NICE National Institute for Health and Care Excellence

Multiple Technology Appraisal

Nusinersen and risdiplam for treating spinal muscular atrophy (MA review of TA588 and TA755) [ID6195]

Guidance review following a period of managed access - Patient organisation submission

Thank you for agreeing to give us your organisation's views on these treatments following a period of managed access. You can provide a unique perspective on conditions and their treatment that is not typically available from other sources.

PLEASE NOTE: You do not have to answer every question. Your organisations involvement in the managed access agreement for these treatments is likely to determine which questions you can answer.

To help you give your views, please use this questionnaire with **NICE's guide for patient organisations "completing an organisation submission following a period of Managed Access for Technology Appraisals or Highly Specialised Technologies".** Please contact pip@nice.org.uk if you have not received a copy with your invitation to participate.

Information on completing this submission

- Please do not embed documents (such as a PDF) in a submission because this may lead to the information being mislaid or make the submission unreadable
- We are committed to meeting the requirements of copyright legislation. If you intend to include **journal articles** in your submission you must have copyright clearance for these articles. We can accept journal articles in NICE Docs.
- Your response should not be longer than 35 pages.

NICE National Institute for Health and Care Excellence

This form has 8 sections

Section 1. About you

Table 1 Name, job, organisation

1. Your name	**SMA UK**: Portia Thorman **Treat SMA**: Andi Thornton **MDUK:** Rob Burley
2. Name of organisation	Spinal Muscular Atrophy UK Treat SMA Muscular Dystrophy UK
3. Job title or position	Portia Thorman : **Head of Advocacy and Community, SMA UK** Andi Thornton: **Trustee, Treat SMA** Rob Burley: **Director of Care Campaigns and Support, MDUK**
4a. Provide a brief description of the organisation. How many members does it have?	**Spinal Muscular Atrophy UK (SMAUK)** is a national charity, founded in 1985, providing support via our Support Service team, and information about SMA to all those living with the condition and their families. Our e-news is sent to 3,736 recipients and our magazine SMA matters is sent to 3889 households. We also advocate on improving access treatment and issues surround the complexities that living with a rare condition brings. All our health information is accredited by the Patient Information Forum (PIF) and is available via our website in the form of webinars, podcasts and information sheets. We host virtual and in person events that connect the SMA Community together offering a space to share information and offer peer support. **Treat SMA** is a UK charity established back in 2017 made up of volunteers living with spinal muscular atrophy (SMA) and their parents and carers who joined hands to improve the diagnostics, standard of care, social support, and access to treatments in this severe genetic disorder. We support the efforts to speed up diagnostics and introduce treatment as early as possible. TreatSMA aims to ensure hospitals across the country can offer the highest standard of medical care to those with SMA. We promote the Standard of Care document and protocols, to reduce the risk of severe complications of spinal muscular atrophy and improve the quality of life.

	We believe that everyone with SMA has a right to treatment and work to ensure that people with all types of the SMA get the opportunity to access effective treatments. We co-operate with all other stakeholders in the UK SMA community to bring about broad access to the most appropriate treatment given the individual circumstances and advocate for appropriate levels of social support, including access to physiotherapy, hydrotherapy, occupational therapy, supportive tools and equipment – everything that reduces the burden of SMA and makes life with this severe disease more bearable. Through our extensive social media and online community reach, we encourage people with SMA, their friends and families to work together and advocate jointly for change. **Muscular Dystrophy UK (MDUK)** is the charity bringing individuals, families and professionals together to beat muscle-wasting conditions. Founded in 1959, we have been leading the fight against muscle-wasting conditions ever since. We bring together more than 60 rare and very rare progressive muscle-weakening and wasting conditions, affecting around 110,000 children and adults in the UK. We fund research, provide vital information, advice, resources and support for people with these conditions, their families and the professionals who work with them. Collaboration lies at the heart of our work and as such this submission has been collated together jointly between our three organisations
4b. Has the organisation received any funding from the company/companies of these treatments and/or comparator products in the last 12 months? [Relevant companies are listed in the appraisal stakeholder list which was provided to you when the appraisal started] **If so, please state the name of company, amount, and purpose of funding.**	**SMA UK** **Roche** — **£** Community communications and connections — **69,810** Consultancy Fees — **6,477** SMA Care UK Project — **67,354** **Biogen** Children's book project sponsorship — **15,000** **Novartis** Support Services — **37,500**

<table>
<tr><td></td><td>
Treat SMA
As a voluntary organisation led by people living with SMA, Treat SMA do not receive any funding from industry.

MDUK
<table>
<tr><th>Roche</th><th>£</th></tr>
<tr><td>European Paediatric Neurology Society congress attendance costs</td><td>1,711</td></tr>
<tr><td>Advocacy Panel event participation</td><td>900</td></tr>
<tr><td>Conference fee costs and accommodation expenses to participate in Health and Care Forum fringe event at Conservative Party Conference</td><td>608</td></tr>
<tr><td>Virtual seminar sponsorship</td><td>2,750</td></tr>
<tr><td>Health inequity co-creation exercise participation</td><td>600</td></tr>
<tr><td>Conference fee costs and attendance expenses for the Muscular Dystrophy Association Conference 2023</td><td>TBC</td></tr>
<tr><td>UK SMA Newborn Screening Alliance</td><td>50,000[1]</td></tr>
<tr><td>Novartis</td><td></td></tr>
<tr><td>UK SMA Newborn Screening Alliance</td><td>45,000[2]</td></tr>
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</td></tr>
<tr><td>4c. Do you have any direct or indirect links with, or funding from, the tobacco industry?</td><td>No for all 3 organisations</td></tr>
<tr><td>5. How did you gather information about the experiences of patients and</td><td>SMA UK, Treat SMA and MDUK conducted two surveys of the SMA community to help form this response. The surveys were open between 22nd February and 22nd March. One survey was for carers and one was for people living with SMA. The carer survey received 145 responses (135 informal carers/ 10</td></tr>
</table>

[1] This is funding for the work of the UK SMA Newborn Screening Alliance and is not being retained by MDUK.
[2] This is funding for the work of the UK SMA Newborn Screening Alliance and is not being retained by MDUK.

carers to include in your submission?	professional carers); and the survey for those living with SMA received 114 responses. We are grateful to all those who shared their experiences with us in this way. In addition, 13 detailed case studies provided by members of the SMA community have been used in this response. When we summarise the experience of an individual that has been shared with us in this submission, it has been gathered through this activity. **SMA UK :** • Membership of SMA UK social networks: -Family network- 88 members -Adult network: 23 members -Young adult network: 43 members • Working closely with SMA UK's support team who responded to 207 families through our direct support line in 2023. • SMA UK's Adult advocacy steering group • SMA UK's community podcasts • Personal experience of living with a son with SMA type 1 **Treat SMA:** • Facebook group 2000 members • Treat SMA facebook page 4,400 followers • Adult facebook group 200 members Conclusions were formed from reaching out to the UK Spinal Muscular Atrophy Community in the UK via our social media platforms, specifically facebook.

	Due to the large amount of people in the group we had a fantastic response to our requests which enabled us to cover the wide spectrum which is SMA from all types to ages on both treatments taking into account variables. Visually we had many videos and photos submitted which backed up evidence submitted on how both treatments are working for individuals and how this has not only changes their life but those around them including their siblings, partners, parents, carers and PAs.

Section 2 Living with the condition and current treatments

Table 2 What it's like for patients, carers and families to live with the condition and current NHS treatments

6. What is it like to live with the condition? Consider the experience of living with the condition and the impact on daily life (physical and emotional health, ability to work, adaptations to your home, financial impact, relationships, and social life). For children, consider their ability to go to school, develop emotionally, form friendships and participate in school and social life. Is there any impact on their siblings?	While SMA is categorised under 4 specific types, the range and impact it has on patients in all groups is highly variable and subjective. Two type 1 patients can be impacted in very different ways, even with the same clinical diagnosis in terms of SMN2 copies. The views in this document are heavily summarised and we would urge those reading the document to take time to review the specific patient comments and feedback listed in the appendices to get a far better understanding of how the condition impacts those individuals with and those caring for people with SMA . **Executive Summary** • **Ability to work or gain an education:** Limitations in workplace and educational settings due to physical and care needs, though Access to Work scheme and EHCPs can provide support. • **Emotional health and well-being:** The continuous loss of abilities and chronic sorrow significantly impact mental health, necessitating tailored support strategies. • **Adaptations to the home:** Financial and logistical challenges of home adaptations for accessibility and independence. • **Financial impact:** Significant expenses related to care, equipment, home adaptations, and the need for specialized vehicles, putting a strain on personal finances. • **Relationships:** Strain on family relationships due to care demands and the impact of SMA on siblings' emotional well-being. • **Diet:** Dietary adjustments and assistance required due to difficulties with swallowing and feeding. • **Exercise:** Limitations on physical activity due to mobility and respiratory issues, though specialized physiotherapy can help. • **Travel independently:** Challenges in accessing public transport and the need for specialized vehicles to maintain mobility and independence. 1) Mobility a) Use of Wheelchairs

	i) **Manual and Powered Wheelchairs**: The condition necessitates the use of both manual and powered wheelchairs, tailored to the individual's specific mobility limitations and lifestyle requirements. ***"In my early 20s, I used to be able to go around the house on my knees, but I can't do that now,".*** Adult ii) **Additional Modifications**: To enhance comfort, independence, and quality of life, wheelchairs often require additional modifications not covered by standard healthcare services., b) Challenges in Mobility and Independence i) **Environmental Adaptations**: . home adaptations, widening doorways, installing ramps, and modifying bathrooms are vital for allowing individuals with SMA to navigate their living spaces independently and safely. ii) **Financial and Logistical Hurdles**: The financial burden of acquiring such specialized equipment and making home adaptations can be immense. ***"Financially it is extremely tough, we have spent a lot of money adapting our house and garden for our son's needs."*** Carer of child iii) **Specialized Equipment Needs**: Beyond mobility aids, individuals with SMA may require other specialized equipment to facilitate their daily living. This includes adaptive beds, hoists for transfers, and standing frames to support physical health. The process of integrating this equipment into the home requires careful planning and can significantly impact the family's living space and finances. 2) Self-Care a) Dependency for personal care i) **Total Reliance on Others**: Individuals with SMA, particularly those with types 1 and 2, exhibit profound muscle weakness, rendering them entirely dependent on others for most aspects of personal care. This includes assistance with transfers from a wheelchair to a bed or other seating, personal hygiene tasks, and even turning in bed to prevent pressure sores. ii) **Impact of Reduced Arm Strength**: For many, especially those with types 1 and 2 SMA, limited arm strength necessitates total reliance on others even for basic self-care tasks. The

loss of autonomy in these areas significantly impacts individuals' quality of life and mental health, as they navigate the challenges of needing constant care while striving to maintain some degree of independence.

b) Eating and swallowing difficulties

i) **Challenges with Swallowing**: As SMA progresses, it affects bulbar muscles responsible for swallowing and facial expressions. Individuals may experience difficulties with chewing and swallowing, necessitating modifications to their diet to ensure safety and nutritional intake. This often involves careful selection of food textures and assistance with cutting food into small pieces or moistening it to facilitate safer swallowing

"The loss of my son's ability to swallow, smile, and effectively communicate are probably the most difficult aspects of SMA for me to come to terms with…," Carer of child

3) **Dependence on Others for Feeding**: Many individuals with SMA require help with feeding, either due to the physical inability to lift utensils to their mouth or because of the need for mechanical arm supports. The social and emotional implications of these dependencies are significant, affecting individuals' participation in shared meals and social interactions.

, **"The inability to feed myself…has massively impacted my social life. Through extreme anxiety, I am forced to exclude myself from any social events both personal and work due to feeling extremely self-conscious about needing assistance."** Adult

4) Usual Activities

", SMA significantly impacts daily life, affecting individuals' ability to participate fully in the world around them

a) Impact on Education and Employment

i) **Educational Challenges:** Despite cognitive abilities being unaffected by SMA, physical limitations can hinder access to mainstream educational opportunities. Finding a school that is both physically accessible and offers the necessary support for toileting and other personal care needs is a formidable challenge for many.

‘ I looked at 15 nurseries and 28 primary schools and accessibility was very poor at most of them. The attitude of staff is the MOST important thing, though. It doesn't matter if they have previous experience with disabled pupils but they need to have a can-do attitude and not be afraid of them. They need to see the child as a human and not a problem! They need to be able to think outside the box and ensure inclusion.’

Carer of child

ii) **Employment Limitations:** SMA also significantly impacts individuals’ capacity to engage in employment. Workplace adaptations and flexible working arrangements are essential for accommodating the unique needs of those with SMA..

“When my son was diagnosed with SMA Type 1 at 3 months old, I had no choice but to give up my job,”

Carer of child

Social Isolation

iii) **Isolation from Peers:** The need to minimize health risks, especially respiratory infections, often leads families to isolate themselves, significantly limiting social interactions, independence and impacting family dynamics. The quote in section 3 above, about assistance with feeding, highlights how anxieties around needing assistance in public settings hugely impacts social inclusion.

iv) **Limited Access to Social Activities:** The challenges extend to social and leisure activities, where physical and health considerations restrict participation. This limitation not only affects the individuals with SMA but also their family members, altering family dynamics and leisure opportunities.

v) **Challenges in Maintaining Relationships:** The strain on relationships extends beyond the immediate family to affect friendships and romantic relationships. The presence of a carer during personal or intimate moments, for example, can significantly alter the dynamics of these relationships, highlighting the nuanced ways in which SMA impacts personal and social interactions.

vi) **Impact on siblings**

Siblings report feeling that things are all focused on their brother or sister, missing out on attention from parents. They may feel anxious or worried about their sibling’s disability. Options for day trips and family

	holidays are significantly limited, giving SMA siblings fewer opportunities than their peers. As an adult sibling the caring role for their brother or sister with SMA may continue alongside formal and/or informal care provision. '***Having an SMA brother is not completely different to having a brother without SMA, we can still make up games and play, just in different ways. I treat him like a normal brother. But it does make me sad that he cannot eat or walk and run. When he is poorly in hospital, I do feel very sad and worried, and I miss my mum a lot'*** 10 year old sister of child 5) Pain and discomfort in individuals with Spinal Muscular Atrophy (SMA) brings significant challenges that directly affect their quality of life and ability to engage in daily activities. Spinal Curvature and Contractures i) **Development of Spinal Curvature (Scoliosis):** Scoliosis is a common issue for individuals with SMA, impacting mobility and overall health. The curvature of the spine can compress internal organs and cause pain ii) **Contractures and Joint Issues**: Contractures, where muscles or tendons shorten, leading to stiffness and restricted joint movement, pose daily challenges. The development of contractures contributes to a cycle of pain, reduced mobility, and further physical decline, illustrating the interconnectedness of SMA's physical impacts. b) Respiratory Issues and Discomfort i) **Breathing Difficulties**: Individuals with SMA often experience significant respiratory compromise, leading to discomfort, fatigue, and anxiety. Daily management involves routine respiratory physiotherapy, cough assist devices, and sometimes overnight non-invasive ventilation. ii) **Impact on Daily Life**: The challenges of managing respiratory issues significantly affect social interactions and independence. Reduced lung capacity leads to fatigue and decreased voice volume, making even simple conversations exhausting. Many families choose to isolate themselves to minimize health risks, leading to a secluded lifestyle. One individual described how respiratory compromise affected their ability to participate in social activities, stating that even a decrease in voice volume could limit their social interactions, illustrating how respiratory issues compound the challenges of living with SMA.

6) Anxiety and depression

Emotional Toll of SMA

i) **Chronic Sorrow**: The progressive nature of SMA means that individuals are constantly facing the loss of their physical capabilities, a process that engenders a state of ongoing grief or “chronic sorrow.” Unlike acute grief, which might diminish over time, chronic sorrow is a persistent mourning over the progressive losses experienced.

ii) **Impact on Mental Health**: The relentless progression of SMA can make traditional depression treatments less effective, as they are not designed to address the ongoing loss of function. The psychological impact extends beyond the individuals with SMA to affect their families and caregivers, who also experience stress, anxiety, and grief.

“Living with a child with SMA is emotionally draining… It is a constant worry about the future and his independence,” illustrating the pervasive anxiety about the disease’s progression and the future.” Carer of child

b) Anxiety Over Health and Future

i) **Fear of Respiratory Illnesses**: The vulnerability to respiratory complications is a constant source of anxiety for those with SMA and their families. A common cold can lead to life-threatening situations, creating a backdrop of fear and uncertainty that permeates daily life. This fear often leads to social isolation in an attempt to protect the individual with SMA from potential infections, further impacting mental health and quality of life.

ii) **Worry About Independence and Care**: As SMA progresses, the increasing dependence on others for basic needs can significantly impact self-esteem and mental health. The worry extends to the availability and quality of care, particularly as caregivers themselves face burnout.

‘I currently rely on twenty-four-hour care, which is shared between the carers I employ and my family. Independence is a factor that contributes the most to health and it can be hard in a care crisis to have your needs and wants fulfilled’ Adult

“Numbers can’t come close to showing how I battled through university – exhausted, bruised, often bleeding – determined to keep up “ Adult

	"You never know what is round the corner… There are days when the disease wins," Adult
7. What do carers experience when caring for someone with the condition?	**Appendix 2:1: Quantitative data Appendix 2:2 -2:5: Qualitative data** Caring for someone living with SMA impacts on every part of an individual's life. It is common for one family member to give up a career to take on a full-time caring role. Depending on the severity of the individual living with SMA, the carer role involves supporting with everyday activities as well as learning and delivering more specialist care at home including: - Respiratory physio (cough assist and suction) and ensuring proper use of any ventilatory support. - Physiotherapy and stretches - Personal care and transfers - Planning and risk assessing trips - Ensuring comfort through the night – inc turning and saturation monitoring in some cases. - Managing prescriptions and appointments - Sourcing specialist equipment and adaptations Aspects explored in the survey showed: **Mental health:** 67% of carers occasionally or frequently feel anxious, stressed or down because of their role as a carer. ***'Massively stressful and exhausting always being the sole carer to someone. You don't get a break or time to yourself. Outside services are limited and a lot of the time we feel very alone.'*** Carer of Adult With a lack of capacity in the NHS, patient groups support carers with access to counselling services. **Social Life**: 78% of carers felt their caring role impacted their social life, with 25% reporting that it made it almost impossible to have a social life. ***'I am fortunate enough to have excellent parents and a partner who all support me in being able to maintain some sort of social existence. However, this is still different to that of my friends who have children who don't have sma. Trying to find babysitters or carers outside of your immediate circle is virtually impossible with the higher level of needs required'*** Carer of child **Relationships:** 65% of carers felt their role occasionally of significantly affected their relationships. 5 respondents perceived their caring role to be responsible for their divorce.

	'Relationships in the household can become very strained. My daughter needs can impact everyone in the household with the constant care needed. I would say it has impacted my marriage significantly due to the tiredness and day to day routines. It's certainly not easy but we try our best' Carer of child **Finances:** 89% of carers felt their caring role had an impact on their finances, 51% reporting a significant impact. ***'Electric, fuel for the van, insurance, food, extra hotel room for carer when we go away overnight impact us massively. I can't work apart from 10 hours per week I get paid as part of my son's care team as I'm always on call/ home alone with him.'*** Carer of adult
8. What do patients and carers think of current treatments and care available on the NHS Please state how they help and what the limitations are.	**<u>Current treatments</u>** The only disease modifying treatment routinely available on the NHS to treat SMA is Onasemnogene abeparvovec, branded Zolgensma. ***Limitations*** Only suitable for babies and young children weighing up to 21kg , with up to 3 copies of SMN2, Zolgensma leaves the majority of the current SMA population in the UK without routine access to a disease modifying therapy. When administered early enough, preferably before symptoms appear, Zolgensma can modify the natural path of the disease and we are now seeing children living with the most severe type of SMA following normal developmental patterns, walking, eating and breathing independently. However, Zolgensma is not always suitable for those who fall within the eligibility criteria. There have been children who cannot access it due to initial blood tests revealing antibodies to the AAV9 virus (around 5 in 100 children tested). If the results of the other tests (liver function, full blood count, kidney function, cardiac enzymes) aren't clear, these may indicate it wouldn't be safe to administer Zolgensma. Families are careful not to expose their children to any viruses before the infusion, as any clinical instability would mean the infusion would be postponed. Following Zolgensma infusion, patients with underlying active infection, could be at an increased risk of serious systemic immune response, potentially resulting in more severe clinical courses of the infection, therefore many families choose to shield for all or part of the average 3 month monitoring phase post Zolgensma. This shielding process both pre and post Zolgensma

	puts serious limitations on family's lives, impacting siblings ability to go to school and parents' ability to go to work. In addition to the above, even if administered successfully Zolgensma is not always effective. There are rising number of cases that require additional treatments post Zolgensma infusion. '***The shielding process was pretty long after already spending 5 weeks in hospital, more for my partner being self employed. He had nearly 3 months off work not being paid because of hospital and shielding.'*** Carer of child ***'We are about 8 weeks nearly 9 weeks in from my daughter having Zolgensma, we are still having to shield as best as we can because her liver levels are to high from Zolgensma, she's also had to start a new medicine alongside the steroids because of the liver levels being too high , so lots of extra blood tests. She also had to try the steroids on drip for 3 days, but we knew this could be a side effect from Zolgensma, it can be hard with having other children who still need to go school I feel like it's pretty hard going on them, I'm not able to do anything with them etc.'*** Carer of child Access is also limited by geographical area, with only seven infusion centres across the UK, many families will have to travel long distances and stay away from home to get access. **<u>Current Care</u>** **Management interventions**, particularly for infants with Type 1, focus on **correct positioning** and ameliorating **breathing difficulties**. These include: chest physiotherapy; oral suctioning; medication to reduce secretions; cough assist; non-invasive ventilation. This is very time-consuming for parents and can be distressing for both them and their child. **Spinal scoliosis and kyphosis**, with its physical and emotional impact, is often managed initially with a lycra suit, spinal brace or jacket but surgery may be recommended if it is contributing to breathing difficulties, preventing comfortable sitting or the curvature has progressed beyond a certain point. The majority of adults living with type 2 SMA will have had spinal surgery, usually in their early teens, as will the later treated type ones as they grow up.

	Physiotherapy, Knee-ankle-foot orthosis (KAFOs) and Ankle-foot orthosis (AFOs) as well as standing frames (predominantly paediatric) help manage contractures and pain, chest physiotherapy helps manage breathing difficulties. For those children treated early, regular physiotherapy is now being used to facilitate standing and walking. Interventions, particularly for those with Type 1 and 2, to manage choking, swallowing, fatigue with feeding, digestion, constipation and managing weight, may include **tube feeding, gastrostomy, medication** and **dietary management**. A major management tool, however, is vigilance and time on the part of carers. **Standards of Care in SMA** The standards of care for SMA, published in 2017 are now out of date. The advent of new treatments have brought huge changes to the SMA landscape. Standards of care and management of the condition on the NHS vary across the UK. A real world study in 2022 showed that: *'Access to certain professionals for people with SMA is limited in the UK. Striking differences were noted between paediatric and adult populations. Limited access to care were regularly reported, with half of the study population consistently not accessing full multidisciplinary care. Access to interventions for contracture management were recorded to have significant limitations. Mobility aids and home adaptations are widely available and were also reported as the most valued interventions. Access to nutritional support or speech and language therapy appears only to be available for a small proportion of the participants. Access to respiratory care was good especially in severe forms of SMA. We found pockets of good practice in the UK that align with the SoC. However, access is not equal for adults and children and access to certain professionals is significantly limited.'*[3] The findings of this study reflect what patient groups see in the SMA community. Inconsistencies in provision of therapies, equipment and orthosis across the UK mean many people living with SMA will pay privately for mobility equipment, physiotherapy and physiotherapy equipment, orthotics and other

3 **Real-World Data on Access to Standards of Care for People With Spinal Muscular Atrophy in the UK**

Robert Muni-Lofra et al

	interventions such as neuromuscular electrical stimulation, often on the recommendation from other families via social media and not on specialist clinical advice. Other barriers to optimum care are the lack of clinical evidence in SMA and a lack of communication between tertiary, secondary and primary care providers. People of all ages and all severities of SMA experience a lack of capacity, knowledge and understanding at local level. Capacity for therapies in adult local services is particularly strained.
9. Considering all treatments available to patients are there any unmet needs for patients with this condition? If yes please state what these are	Zolgensma is only available for young children with 3 or less copies of SMA2 and under 21kg who have passed all the clinical assessment. For those living with SMA (which is the majority of prevalent cases) who do not meet Zolgensma's access criteria, there is currently no disease modifying treatment treatment to halt the progression of the disease. Therefore, both children and adults living with SMA across the UK will be living with a progressive decline, losing the ability to walk, sit, breathe and swallow at different rates depending on their severity level. Despite Spinraza having a license to treat all those living with 5Q SMA, those living with type 4 SMA have never had any access to DM treatment. This has caused significant distress. See appendix 1:4 for case study.

Section 3 Experience during the managed access agreements (MAA)

Table 3 Experience, advantages and disadvantages during the MAA period

Please present your responses by treatment under each section.

10. What are patients' and carers' experience of accessing and having these treatments?	**Appendix 3:1 Quantiative data** **Appendix 3:2 Qualiatative data** Ease of access to treatment varies depending on age, location and year of access, with access improving as the MAA rolled out across the UK and awareness of it grew among patients and health professionals.

• Please refer to the MAA re-evaluation patient submission guide	From the qualitative data, we saw some other themes emerge amongst those that struggled to get timely access the treatments on the MAA: • A lack of knowledge of the advances in treatment for SMA amongst local health providers was a barrier for many, with some people having to educate their GPs to get a referral: ***'Had to travel out of area to see a neurologist who was able to prescribe it. It took approximately one year to get this appointment. Once seen by this neurologist I received the prescription quickly.'*** Adult ***'The referral process took extremely long, six months to see a local neurologist and then a further eight months before seeing the specialist clinic'*** Adult • Geographical inequities ***'Living in the South West of England we are always the last to receive new treatments.'*** Adult • Extended timelines due to the MAA exclusion criteria For those falling within the descriptors of the exclusion criteria, access was a longer process involving a multi-disciplinary team of specialist clinicians. We heard form the parents of 3 young babies who were permanently ventilated in PICU when they first accessed treatment. **(See appendix 3:3 for case study).** ***'Being a young parent and having a recent diagnosis of SMA 1 is stressful enough on its own without having the fight we have to go through. Due to my little girl being intubated no treatment was available until we pushed and pushed and eventually got a trial for 3 months of risdiplam (which has worked wonders) now because my daughter is still intubated and the 3 months is nearly up we have to wait for it to go back to a panel meeting to see if treatment can carry on. It is so so disappointing as a parent to have to fight so much for treatment which could prevent so much for***

***children with SMA. And I think it is disgusting that children who are intubated or have tracheostomy's are not eligible for this treatment it is so so cruel*!'** Carer of child

SMA type 1 progresses at an extremely fast pace. Delaying treatment for the most severely affected has caused huge stress for parents and further irreparable damage to the child living with SMA.

'We accessed Spinraza when it was available through the EAP, I am thankful that it was not on the MAA as we would not have been eligible due to the fact he was intubated at the time.'
Carer of child

We also saw some positive comments about the speed of access to treatment, particularly with Risdiplam.

'Very smooth process that was dealt with well by my clinic most of the way but difficult to access sperm banking, which I ultimately didn't pursue as it wasn't important to me'
Adult

'I was amazed that I got a phone call from Polar speed & they keep control of the drug being given. which is nice if I was to ever forget ordering. Polar speed are a friendly team and I felt supported.'
Carer of child

Summary of data appendix 3:1

Benefits of access to Risdiplam	Negatives of access to Risdiplam
Convenient, delivered to your home Non-invasive No hospital admission required Minimal impact on daily life	Taste Liquid is difficult to draw up independently.

Benefits of access to Spinraza	Negatives of access to Spinraza
Only 3 times a year Patients feel safe and well cared for	Specialist hospital can be far from home Takes a day or more out of daily life Invasive procedure

11. What do patients and carers think are the advantages of the treatments? Please refer to the MAA re-evaluation patient submission guide	**Appendix 4:1 Quantiative data** **Appendix 4:2 Qualiatative data** For the youngest and most severely affected, treatment has given a life that would have otherwise lasted less than two years. It has brought physical gains and stability to many. Case studies and social networks show it has also brought hope to the SMA community. Our survey captures the real world impact of Nusinersen and Risdiplam across both physical and mental health. **Strength** The quantitative data from the survey shows majority of people on both treatments perceive their strength to either have stayed the same or to have improved. The free text comments from both treatment options report real world examples of how valuable stability and small gains are to people who, before these treatments were available, were facing a progressive disease and had no hope of maintaining the strength to do everyday tasks. ***'I am now able to lift my hand from my lap to the control of my wheelchair without help'*** Adult ***'I have maintained my strength and improved in some aspects. For example, putting on my headset is very important to me and I no longer strain as much as I did.'*** Teenager **Respiratory Function** Apart from two respondents, everyone living accessing treatments on the MAA feel their respiratory function has either remained the same or improved. Many commented on the obvious gains they have seen in their respiratory function since starting treatment: ***'He was in intubated for every common cold he got when he was little, 10 times in his first 3 years. Now, [aged 7] he manages common colds at home with chest physio and bi-pap.'*** Carer of child ***'I was ventilated 24 hours a day just to stay alive I now only need my ventilator when I'm asleep and can mange all naps off it. I'm so much stronger and haven't had a hospital admission for a common cold in 4 years '*** Adult

	Others commented on the less obvious gains that have had a significant impact on their quality of life: ***'My breathing was always okay, but my cough and strength of breathing have increased greatly. I can now recover from colds quicker and unblock my airways when ill.'*** Adult ***'I can now cough up phlegm a lot easier preventing hospital admissions.'*** Adult The positive impact on social communication was also highlighted by a number or respondents in the free text, all adults living with SMA; ***'I can shout much louder and hold my breath for longer'*** ***'I feel that I can speak longer than any time before without being out of breath. All my friends and relatives noticed that my voice became louder.'*** ***'I no longer run out of breath while talking. This has helped massively with both my energy levels and my ability to interact with people.'*** **Swallow** Only one respondent across both treatments available on the MAA that reported any regression in the ability to swallow. Some have seen gains, but most have noticed that there has been no change. With fear of choking a very real thing in the SMA community, stability in this area is a huge positive for the SMA community. **'There has been no minor or major progression - there has been perhaps less aspiration'** Adult **'My swallow ability is stable and it is very important for me too. Because it is in a rather poor condition and if it progresses, I could lose the ability to eat tough food.'** Adult Some have seen more noticeable gains:

	'I was starting to have difficulty swallowing around foods that were dry but I don't struggle as much now. I always grew up having olive oil to assist with the food so now I just use olive oil so it's back to how it was' Teenager ***'Was told to start thickening powder for fluids as was aspirating. That is no longer needed'***. Carer of child **Fatigue** Levels of fatigue are difficult to capture in clinical data, and the definition of fatigue is a subjective one that varies depending on baseline. Many respondents to this sliding scale question perceived their energy levels to have stayed the same or to have improved since treatment started. Some believed that although their fatigue levels had stayed the same, or increased a little, this could be due to the fact that they felt able to do more without resting during the day. ***I am tired but I do more than before as my left arm has more strength and range. I have increased hours at work so whilst I am tired at the end of a day, I am doing more because I now can.*** Adult '***I no longer need short naps in the day to recover from bursts of activity and feel I can manage a full days school/travel/play without sleeping/resting which wasn't the case before'***, Adult **Mental Health** Living with SMA with or without treatment is a burden on mental health for the individual and the whole family. Treatments on the MAA stop the progression of the disease but they do not reverse the impact up to that point. Maintaining a positive mindset whilst living in a world built for able bodied people will always be a constant mental battle for those living with SMA and their carers but new treatments bring hope. A lack of mental Health services on the NHS impacts the whole SMA community. ***'It's been a real mental soother to know I'm not getting weaker in theory and my results prove it.'*** Type 2 SMA 15-20 yrs ***'It is amazing to know that something is being done to aid sma and it makes me feel a lot less worried about the future'*** Adult living with type 3 SMA

Quality of life

Quality of life can mean different things to different people. The chart below summarises the frequency of 4 identified themes from the free text responders.

Everyday examples of how quality of life has been impacted:

1. Increased independence inc work and social life	**23**
2. Improved health	**10**
3. Stabilisation of condition inc less fear of death	**19**
4. Living not dying	**5**

1. Independence inc work and social life

'Through treatment our daughter is able to walk, a skill that was in decline prior to the commencement of treatment. She currently lives a full, happy, and high quality life including playing with friends' Carer of child

2. Health

'Huge improvement. Able to go to preschool and engage in age appropriate activities alongside peers. Improved respiratory function has also meant that we no longer avoid infection like we used to as a family, so we socialise more and lead a more normal life' Carer of child

3. Stabilisation of condition inc. less fear of death

'I'm not quite sure how to put this. Risdiplam has improved every part of my life. I can now talk to people and they understand every word because my voice box works again. I no longer feel like I'm dying. At all. Let alone soon.' Adult

4. Life itself

'He would not have a life if it was not for treatment' Carer of child

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Carer Quality of Life

The carer survey saw some different themes emerge as to what they perceived had the greatest impact on their quality of life. Alleviation of stress relating to the poor physical health of the people they care for was one of the most common responses in the free text. The frequency of themes found are summarised below, some respondents mentioned more than one of the themes;

<table>
<tr><td>Increased independence of person living with SMA</td><td>20</td></tr>
<tr><td>Increased independence of carer</td><td>7</td></tr>
<tr><td>Improved physical health of person living with SMA</td><td>37</td></tr>
<tr><td>Stabilisation of the condition</td><td>24</td></tr>
<tr><td>Living not dying</td><td>2</td></tr>
<tr><td>Less stress/ worry for carer</td><td>27</td></tr>
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12. What do patients or carers think are the disadvantages of the treatments?

Please refer to the MAA re-evaluation patient submission guide

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The data collected as well as experience supporting people through patient organisations, shows that the treatments do not impact individuals living with SMA in the same way. Two individuals with the same SMN2 copy numbers and presenting similarly clinically will not necessarily have the same treatment outcomes. For a minority of individuals, 2 in our data sample, treatment is not effective, or side effects decrease quality of life.

SMA social media groups and forums have taken a toll on some of the SMA community. People will always compare themselves to those in similar situations and the fact that treatments effect everyone differently has been difficult for many, with unfulfilled high expectations for treatment outcomes.

Treatment has also introduced disruption into some people's lives, adjusting to the treatment and monitoring schedule has been difficult for some:

'***I think one of the challenges that has come with being on treatment is the patient work/life balance. I think that there is a misconception that clinicians have about people living with SMA. It's almost as if they don't realise we are actually capable of acquiring jobs and contributing to society. So***

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	cloying to balance regular hospital checkups that usually take you away from home for either the whole day or multiple days is sometimes challenging. 'Adult Some patients have reported side effects from both treatments that have impacted their quality of life such as headaches from lumbar punctures or gastric problems from Risdiplam. See section 10 for disadvantages of how treatment is accessed. There were not a significant amount of disadvantages reported by the community.
13. What place do you think these treatments have in future NHS treatment and care for the condition? Consider how these treatments have impacted patients and how it fits alongside other treatments and care pathway.	<u>Choice</u> It is important for the SMA community to have a choice of all available treatments on the NHS. There is not one treatment that is effective for all, both clinical and real world evidence has shown that there are non-responders to all of the treatment options, where one treatment is ineffective, another might get better outcomes. Choice and trial and error is currently the only way to optimise treatment outcomes for SMA. When newborn screening for SMA is in place, having the choice of three treatments for up to 4 SMN2 copies will allow a treatment option for all, with the Sprinraza license not limited by SMN2 copies. <u>Access for all</u> Patients have seen benefits from treatment across the severity spectrum. Access for all from those fully ventilated to those living with type 4 is the only way to ensure equity of access for the whole SMA community. <u>Newborn Screening</u> Will health outcomes directly related to speed of access, the future has to be one where people living with SMA are diagnosed through newborn screening, the only way to ensure timely access and optimum outcomes for all living with SMA. <u>Combination therapy</u> Both Risdiplam and Nusinersen impact the function of the SMN2 gene, Zolgensma effectively replaces the faulty or missing SMN1 gene. Clinical trials are currently assessing the efficacy of using dual therapy to maximise the production of the SMN protein.The future could see either of the treatments being used as a combination therapy with Zolgensma.

Section 4 Patients views on assessments used during the MAA

Table 4 Measurements, tests and assessments

Please present your responses by treatment under each section.

14. Results from tests and assessments are used to help reduce uncertainty about the effectiveness of treatment. **How well do you think these tests and assessments worked in measuring the effectiveness of these treatments?**	**Appendix 5:1 Quantiative data** **Appendix 5:2 Qualiatative data** Many agreed the MAA assessments were effective at measuring some physical outcomes of treatment and the official recording of outcomes was appreciated. Perspectives also showed the difficulties of capturing how treatment has impacted daily life. The themes captured by the free text responses are summarised below: 1. No assessment of real-world milestones or daily life activities. ***'Luckily the tests showed a lot of positive impact, however its not the whole picture. Seeing a child every day on treatment, I get to see all the small things she can now accomplish that a test cannot - such as the length of time she can now weight bare or the fact she can now eat her dinner without getting tired.'*** Carer of child ***2.*** A snapshot in time is not a fair assessment, may be assessed when fatigued or having an 'off' day. ***'Time of day the assessment is carried out impacts the results. The later the day the more fatigued' '*** Carer of child **3.** Especially difficult for children in a clinical environment. ***'They look at a snapshot in time on that particular day, at that particular time. Our little boy is often shy when he first meets people/sees people for the first time in a while, so takes a while to warm up. Early on tests may not show real-life results as he'll be more nervous about doing anything, particularly as there are usually other conversations going on in the room at the same time. Additionally at his age he doesn't understand everything that he's asked to do, with some of***

	the tests being things he's never been asked to do before so there's no opportunity to learn/understand what's being asked of him at the time.' Carer of child 4. No measurement of improvements in mental health or confidence. ***'The assessments and tests are good but do not pick up necessarily on how much benefit mentally as well as physically being on the drug gives. It has given my wife and myself hope about the future as even if the drug only slowed down the effects of SMA this would be a massive achievement but as it stands we have actually seen gains with her swallowing and ability to move her arms***.' Carer of adult 5. Some important factors are not included in the assessments. ***'No assessments or tests for bulbar function which has been our biggest improvement. Gone from completely tube fed to mostly oral eating since being on risdiplam.'*** Carer of child
15. Were there any tests or assessments that were difficult or unhelpful from a patient's or carer's perspective?	Whilst the tests were generally considered as effective at measuring gross and fine motor skills, they do not accurately represent outcomes in what is a multi-system condition. Formal assessments of bulbar function and respiratory drive for example would give a more holistic picture of efficacy. The Patient reported outcomes (PROMS) could be an excellent way of collecting real life qualitative data, but will only be successful if embedded into clinical practice with good communication. Many people were not aware of these assessments at all until the end of the MAA period. As the requirement was to complete the PROMs near to the time of your clinic appointment, it would have made sense to complete it whilst in clinic, or whilst waiting for the appointment. Adults living with a slower progression have found the 6 monthly assessments a burden. The appointment, often far from home can take a lot of organising and also a whole day out of work for some. When assessments 6 months apart rarely show any significant differences for adults living with SMA, it would be more helpful and less of a practical and emotional burden to have an annual clinical assessment. ***'[We need] new tests designed specifically for adults with SMA which can measure improvement in much smaller increments. A more joined up and robust approach to the collection of qualitative data which reflect more accurately the positive impact treatment has on the individual.'*** Adult

	There were also several comments made in the survey about a lack of continuity, variations in equipment or clinician from one assessment to the next made people concerned about the validity of the outcomes. ***'I think the test should be videoed, so the assessments are carried out exactly as the previous assessment.'*** Adult The knowledge that any regression in assessment scores could result in removal of treatment causes the SMA community significant distress. If it was made clear to patients that the quantitative data from assessments is looked at holistically with qualitative data collected by a range of methods, there would be less stress on people living with SMA and their carers.
16. Do patients and carers consider that their experiences (clinical, physical, emotional and psychological) were captured adequately in the MAA tests and assessments? If not please explain what was missing.	See section 14
17. What outcomes do you think have not been assessed or captured in the MAA data? Please tell us why	**Respiratory Health** Good respiratory health is often what keeps people living with SMA out of hospital. Lung function tests are carried out by some centres but not all (these tests are not suitable for the more severely affected as creating a seal around the mouthpiece can be very difficult with weak facial muscles). Everyone should experience a multi-disciplinary approach to assessment, with effective collaboration between neuromuscular and respiratory teams.

	Bulbar function Whilst information on bulbar function is collected anecdotally, a more formalised approach is required to provide clinical evidence on the impact of treatments on swallowing, chewing, voice strength and mouth opening. All of these have a significant impact on quality of life for those living with SMA. **Everyday tasks** The main theme running through the research for this submission has been the positive impact of treatment on daily life. Tailoring formal but individualised assessments to capture this would be a step towards more realistic data. For example, speed to fasten buttons or type on a keyboard, whatever measures the individual feel represents improvements in their personal daily life tasks. Improving communication around PROMs would also facilitate this.

Section 5 Patient population

Table 5 Groups who may benefit and those who declined treatment

Please present your responses by treatment under each section.

18. Are there any groups of patients who might benefit more or less than others from these treatments? If so, please describe them and explain why.	Since SMA is a spectrum condition, inevitably some will benefit more than others. Furthermore, some may not even wish to change their on-going lifestyle for personal reasons. However, we must be careful defining benefit as this is a non- quantifiable variable and almost always personal. The truth is – treatment should be available to ALL those who want it and only withdrawn in cases where declines continue to be observed. The lifetime costs of managing the impact of SMA – the healthcare, equipment and home adaptations, and the support at school and work – can be huge. For adults, the value of stabilisation of the condition cannot be underestimated.

19. Were there people who met the MAA eligibility criteria who decided not to start either of these treatments? Please state if known the proportion of eligible patients who did not start the treatment and any reasons for this.	It is estimated that globally, 1/3 of eligible adults have not started treatments. There is currently no knowing how accurate this estimate is, Many adults not accessing treatment are also not engaging with patient organisations or completing surveys. Anecdotally however, we can say that adults living with SMA choose not to access treatment due to concerns about their fertility, or because of a lack of long term evidence. Some, who are experiencing a slow disease progression, are content living with SMA and have adjusted to the lifestyle that it demands. In the paediatric population, now with improved information and communication around treatments there are not currently any families that we know of as patient groups that choose to not access treatment. Historically, there have been a few families who, with clinical support, have chosen not to access treatment due to the progressed nature of the disease and the impact that would have on the quality of life of the child and the family for a lifetime. This could be a decision other families may take in the future which presents ethical issues.

Section 6 Equality

20. Are there any potential equality issues that that should be taken into account when considering this condition and the treatment? See NICE's equality scheme for more details.

We have reported on survey responses from 11 people living with SMA in the home nations (5 Scotland, 3 Northern Ireland, 3 Wales) NICE guidance do not have jurisdiction in these home nations. The Health and Social Care (HSC) in Northern Ireland and Scottish Medicines Consortium (SMC) make decisions on guidance and assessments of these disease modifying treatments.

Nusinersen needs to be administered in treatment centres equipped with the resources for intrathecal administration (injection into the spinal canal). There are no paediatric treatment centres in Wales and no adult treatment centres in any of the Devolved Nations. This means that

patients must either travel very long distances for treatment – potentially hundreds of miles – or have access to a more limited range of treatment options

Section 7 Other issues

21. Are there any other issues that you would like the committee to consider?

Section 8 Key messages

In up to 5 sentences, please summarise the key messages of your statement:

- There is a clear unmet medical need in the case of SMA with fatalities and ongoing deterioration of health in affected individuals that could be immediately addressed through proposed treatments which can stop deterioration and bring about stability, improved respiratory health, preventing the life threatening impact of relatively minor illnesses.
- All patients regardless of type, age, copy number or disease progression must have access to treatments that meets both their clinical and non-clinical circumstances and ability to choose or switch treatments that suit their individual needs in line with licencing agreements.
- The natural history of SMA is progressive. Anything better than deterioration (e.g. stability) should be considered a positive outcome.
- The mental health of people living with SMA and their carers has an immeasurable impact on lives. Receiving treatment (that is not designed to treat psychological issues), has a huge positive influence on the emotional wellbeing of the whole SMA community and their support networks.

- The availability of these two treatments through the MAAs has changed the lives of the SMA community, and combined with the availability of Zolgensma has completely altered the lived experienced of this still devastating condition for individuals and families

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