nusinersen in type 1 SMA infants, children and young adults: Preliminary results on motor function <i>Neuromuscular Disorders</i> 28 (2018) 582-585 30 May 2018 <p>Also:</p> <ul style="list-style-type: none">• Hoy, S (2018) Nusinersen: A Review in 5q Spinal Muscular Atrophy <i>CNS Drugs</i> (2018) 32:689-696 Published online 20 July 2018 © Springer Nature Switzerland AG 2018 <p>In summary we ask NICE to include in their evidence base the outcomes of 5 ‘real world’ studies of 235 patients age range 1 month – 35.7 years receiving treatment via the global SMA Type 1 Expanded Access Programme.</p>
3	<p>Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?</p> <p>Consultation Paper 3.6 NICE’s conclusion re: clinical effectiveness in terms of survival and improved motor function.</p> <p>We note Hoy’s overview (cited above) which supports NICE’s conclusion.</p> <p>‘Results from an expanded access programme support the efficacy of nusinersen in the real-world setting.’</p>
4	<p>Is the summary of clinical effectiveness a reasonable interpretation of the evidence?</p> <p>Consultation Paper 3.7. NICE’s discussion of other health benefits for early onset SMA.</p> <p>This focuses on discussion of outcome measures used in the trials. It acknowledges the patient experts view of these ‘other’ valuable benefits and the importance of any stabilisation and even small improvements in symptoms, especially improvements in motor function. Aragon-Gawinska, K <i>et al.</i> confirm this and describes parental reports of the wider impacts, impacts that are significant for quality of life:</p> <p>‘It should be noted that many parents reported improvements during treatment with nusinersen that were not captured by the measures used and that were not predefined in data collection such as louder voice, better endurance, and more efficient coughing. Better definition of these outcomes might be useful for long-term follow-up of these patients.’</p>

Please return to: TACommE@nice.org.uk / NICE DOCS

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

Pechmann, A *et al.* also note in their study, 'Further research is needed to evaluate the impact of changes in CHOP INTEND score on daily life and on quality of life in children with SMA type 1, which are not as obvious as changes in motor milestones.'

Aragon-Gawinska, K *et al.* confirm NICE's conclusions when they state:

'Our results are in line with the phase 3 study for nusinersen in patients with SMA1 treated before 7 months of age and indicate that patients benefit from nusinersen even at a later stage of the disease.'

And

'Despite its limitations, this study provides Class IV evidence that nusinersen is beneficial for patients with SMA1 between 7 and 113 months of age.'

ENDEAR's respiratory function, time on ventilator and hospitalisations evidence is currently in confidence and therefore not discussed in NICE's conclusions. With regard to this, though not 'clinical evidence' and already submitted, we remind the committee of the results of our own survey in the UK when we heard from 29 parents whose children had received nusinersen treatment, many of whom had had this for longer than six months:

- **Numbers:** Type 1 - 19; Type 1 / 2 - 9; Type 2 - 2; Type 3 – 1.
- **Age range:** <7 months – 9+ years.
- **Treatment duration:** 0-4 injections – 8; 5-7 injections – 18; 11+ injections -1).

The % reports from 20 parents giving open comments of their observed outcomes of their treated child was as follows:

- Physical / muscle improvements 95%
- Much happier 40%
- Respiratory gains 35%
- General improvement in health 20%
- Increased vocalisation 10%

Typical quotes, taken from the qualitative part of our study, that **highlight the impact of the motor milestones on daily living** are:

'Practically she is able to perform more tasks herself and gained strength to use her own wheelchair.' **Type1, treatment started age 13 - 24 months, 5-7 injections**

Typical quotes that **highlight the gains are not just with mobility and suggest an impact on**

Please return to: TACommE@nice.org.uk / NICE DOCS

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

	<p>respiratory function are:</p> <p>‘He has been managing colds all through winter at home whereas before he was in intensive care on life support for every cold he got. He is a happy boy who can now start to explore his surroundings, he is also beginning to talk and can say Mum and dad and can sing and clap.’ Type 1, treatment started < 7 months, 5-7 injections</p> <p>‘My child required/relied on bipap before treatment and her lungs were getting worse and worse.However, nusinersen has stabilised / improved her breathing. She now only requires bipap for sleep and her settings have been turned down following sleep studies.’ Type 1 treatment started 13-24 months, 5-7 injections</p> <p>‘He can tolerate sitting up for hours without any respiratory support.....Respiratory wise he has gone from being ventilated 22 hours a day to 16 hours a day.’ Type 1, treatment started <7months, 11+ injections</p> <p>‘Her biggest joy is being able to cough better, and deal with mucus plugs without so much chest physio and cough assist. Also, previously every illness (respiratory or gastric) meant non-reversible deterioration, and now she bounces back almost to the same level as before the illness.’ Type 1 / 2, treatment started 37 months +, 5-7 injections</p> <p>In summary: we are pleased to see NICE recognising that any improvements would be highly valued by patients and that it provides important health benefits for early-onset SMA. We suggest that real world studies that comment on parent views and our own survey indicate less uncertainty than NICE concludes.</p>
5	<p>Is the summary of clinical effectiveness a reasonable interpretation of the evidence?</p> <p>Consultation Paper 3.8 Nusinersen substantially improves motor function for people with later-onset SMA</p> <p>We note and agree with this conclusion.</p> <p>The real-world studies (see 2) of patients with SMA Type 1 aged 1 month to 35.7 years indicate, as summarised by Pechmann, A et al that, ‘Although this study does not provide evidence comparable to a randomized controlled trial, the results indicate that even in advance stages of the disease, nusinersen can lead to improvement of motor function as measured by CHOP INTEND’. Given these real-world studies have necessarily been restricted to delivery to those with SMA Type 1 the most severe form of SMA, it may not be unreasonable to suggest, as shown in CHERISH that these findings will be at the very least replicated with SMA Type 2 and 3 with all the very positive implications of such outcomes.</p> <p>We also remind NICE that this conclusion was confirmed in our submission which drew</p>

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

	<p>attention to the very positive outcomes of treatment, not just in terms of motor function, for a teenager with SMA Type 3 and the impact that the gains have had on all aspect of his daily living. We understand his treatment has continued and this parent will be giving NICE a further update on progress.</p>
6	<p>Is the summary of cost effectiveness a reasonable interpretation of the evidence?</p> <p>Consultation Paper 3.10 Transition probabilities based on assessment of motor milestones</p> <p>We agree with the Evidence Review Group (ERG) comments that the model structure fails to take account of other key factors affecting health-related quality of life such as; participating in activities, respiratory function, pain and physical impairment.</p> <p>We note that the committee concluded that the models had limitations but were nevertheless suitable for decision making as they were consistent with the main outcomes of the clinical trials.</p> <p>We are not confident that we agree with this conclusion because it is questionable whether the main outcomes were an adequate reflection of the effectiveness of treatment. In Ethical Challenges Confronted When Providing Nusinersen Treatment for Spinal Muscular Atrophy Journal of American Medical Association Feb 2018 Volume 172 Number 2, Burgart, A.M et al. comment on the motor milestone measurements used in the trials as follows:</p> <p>‘Maintaining the most marginal function may be the key quality of life indicator for a patient seeking nusinersen treatment. The measurements used during the trials, while sufficient for patients who met study criteria, may not be sensitive enough to detect minute differences in strength maintained or gained.’</p> <p>Additionally, as shown above (see 4), the range of outcomes measured was limited and did not adequately show their breadth.</p>
7	<p>Is the summary of cost effectiveness a reasonable interpretation of the evidence?</p> <p>Consultation Paper 3.13 Utility values in the economic model are highly uncertain</p>

Please return to: TACommE@nice.org.uk / NICE DOCS

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

We agree with NICE's concerns that identifying robust utility values in babies and young children is exceptionally challenging and draw attention to the flaws the measures present as summarised by Griebisch, I *et al.* **Quality-Adjusted Life-Years Lack Quality in Pediatric Care: A Critical Review of Published Cost-Utility Studies in Child Health** [Pediatrics May 2005, VOLUME 115 / ISSUE 5](#) summarises the issues that this measurement brings:

- Children undergo dramatic changes in growth and function (e.g., mobility, self-care) at different rates, difficulties may arise to attribute improvements to health care interventions rather than to normal development. There is no methodologic guidance about how this should or even might be dealt with.
- All current generic measures (with the exception of the Health Utility Index Mark 2) are derived from adult populations, and additional attributes that are particularly relevant to child health, including, for example, autonomy, body image, cognitive skills, and family relationships, may not be captured by these measures. Furthermore, no generic instrument for children and infants **younger than 5 years** is available.
- Children, particularly young children do not have the cognitive ability to comprehend and complete valuation or even measurement tasks. The implication is that, for very young children, some form of proxy inevitably will be used for measurement tasks, whether this be the clinician or the parent. Although parents may be perceived by economists as the more appropriate source of measurement and/or valuation, the potential for interaction between the utility function of the parent and the proxy (their child) for whom he or she is making the measurement/valuation may lead researchers to choose to use clinician judgment to avoid this problem. The issues with this are that: clinicians only see and record a 'snapshot' which may not truly represent the changes taking place and impact on daily living for both child and parents; measurement tools are insufficiently subtle and limited in their measurements.

This last point is confirmed by the above comments (see 4) and the many studies that show this, for example, **Srikrishna S, *et al.*(2009) Is there a discrepancy between patient and physician quality of life assessment?** *NeuroUrol Urodyn.* 2009;28(3):179-82. doi: 10.1002/nau.20634.

In summary: we agree that both the company and the ERG approaches had serious limitations. We understand NICE's decision to use both approaches sought to address this, but are concerned that the final values may not appropriately reflect the impact of the worst health states caused by untreated SMA as reported in clinical and patient

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

	expert evidence.
8	<p>Is the summary of cost effectiveness a reasonable interpretation of the evidence?</p> <p>Consultation Paper 3.14 Carer disutilities</p> <p>We note NICE concluded that quantifying carer -related disutilities was extremely difficult and that the committee was concerned that the proposed model resulted in the counter-intuitive outcome whereby, ‘the largest carer disutility was seen in the best health state.</p> <p>We agree with this concern and remind NICE of our survey in which 56 people with SMA, 55 parents/carers and 21 relatives described the huge ‘carer burden’ of the untreated condition on their lives. In contrast, in ‘open comments’, 20 families with children still at early stages of treatment described the beginning of the reduction of this ‘burden’ in the following ways:</p> <ul style="list-style-type: none">• Given hope 65%• Emotionally positive and happier 40%• Decreased care needs 20% <p>One family summarised the pre and post treatment change in ‘burden’ as follows:</p> <p>‘When your child is unstable and having frequent hospital / ambulance admissions this is very draining both physically and emotionally on the whole family. We are more relaxed and able to enjoy day to day life and activities so much more now. SMA is very tough on you as a carer / sibling, but with his stability and health being so much better we feel a lot more happy as a family.’ Type 1, treatment started <7months, 11+ injections</p>
9	<p>Is the summary of cost effectiveness a reasonable interpretation of the evidence?</p> <p>Consultation Paper 3.15 The ICER is uncertain Consultation Paper 3.18 Uncaptured health benefits</p> <p>We agree with NICE that there is uncertainty and acknowledge the committee’s efforts to address flaws in the models in its conclusions. We note that the paper states ‘It was not presented with any data to show other distinct and substantial benefits of nusinersen that have not been captured in the economic analysis.</p> <p>We acknowledge that our submission data was qualitative and anecdotal, but it was directly from members of the UK SMA community. We therefore seek an assurance that the economic analysis covered all direct health and personal health and social services costs</p>

Please return to: TACommE@nice.org.uk / NICE DOCS

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 **email:** TACommE@nice.org.uk /NICE DOCS

and reflect the observations submitted in our survey results, namely:

- **mental health:**

- 56% of 132 of ‘untreated’ respondents reported the person with SMA did not have enough support and intervention to keep emotionally well
- 54% of 132 of ‘untreated’ respondents reported the person with SMA did not have enough support and intervention to get enough sleep
- 67% of 132 of ‘untreated’ respondents reported the main carer did not have enough support and intervention to keep emotionally well
- 73% of 132 of ‘untreated’ respondents reported the main carer did not have enough support and intervention to get enough sleep

- **equipment costs and housing adaptations:**

- our survey detailed the huge range required

- **emergency hospital stays, surgery and clinic time:**

- again, these events and related costs are enormous

- **continuing health care (CHC) cost:**

- these can be significant and, combined with social care / personal budget, up to 24 hour

Though we accept there is uncertainty as to future long-term outcomes for those treated with nusinersen, the evidence to date clearly indicates that these wider costs will potentially reduce significantly. We would like assurance that this potential is adequately reflected in the ICER.

We also seek assurance that the model reflected that the health impact is not on **one** carer but on many e.g. grandparents who also often play a key role. Also that due to the ‘carer burden’ of caring for someone with SMA, that it impacts on other caring responsibilities of the carer.

In our survey:

- 32% of 128 respondents reported the carer had caring responsibilities for **ageing parents** – with the potential that they would not be able to give those parents the care they will need and that these costs will therefore fall to health and social services
- 51% had caring responsibilities for **other children** with some reporting that their focus

Please return to: TACommE@nice.org.uk / NICE DOCS

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

on the child with SMA and their needs was impacting negatively on siblings' mental health and behaviour with potential health related costs

We are concerned that however much effort NICE has made to adjust the ICER's to better reflect the evidence presented and address shortcomings that do not reflect 'real-world patient expert reports, the appraisal system remains fundamentally flawed. From our perspective there needs to be a much more holistic inter-departmental approach to assessing the costs and benefits of treatment. Only then can the ICERs really begin to reflect the true potential value of this treatment.

As examples of this, SMA impacts on:

- **education costs:** requiring Teaching Assistants, school adaptations, University PAs
- **work costs:** carers (parents and grandparents) and patient – loss of potential productivity and contribution to the economy through work / taxes. In our survey:
 - 52% of 132 respondents reported that the interventions and support they have is not enough for the person with SMA to work / study for the hours they wish
 - 70% of 132 respondents reported they were not enough for the carer to work / study for the hours they wish
- **health and social care costs borne by families:**
 - 45% of 132 respondents reported that the interventions and support the person with SMA and their carers have are not enough for that person to manage financially
 - 60% of 132 respondents reported that they are not enough for the carer to manage financially
- **equipment and housing adaptation costs borne by families:**

Examples from our survey of items that many respondents reported were not NHS funded:

- 71% of those using a wizzybug
- 70% of those needing a specialist car seat
- 57% of those needing a wheelchair accessible vehicle
- 52% of those who had needed home adaptations
- 50% of those needing a powered wheelchair

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

	<ul style="list-style-type: none">○ 50% of those requiring assistive technology <p>SMA is a progressive condition which mean these costs increase over time. Treatment that results in stability alone can result in a huge reduction in these costs.</p> <p>In summary: we seek an assurance that the economic analysis covered all the real-world costs of all the health and personal health and social services required to support a person with SMA and their family and included the impact of SMA affecting more than one carer. We also wish it to be noted that we consider the model falls short in that it fails to cover the real-world costs that lie outside the realm of health and social services. We are aware this is not possible within this appraisal but consider that this needs to be urgently addressed by NICE.</p>
10	<p>Are the provisional recommendations a sound and suitable basis for guidance to the NHS?</p> <p>Consultation paper 3.16. states</p> <p>‘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.</p> <p>Due to nusinersen having been assessed via a Single Technology Appraisal (STA), we consider the ICER threshold is inappropriate and urge flexibility when establishing what will be an appropriate range.</p>
11	<p>Are the provisional recommendations a sound and suitable basis for guidance to the NHS?</p> <p>Consultation Paper 3.20</p> <p>We note NICE’s statement that its decision to appraise the treatment via an STA rather than via a Highly Specialised Technology (HST) was ‘because the population covered by the marketing authorisation is larger than that which can be considered in HST evaluations’. We refer back to our previous comments (See 1) highlighting our concern about the figures used by NICE to draw this conclusion.</p> <p>We also wish to draw attention to the thresholds comparable regulatory bodies use for considering rare orphan / ultra orphan medicines:</p> <ul style="list-style-type: none">● Scotland is introducing a new definition of 'ultra-orphan medicines' that can treat very rare conditions affecting fewer than 1 in 50,000 people - around 100 people or less in Scotland. This will include SMA and allows the Scottish Medicines Consortium (SMC) the

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

ability to treat some medicines for rare orphan diseases as ultra-orphan medicines.
www.news.gov.scot/news/treatments-for-rare-conditions

- **The European Medicines Agency** states that for orphan designation, the **prevalence** of the condition in the EU must not be more than 5 in 10,000 (1 in 2,000) or it must be unlikely that marketing of the medicine would generate sufficient returns to justify the investment needed for its development;

Though it is not clear what population threshold NICE uses given its HST guidance (August 2018) now states that for a topic to be selected, ‘the target patient group for the technology in its licensed indication’ has to be ‘so small that treatment will usually be concentrated in very few centres in the NHS’ we understand that previously **NICE’s commonly accepted threshold** for considering scoping a treatment as an HST was, that it would be accessed by fewer than 500 patients in England and Wales. If this were the case this would be the equivalent of **1 in 110,000 (Population for England and Wales 2017)**. If the threshold moved in line with Scotland it would in contrast, include **1,313 patients**. As outlined in (1) above, the total target population would come well within this.

We also note that the treatment was excluded from being appraised via an HST because it is ‘not commissioned through a highly specialised service.’ We question how appropriate such a barrier to HST appraisal is for a condition such as SMA which is clearly rare but for which, for safe and efficient delivery, treatment needs to be delivered as close to a person’s home as possible.

We note that Biogen’s EAP, which has given the drug free has been opened in both highly specialised and specialised centres in response to strong advocacy from patient groups and clinicians which highlighted:

- A need to circumvent a postcode lottery
- The need for children not to travel (health risks, burden on families)
- The capacity issues of centres that were open.

In view of this, we consider this range of centres is an appropriate response to the treatment needs of this population. It is a credit to Biogen that they agreed to provide the drug to a wide number of centres and that as a result, more than 80 children are having treatment in across the UK. In so doing we imagine Biogen was aware that this very move would offer one more reason to push the drug out of the HST appraisal route into that of an STA for common diseases.

We understand that this treatment did not meet 4/7 of the HST topic selection criteria (Sir David Haslam letter to clinicians 3 September 2018). As such it has missed out on being assessed against the higher HST ICER threshold and has instead been assessed as an STA for

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

	<p>common diseases. We strongly contest that this is an inappropriate threshold and that the choice of only these two routes has created undue delays and difficulties with the assessment of this treatment and condition. This has meant that, despite the clinical evidence available, there has been no access for anyone other than those with Type 1 < 7 months of age.</p> <p>In contrast, in July 2018 Biogen reported 20 European countries had access to nusinersen via routine reimbursement. We have provided information and emotional support to one family already who has chosen to move to one of these countries as they are desperate to access treatment. This is not a choice they wanted to make and has been a hugely complex and distressing decision. We know of other vulnerable families also feeling forced to consider this. This is only going to get worse with the imminent closure of the EAP for Type 1 on 1st November. If not resolved before then we will see infants with SMA Type 1 missing the critical early treatment window which gives the best opportunity for positive outcomes and the very real prospect of these infants dying.</p> <p>In summary: We urge NICE to:</p> <ul style="list-style-type: none">• Take account of the STA presenting what we regard as an inappropriately low ICER threshold for this treatment and reflect this in a more flexible approach to an agreed higher price threshold within a timely Managed Access Agreement (MAA).• Ensure that England and Wales offer access in line with Europe
12	<p>Are the provisional recommendations a sound and suitable basis for guidance to the NHS?</p> <p>Consultation Paper 3.23 We agree with the committee that ‘it could be unreasonable to apply a different level at which nusinersen would be considered cost effective depending on age of onset of SMA’</p>
13	<p>Are the provisional recommendations a sound and suitable basis for guidance to the NHS?</p> <p>Consultation Paper 3.24 We acknowledge the committee’s comment, ‘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 that may not be cost effective’ However we point out that many families have expressed that they see this treatment as a vital bridge to further new treatments which are coming close to completion of clinical trials and, one imagines possible applications for licences (AveXis’ AVXS-101, Roche’s RG7916 / risdiplam). In the light of this, we ask the committee to consider that this risk may not be very long term.</p>

Please return to: TACommE@nice.org.uk / NICE DOCS

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

	<p>We were also pleased to read the committee is, ‘Willing to be flexible around uncertainty, particularly if access could be managed such that risk to the NHS was reduced’ and consider it possible, via a Managed Access Agreement, to collect data that will reduce uncertainty. We suggest collection of the data could include reviewing and incorporating the work of Chad Heatwole, MD, at the University of Rochester, who, in his project, " Development of a Clinically Relevant Outcome Measure for Pediatric SMA Therapeutic Trials." is working to develop SMA-specific patient reported outcome measures for use in SMA clinical trials and clinics. One such instrument, the Spinal Muscular Atrophy Health Index (SMA-HI), was developed and validated using FDA guidelines for SMA patients age 8 to 85. This instrument is currently being utilized to measure therapeutic response in clinical trials. The new work will look at developing properly validated, disease-specific, observer-reported outcome measure for infants and children (under 8 years of age) with SMA.</p>
14	<p>May the preliminary recommendations need changing because they could have an adverse impact on people with a particular disability or disabilities?</p> <p>We would argue ‘yes’, most definitely this decision has an adverse impact on all with SMA who would have wanted and for whom it would have been clinically safe to access the treatment. This decision deprives these people of the possibility of accessing a life-changing treatment that has the potential to have a huge impact on both their quality of life and the quality of life of their families.</p>
15	<p>Is there a clinically distinct subgroup of people in whom nusinersen is expected to be more clinically effective? How could this group be identified in clinical practice?</p> <p>We note that the cost of the drug is covered by Biogen’s EAP for all those currently living with SMA Type 1 (prevalent population). We assume that NHS England’s 9 March 2018 commitment to cover the costs of administration of the drug remains in place.</p> <p>We note that there is no clinical evidence for treatment of those with SMA Type 0 and Type 4</p> <p>We suggest that there are three groups all of whom are of equal importance and for all of</p>

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

whom there is potential for clinical effectiveness. They are differentiated only so that different ‘work streams’ can be established within any MAA:

Group A

Clinical evidence (ENDEAR and CHERISH Trials) and ‘real-world’ studies cited above indicate that early treatment provides greater effect. This includes those with Type 1, 2 and 3 where it is clinically safe, and the clinicians and family agree on treatment. Note that, for a range of (personal) reasons, not all will want treatment. For example, **Farrar, M *et al.*** cite, that 4 of 20 families with children eligible for treatment chose not to go ahead. It is a very individual decision requiring informed consent.

- **How could this group be identified in clinical practice?**

We suggest this group could be easily identified at the time of diagnosis and that for England in any one year, given the incidence (see references and calculations in 1) is likely to be **68 children** including those diagnosed with:

- Type 1: 60% - 41 infants age < 6 months
- Type 2: 21% - 14 children ages 6 – 18 months
- Type 3: 19% - 13 children including
 - Type 3a ages 18months – 3 years
 - Type 3b age 3 years plus

Though outside the scope of this appraisal, we note and agree with the comments made by **Farrar, M *et al.*** (2018) **Nusinersen for SMA: expanded access programme** J Neurol Neurosurg Psychiatry 2018;**89**:937–942. doi:10.1136/jnnp-2017-317412

‘that further education of healthcare professionals seeing infants at risk of SMA type 1 is necessary.’

And that ‘Newborn screening (NBS) presents as the best opportunity to considerably reduce medical morbidity resulting from a delayed diagnosis of SMA type 1’ and indeed the impact of other types of SMA.

We note that the UK national screening consultation for SMA is currently calling for

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

comment as to whether criteria for this to be recommended have now been met. One of these is that a viable treatment is available. This relies on a positive recommendation by NICE, at which point there could be the potential for even earlier treatment for these 68 infants each year.

We are aware that there are sensitive considerations around the ethics of screening for a condition when the potential impact varies greatly, and the treatment delivery is invasive and requires a long-term commitment but understand that the screening consultation will be addressing potential issues.

We note that several US states have recently introduced newborn screening and those with between 1 and 3 *SMN2* copies are offered treatment. However, we note from the internationally agreed Standards of Care the variance between the 'usual' number of *SMN2* copy numbers compared with the possible 'range' (**Tillmann, A et al.**):

- Type 2 have a 'usual' *SMN2* copy number of 2 but a 'range' of 2-4 copies
- Type 3a have a 'usual' *SMN2* copy number of 3 but a 'range' of 3 – 5 copies
- Type 3b have a 'usual' *SMN2* copy number of 4 but a 'range' of 3 – 5 copies

As stated in the International Standards of Care, at the individual level, perfectly accurate predictions cannot be made about the type or severity of SMA based on the *SMN2* copy number alone. This is likely to be because other genetic and possibly environmental factors have an influence on the disease. Added to this there can be delays in obtaining *SMN2* copy number results which, for this group may impact on what is a critical window for intervention.

Group B

We note Biogen's clinical results (CHERISH Trial) and now the SHINE study. We also note the real world studies of those with SMA Type 1 including recent publication of the study by **Aragon-Gawinska, K et al.** which commented, 'new motor acquisitions were attained even in 8-year-old patients' and **Pane, M et al.** whose treatment of those with SMA Type 1 included people in the age range 3 months to 19 years, 9 months with 95 of the 104 older than 7 months, 'Our results suggest that some therapeutic efficacy is possible even after the first seven months even if the consistency or the magnitude of response was variable and often smaller than those observed with early intervention.'

This returns us to the point that stability alone can make a significant difference to quality of life and reducing the true costs of the condition for the individual, their families and

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

caregivers and health and social services (see 9 above).

We therefore consider that access is **of equal importance** for all with Type 2 and 3 where it is clinically safe, who are at a **critical point** and the medical team and family/adult agree treatment offers a potential benefit.

The need for treatment access for this group is discussed in **Burgart, A et al's** article which gives examples of:

'older patients with advanced SMA may be clinically stable in terms of vital physiological functions but on the verge of losing a key functional ability, such as communicating by computer or operating adaptive equipment'. Achieving stability is critical

Other examples might be a child whose scoliosis is progressing significantly or, as there is a tendency for children to become weaker at times of major growth spurts such as puberty, children who are reaching this stage.

An outcome that maintains stability would be sufficient reason to continue treatment.

Not all in this group will want treatment. It is a very individual decision requiring informed consent.

- **How could this group be identified in clinical practice?**

There would perhaps need to be agreement by a clinical / patient group as to guidelines for what constitutes a 'critical point' and perhaps an overarching national 'appeals group' to ensure equity. If used, as **Burgart, A et al.** point out, this would need to 'incorporate appropriate stakeholders, including patient advocates, clinicians, community members, ethicists, and others'

We suggest, that though we are aware this is a workload for already pressured clinicians, immediate work is undertaken by a group such as the NorthStar network group and also by clinicians who care for adults with SMA Type 2 and 3. This would be to review caseloads and prepare very brief details of anyone with SMA Type 2 or 3 whom they consider would meet agreed 'critical point criteria' so that numbers and geographical location can be ascertained.

If helpful, SMA Support UK could endeavour to assist with identification of this group by contacting the community as we did when we worked with NHS England to trying to

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

establish how many families with children with SMA Type 1 wanted access to the EAP. The UK SMA Patient Registry would be another potential source of assistance – with all working together.

Without this preliminary work being undertaken as a matter of urgency, we cannot know the size of this group.

Group C

This group, **of equal importance**, is all those with Type 2 and 3 who are not at a critical point, where it is clinically safe, and the medical team and family/adult agree that treatment has potential to bring stability. We note again the findings of CHERISH and now SHINE and real-world studies that have included older patients with SMA Type 1 to positive effect.

Treatment of this group will potentially bring benefits in delaying or preventing individuals reaching the ‘critical’ point of Group B. These benefits would impact positively on both quality of life and the true costs of the condition for the individual, their families and caregivers and health and social services (see previous points)

- **How could this group be identified in clinical practice?**

We suggest a similar exercise to the above. SMA Support UK could help gather this information as could the UK SMA Patient Registry – with all working together.

Again, not everyone will want this treatment. It is a very individual decision requiring informed consent. There are adults and young people who won’t want this treatment and would rather wait for one with a less invasive delivery.

In summary we identify three clinical sub groups all of whom can be identified in clinical practice. They are all of equal importance as clinical evidence demonstrates they all have the potential of benefiting from treatment. They are differentiated only so that different ‘work streams’ can be established within any MAA. They are:

- **Group A: all newly diagnosed with SMA Type 1, 2 or 3**
- **Group B: all with Type 2 or 3 who are at a ‘critical point’ in terms of the progressions of their SMA**

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

	<ul style="list-style-type: none">• Group C: all with Type 2 and 3 who are not at a critical point but where treatment will potentially bring stability
16	<p>Is there a clinically distinct subgroup of people in whom nusinersen is expected to be more clinically effective? How could this group be identified in clinical practice?</p> <p>The logistical challenges of providing treatment</p> <p>We are very aware that Centres are limited as to how many people they can manage to treat and, as noted by Burgart, A <i>et al.</i>, the need for, ‘high-level operational planning and coordination.’ Their further comments about the need for different workstreams to meet needs could fit well with our suggested groupings:</p> <p>‘The task of administering the medication consists of at least 3 clinical work flows: the first involves patients for whom lumbar puncture administration is relatively straightforward and can be performed in an outpatient clinic visit, the second involves patients who require a higher level of supportive care to safely undergo the procedure and fully recover to return home, and the third involves patients who are already hospitalized or those whose clinical condition requires recovery in the hospital. These workflows do not necessarily compete with each other for resources, so that patients queued in one work flow are not necessarily ahead of or behind patients queued in another workflow’.</p> <p>In summary: The EAP has ensured that many paediatric centres are ready and delivering treatment. We don’t know how ready adult services are to respond to new work streams. Any exercise to collate numbers for treatment must map out location of patients and a plan for ensuring efficient delivery and geographical equity.</p>
17	<p>Is there a clinically distinct subgroup of people in whom nusinersen is expected to be more clinically effective? How could this group be identified in clinical practice?</p> <p>Including all, and allowing for new developments with delivery methods</p> <p>We note the many developments in delivery for those with spinal scoliosis / who have had spinal surgery as follows:</p>

Please return to: TACommE@nice.org.uk / NICE DOCS

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

- **Germany** – 26 patients

Mousa, M *et al.* (2018) A comprehensive institutional overview of intrathecal nusinersen injections for spinal muscular atrophy # Springer-Verlag GmbH Germany, Springer Nature July 2018

‘Although we achieved 100% technical success in intrathecal nusinersen administration, our practices evolved during the course of this study. As a result of our early experience we developed an algorithm to assist in promoting safe and effective nusinersen administration in children with spinal muscular atrophy regardless of SMA type, abnormal spinal anatomy and complex spinal instrumentation.’

- **USA** – 3 patients ages 12 – 17 years

Veerapandiyar, A *et al.* (2018) Cervical puncture to deliver nusinersen in patients with spinal muscular atrophy Neurology® 2018;91:e620-e624.

‘Cervical puncture is a feasible alternative delivery route to administer intrathecal nusinersen in patients with longstanding SMA and spine anatomy precluding lumbar access when done by providers with expertise in this procedure’.

- **Germany** – 4 children

Weaver, J *et al.* (2017) Transforaminal intrathecal delivery of nusinersen using cone-beam computed tomography for children with spinal muscular atrophy and extensive surgical instrumentation: early results of technical success and safety Pediatr Radiol (2018) 48:392-397

‘Cone-beam CT guidance with two-axis navigational overlay is a safe, effective method for gaining transforaminal intrathecal access in children with spinal abnormalities and hardware precluding the use of standard techniques.’

- **Germany** – 20 children

Strauss, K *et al.* (2018) Preliminary Safety and Tolerability of a Novel Subcutaneous Intrathecal Catheter System for Repeated Outpatient Dosing of Nusinersen to Children and Adults With Spinal Muscular Atrophy J Pediatr Orthop 2018; 00:000–000

‘In summary, nusinersen via repeated intrathecal injection is effective therapy for all types of SMA, but its standard method of interlaminar delivery poses both absolute and relative challenges for a large proportion of patients. More data are needed to determine if nusinersen has comparable efficacy when delivered by subcutaneous port as compared with the standard interlaminar route. However, our initial observations are promising, and long-term administration of nusinersen via the SIC or similar device has the potential to double the number of children worldwide who can safely receive the drug while simultaneously lowering its long-term administration cost 5- to 10-fold.’

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

	<p>‘Although the SIC was designed for SMA patients with advanced disease and attendant spinal pathology, our preliminary observations have implications for younger, less severely affected patients. As private and government insurers adapt to the extraordinary costs associated with new disease-modifying precision therapies, they will likely seek practical innovations like the SIC, which have the potential to safely control administration costs while preserving therapeutic value.’</p> <p>In summary: we urge NICE to ensure that people whose SMA has created challenges in terms of the delivery of the drug are also given the opportunity to discuss the possibility with their clinicians. The ability of clinicians to explore and implement these options in the UK could lead to new methods of delivery and reduction in costs of delivery.</p>
18	<p>In summary:</p> <ul style="list-style-type: none">• We are concerned that NICE’s apparent over estimation of the population who would want this treatment and for whom it would be clinically safe may lead to incorrect assumptions by NICE as to the total budget that would be required• We ask NICE to include in their evidence base the outcomes of 5 ‘real-world’ studies of 235 patients aged 1 month – 35.7 years receiving treatment via the SMA Type 1 Expanded Access Programme.• We suggest that real world studies that comment on parent views and our own survey indicate less uncertainty about treatment outcomes than NICE concludes• We agree with NICE that both the company’s and the ERG’s approaches to economic models had serious limitations. We understand NICE’s decision to use both approaches sought to address this, but are concerned that the final ICER values may not appropriately reflect the impact of the worst health states caused by untreated SMA as reported in clinical and patient expert evidence• We seek an assurance that NICE’s economic analysis covered all the real-world costs of the health and personal health and social services required to support a person with SMA and their family and included the impact of SMA affecting more than one carer. We also wish it to be noted that we consider the model falls short in that it fails to cover the real-world costs that lie outside the realm of health and social services. We are aware this is not possible within this appraisal but consider that this needs to be urgently addressed by NICE• We contend that due to nusinersen having been assessed via an STA, the ICER threshold is inappropriate and urge flexibility when establishing what will be an appropriate range for a Managed Access Agreement.

Please return to: TACommE@nice.org.uk / NICE DOCS

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

- We urge NICE to ensure that England and Wales offer access in line with Europe and that there is no break in the delivery of treatment to infants with SMA Type 1 once Biogen's EAP closes on 1st November
- We identify three clinical sub groups all of whom can be identified in clinical practice. They are all of equal importance as clinical evidence demonstrates they all have the potential of benefiting from treatment. They are differentiated only so that different 'work streams' can be established within any MAA. They are:
 - Group A: all newly diagnosed with SMA Type 1, 2 or 3
 - Group B: all with Type 2 or 3 who are at a 'critical point' in terms of the progressions of their SMA
 - Group C: all with Type 2 and 3 who are not at a critical point but where treatment will potentially bring stability
- The EAP has ensured that many paediatric centres are ready and delivering treatment. We don't know how ready adult services are to respond to new work streams. Any exercise to collate numbers for treatment must map out location of patients and a plan for ensuring efficient delivery of treatment to all three groups and geographical equity.
- We urge NICE to ensure that people whose SMA has created challenges in terms of the delivery of the drug are also given the opportunity to discuss the possibility of treatment with their clinicians. The ability of clinicians to explore and implement these options in the UK could lead to new methods of delivery and reduction in costs of delivery.
- We are concerned that NICE's appraisal system has led to undue delays and difficulties resulting in England and Wales being almost the only countries in Europe not offering access to what is proving to be an effective treatment for so many with this devastating condition.
- We urge NICE to continue to meet with NHS England, Biogen, clinicians and patient groups to agree a Managed Access Agreement with work streams that will provide access to all with SMA Type 1, 2, and 3 whom we have identified in this response.

Insert extra rows as needed

Please return to: TACommE@nice.org.uk / NICE DOCS

Nusinersen for treating spinal muscular atrophy [ID1069]

NICE National Institute for
Health and Care Excellence

Consultation on the appraisal consultation document – deadline for comments 5:00pm on 05/09/18 email: TACommE@nice.org.uk /NICE DOCS

Checklist for submitting comments

- Use this comment form and submit it as a Word document (not a PDF).
- Complete the disclosure about links with, or funding from, the tobacco industry.
- Combine all comments from your organisation into 1 response. We cannot accept more than 1 set of comments from each organisation.
- Do not paste other tables into this table – type directly into the table.
- Please underline all confidential information, and separately highlight information that is submitted under **'commercial in confidence' in turquoise** and all information submitted under **'academic in confidence' in yellow**. If confidential information is submitted, please also send a 2nd version of your comment with that information replaced with the following text: 'academic / commercial in confidence information removed'. See the Guide to the processes of technology appraisal (section 3.1.23 to 3.1.29) for more information.
- Do not include medical information about yourself or another person from which you or the person could be identified.
- Do not use abbreviations
- Do not include attachments such as research articles, letters or leaflets. For copyright reasons, we will have to return comments forms that have attachments without reading them. You can resubmit your comments form without attachments, it must send it by the deadline.
- If you have received agreement from NICE to submit additional evidence with your comments on the appraisal consultation document, please submit these separately.

Note: We reserve the right to summarise and edit comments received during consultations, or not to publish them at all, if we consider the comments are too long, or publication would be unlawful or otherwise inappropriate.

Comments received during our consultations 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 comments we received, and are not endorsed by NICE, its officers or advisory committees.