

Single Technology Appraisal

Intrathecal onasemnogene abeparvovec for treating spinal muscular atrophy in people 2 years and over [ID6556]

Patient Organisation Submission

Thank you for agreeing to give us your organisation's views on this technology and its possible use in the NHS.

You can provide a unique perspective on conditions and their treatment that is not typically available from other sources.

To help you give your views, please use this questionnaire with our guide for patient submissions.

You do not have to answer every question – they are prompts to guide you. The text boxes will expand as you type. [Please note that declarations of interests relevant to this topic are compulsory].

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 10 pages.

About you

1. Your name	SMA UK: Portia Thorman Treat SMA: Dr Gennadiy Ilyashenko MDUK: Dr Charlotte Roy
2. Name of organisation	Spinal Muscular Atrophy UK Treat SMA Muscular Dystrophy UK
Charlotte Roy	Portia Thorman : Head of Advocacy and Community, SMA UK Dr Gennadiy Ilyashenko: Trustee, Treat SMA Dr Charlotte Roy: Life Sciences Policy and Influencing Manager, Muscular Dystrophy UK
4a. Brief description of the organisation (including who funds it). 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 to treatment and issues surround the complexities that living with a rare condition brings. We are accredited to the Patient Information Forum (PIF) This shows that we produce SMA health information that is reliable, current, and based on evidence. We host virtual and in person events and moderate 5 What's App groups that connect the SMA Community together offering a space to share information and offer peer support Treat SMA Currently we have 3 trustees and 2 volunteer members as part of the management team, but we have over 5000 active patients and carers within our social media groups. We are a small but active voluntary organisation which campaigns for access to treatments for Spinal Muscular Atrophy. We also play an active role in supporting the community through webinars relating to physio, treatments as well as provide a 24/7 support service for patients and carers. The organisation is funded purely through public donations, and nobody receives a salary for their involvement. 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-

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	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 bringing the treatment to NICE for evaluation or any of the comparator treatment companies in the last 12 months? [Relevant companies are listed in the appraisal stakeholder list.] If so, please state the name of the company, amount, and purpose of funding.	SMA UK <table border="1" data-bbox="687 528 2038 932"> <tr> <th colspan="4">2025-2026 (April- March)</th></tr> <tr> <th>Name of company</th><th>Type of funding</th><th>Purpose of funding</th><th>Amount</th></tr> <tr> <td>Biogen</td><td>Grant</td><td>Spot the signs national campaign</td><td>£20,838</td></tr> <tr> <td rowspan="2">Novartis</td><td>Grant</td><td>Spot the signs national campaign</td><td>£20,840</td></tr> <tr> <td>Sponsorship</td><td>SMA Care UK</td><td>£80,000</td></tr> <tr> <td rowspan="2">Roche</td><td>Grant</td><td>Spot the signs national campaign</td><td>£11,000</td></tr> <tr> <td>Grant</td><td>SMA Care UK</td><td>£75,000</td></tr> </table> Treat SMA No funding from any of the companies to declare. MDUK No funding from any of the companies to declare.	2025-2026 (April- March)				Name of company	Type of funding	Purpose of funding	Amount	Biogen	Grant	Spot the signs national campaign	£20,838	Novartis	Grant	Spot the signs national campaign	£20,840	Sponsorship	SMA Care UK	£80,000	Roche	Grant	Spot the signs national campaign	£11,000	Grant	SMA Care UK	£75,000
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4c. Do you have any direct or indirect links with, or funding from, the tobacco industry?	No for all 3 organisations
5. How did you gather information about the experiences of patients and carers to include in your submission?	• 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 2024. One survey was for carers, and one was for people living with SMA. The carer survey received 145 responses (135 informal carers/ 10 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 in this submission, it has been gathered through this activity. • Between December 2025 and January 2026, SMA UK ran a second survey focusing on the impact of treatment on mental health, reliance on carers and HCRU. Responses from the 113 participants also informed this submission. The high and wide-ranging response rate was achieved by reaching out to the UK Spinal Muscular Atrophy Community via the three charities' social media platforms, in particular Facebook and What's App groups.

Living with the condition

6. What is it like to live with the condition? What do carers experience when caring for someone with the condition?	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 patients with the same ‘type’ diagnosis can be impacted in very different ways, even when they have the same clinical diagnosis in terms of SMN2 copies. 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 specialised 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 specialised physiotherapy can help. • Travel independently: Challenges in accessing public transport and the need for specialised vehicles to maintain mobility and independence. 1) Mobility
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	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. <i>"In my early 20s, I used to be able to go around the house on my knees, but I can't do that now,"</i> Adult ii) Additional Modifications: To enhance comfort, independence, and quality of life, wheelchairs often require additional modifications not covered by standard healthcare services., 2) 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 specialised equipment and making home adaptations can be immense. <i>"Financially it is extremely tough, we have spent a lot of money adapting our house and garden for our son's needs."</i> Carer of child iii) Specialised Equipment Needs: Beyond mobility aids, individuals with SMA may require other specialised 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. 3) Self-Care i) Total Reliance on Others: Individuals with SMA, particularly those with early onset SMA treated post symptomatically, 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: Many, especially those with early onset SMA treated post-symptomatically, have limited arm strength which necessitates total reliance on others even for
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	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. 4) Eating and swallowing difficulties i) Weak chewing and swallowing muscles: 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. <i>“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...”</i> ii) Dependence on Others for Feeding: Many individuals with SMA require help with feeding, either due to their physical inability to lift utensils to their mouth or because of their 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 5) Access to education and work 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>‘ 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</i>
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	<i>the child as a human and not a problem! They need to be able to think outside the box and ensure inclusion.'</i> Carer of child ii) Employment Limitations: SMA can also significantly impact individuals' capacity to engage in employment. Workplace adaptations and flexible working arrangements are essential for accommodating the unique needs of those with SMA. <i>"When my son was diagnosed with SMA Type 1 at 3 months old, I had no choice but to give up my job,"</i> Carer of child 6) Social Isolation i) Isolation from Peers: The need to minimise 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. ii) 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. iii) 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. 7) 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.
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‘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

8) Bones and joints

- i) **Development of Spinal Curvature:** Scoliosis and kyphosis are common issues 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.

9) Respiratory Issues

- 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.

10) Anxiety and depression

- 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. <i>“Living with a child with SMA is emotionally draining... It is a constant worry about the future and his independence,”</i> Carer of child iii) 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. iv) 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>‘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’</i> Adult <i>“Numbers can’t come close to showing how I battled through university – exhausted, bruised, often bleeding – determined to keep up”</i> Adult

Current treatment of the condition in the NHS

7. What do patients or carers think of current treatments and care available on the NHS?

Current treatments

The only disease modifying treatment routinely available on the NHS to treat SMA is Onasemnogene abeparvovec, branded Zolgensma, this is only available to patients under 21kg aged up to 2 years old (or older with the guidance of a multidisciplinary panel if still within this weight limit).

Risdiplam (Evrysdi) and nusinersen (Spinraza) are not currently recommended for routine use by NICE, but are offered under a Managed Access Agreement (MAA), currently under review. While patients appreciate current access to nusinersen and risdiplam, the MAA framework is viewed with significant anxiety rather than security. For a degenerative condition like SMA, the fear that a life-sustaining treatment could be withdrawn due to a change in funding (rather than a change in clinical need) creates significant psychological distress.

Despite this uncertainty, both risdiplam and nusinersen have had a substantial positive impact on the SMA community. Real-world evidence shows that, for the majority, these treatments stabilise symptoms, which people with a progressed form of SMA describe as a major clinical success. Preventing the loss of fine motor skills, such as being able to use a computer mouse or feed themselves, allows individuals to maintain independence, education, and employment. Stabilising respiratory function reduces emergency admissions and provides confidence that essential abilities such as swallowing or transferring independently are unlikely to deteriorate. This stability directly supports mental wellbeing, confidence, and quality of life; in a survey of 113 people receiving either therapy, 63% reported increased confidence and 62% reported improved mental wellbeing.

"Without treatment, I would face severe disability and a negative impact on my future prospects. Now, I am well integrated into university and plan for my career with confidence." Adult living with SMA

"The constant fear of 'what will I lose next year?' has been replaced by a sense of security. That peace of mind is worth as much as the physical strength." Adult living with SMA

Reduced reliance on Healthcare Resources

Treatment has also reduced reliance on healthcare resources. More than half (55%) of the 2025/26 survey respondents reported fewer GP visits, and 47% reported reduced need for emergency services. Additionally, 32% reported a decreased reliance on specialist equipment such as cough-assist or suction devices, while 44% reported no increase, indicating that treatment helps prevent progression to more complex or intensive equipment needs.

Reduction in daily care needs

Carers reported significant benefits as well. The 2025/26 survey saw on average, there was a 23% reduction in daily care needs, freeing nearly three hours per day for work, family responsibilities, or rest. Many described feeling less anxious and more hopeful, and improved patient stability also enhanced carers' sleep and overall wellbeing. Several respondents noted that reduced care demands enabled them to return to work or increase their hours, highlighting the broader social and economic value of maintaining stability in SMA.

"My child can now attend birthday parties and play dates without me worrying they will be too exhausted to function the next day. They feel like 'one of the kids' now."
Parent of child with SMA

Treatment choice is dependent on individualised clinical and social priorities and discussions with specialist clinical teams. There is not a one fits all solution to SMA treatments. Some experience side effects to one or the other treatment, and there are a range of further considerations:

Risdiplam (Evrysdi) pros

- **Convenience:** Risdiplam is highly valued for its oral administration, which has transformed the daily lives of many people. It avoids the need for frequent hospital stays and invasive procedures. The tablet version has improved people's freedom of movement, enabling easier storage and travel, without the concern of keeping a liquid cool.
- **Surgical Barriers:** Many SMA patients have had spinal fusion surgery for scoliosis, making the lumbar punctures required for nusinersen difficult or impossible. For these patients, risdiplam is often their only viable treatment.
- **Mental Health:** Carers report significantly lower anxiety levels when treatment can be administered at home rather than via a stressful hospital procedure, which for some, involves sedation.

Nusinersen (Spinraza) pros

- **Long term evidence:** There is longer term evidence of the safety and efficacy of Spinraza across the SMA spectrum, this is hugely persuasive for many.
- **Reduced responsibility:** The responsibility of handling and administering such an expensive and crucial treatment (risdiplam) can be too burdensome for some. They are reassured by the security of having treatment administered in a clinical setting and appreciate the regular contact with the specialist clinical teams that nusinersen brings.

- **Reduced burden of the daily dose:** Many prefer having three treatment days a year, knowing they are free to forget about treatment for most of the year.
- **Fertility:** Risdiplam comes with a caution of a possible impact on fertility, particularly in men. Whilst the impact on fertility in humans needs further research, this does influence the treatment choices of some. nusinersen allows for treatment throughout family planning for men.

No access to treatment

While significant progress has been made in treatments for SMA, there remains a group of individuals who are still unable to access, tolerate, or benefit from currently available therapies. This includes people who:

- are unable to receive nusinersen due to complex spinal fusions, scoliosis, or because they cannot tolerate the respiratory risks associated with repeated sedation or the invasive nature of lumbar punctures
- have experienced severe or intolerable side effects with risdiplam
- have started a treatment but not achieved meaningful clinical benefit, meaning that despite best efforts the therapy is not suitable or effective for them

As a result, there is still a cohort of patients with clear unmet need who currently remain without an appropriate treatment option.

Current Care

Management interventions, particularly for those living with Type 1 and 2, focus on correct positioning and ameliorating breathing difficulties. These include: chest physiotherapy; oral suctioning; medication to reduce secretions; cough assist; non-invasive ventilation. Interventions require regular monitoring and assessment, usually in 6 monthly specialist respiratory clinics, often involving overnight sleep studies in specialist hospitals. This is very time-consuming for parents and carers and can be distressing.

Spinal scoliosis and kyphosis, with its physical and emotional impact, is often managed initially with an orthotic 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. Most adults living with type 2 SMA will have had spinal surgery, usually in their early teens, as will the post-symptomatically treated type 1s .

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.

Other interventions

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 (SoC) in SMA

The standards of care for SMA, published in 2017 are now out of date. The advent of new treatments has 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.’¹

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 interventions such as

¹ Real-World Data on Access to Standards of Care for People With Spinal Muscular Atrophy in the UK

[Robert Muni-Lofra](#) et al

	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 challenging.
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9. What do patients or carers think are the advantages of the technology?

Permanent solution

The most transformative advantage of IT-Zolgensma is that it is designed as a one-time administration.

- Patients on risdiplam must take a daily oral solution for life. Patients on nusinersen require lumbar punctures every four months (maintenance phase) indefinitely.
- By delivering a functional copy of the SMN1 gene directly into the cerebrospinal fluid (CSF), it addresses the root cause of the disease in a single event. This removes the treatment burden and eliminates the risk of missing doses.
- It removes the medicalisation of daily life. Patients and carers value the freedom from the lifelong anxiety of ongoing medication schedules, repeated hospital visits, and the cumulative physical strain of long-term therapies.
- As a one-time intrathecal injection, IT-Zolgensma may be more feasible for individuals who cannot tolerate repeated lumbar punctures required for nusinersen and also offers an alternative for people who cannot continue risdiplam due to severe side effects or lack of meaningful clinical benefit, providing a potential option for those with limited or no accessible treatments
- In a world where current treatments feel fragile due to managed access agreements, the one and done nature of gene therapy offers the psychological and physical security required to plan for a future defined by ambition rather than degeneration.

New Options for All Ages and Types of SMA

- This treatment uses a proven gene-replacement method designed to help stabilise the condition and prevent further progression. While the original intravenous (IV) version of Zolgensma has already changed lives for infants with SMA, people living with SMA are excited to see that the intrathecal (IT) version adapts this same technology for a wider range of patients.
- By delivering the treatment directly into the spinal fluid, IT-Zolgensma opens the door for older children, teenagers, and adults to receive gene therapy, many of whom previously had no access to this type of treatment.
- Early clinical data for IT-Zolgensma suggest the potential for stabilisation in older individuals, and the lived experience of people on existing therapies helps illustrate why this outcome is so meaningful. For many, preventing further decline is the difference between maintaining independence and losing it; between remaining in work or education and withdrawing; and between feeling secure about the future or living in fear of deterioration.

- This treatment also opens a door to gene therapy for young children diagnosed with type 2 or 3 SMA. This is also the case for older, heavier type 1 children who narrowly missed out on the first version of Zolgensma due to safety concerns related to weight restrictions. Accepting this exclusion has been very difficult for the families of these cohorts. There are clinically weak children who have been diagnosed with type 2, who on clinical assessment are similar to some diagnosed with type 1. Because of the overlaps on the SMA spectrum, a diagnostic classification of 'type' is not appropriate for drug access criteria.

Direct Central Nervous System Targeting

- For patients and their families, the shift to intrathecal delivery is more than just a medical update, it is an expansion of hope. It addresses the physical realities of growing older and heavier with SMA, offering a path to treatment that was previously unavailable.
- Because traditional IV doses must increase as a patient grows, the viral load eventually becomes too high for the liver to handle safely. IT delivery uses a smaller, concentrated dose that is not based on weight. This allows teenagers and adults to receive gene therapy without the safety risks associated with high-dose IVs.
- Some people with SMA report that they worry about whether a systemic medicine is actually reaching their nervous system. The body's natural blood-brain barrier can act as a wall, keeping treatments out. By injecting the therapy directly into the spinal fluid, the medication bypasses that barrier. It goes straight to the motor neurons, giving patients confidence that the treatment is reaching the 'target zone' immediately.

Safety Profile

For older and heavier populations, systemic medications can impact other organs over decades of use. High-dose systemic gene therapy can significantly impact organs such as the liver. By using the IT route, the total viral load introduced into the body is significantly lower than the IV version, potentially reducing the risk of systemic side effects while still providing the necessary SMN protein to the motor neurons.

Equity and Social Inclusion

Expanding access to gene therapy is a significant step toward medical equity. By extending this technology to older individuals and covering all types of SMA, we ensure that life-changing innovation is not restricted to a small group of infants.

Access for the whole SMA Spectrum

For years, many families felt 'left behind' by the eligibility criteria of the original IV therapy, only available post-symptomatically to type 1 babies. This was particularly difficult because SMA is a clinical spectrum, yet treatment access was often dictated by rigid 'Type' classifications. While SMA is often categorised into Type 1, 2, 3 or 4 these are clinical snapshots rather than absolute boundaries. Two patients with nearly identical symptoms might receive different diagnoses depending on when or where they were assessed. We have seen this issue in the current population. By moving toward a treatment that is accessible regardless of age or specific Type classification, we acknowledge that every person living with SMA deserves the opportunity to access gene therapy.

10. What do patients or carers think are the disadvantages of the technology?	Lack of data and decision making For many people living with SMA and their families, the possibility of accessing a one-time gene therapy in the future introduces a complex and highly individual set of considerations. While some may welcome the idea of a potentially long-lasting, single-dose treatment, others may approach the choice more cautiously – particularly given the limited long-term data available for older or heavier individuals who would receive an intrathecal gene therapy. Although intravenous gene therapy has been used widely in infants, the IT formulation remains relatively new in the clinical landscape, and evidence on its long-term safety, durability and comparative effectiveness is still emerging. Satisfied with current treatments These uncertainties may result in some individuals or carers adopting a “wait and see” approach. People who have experienced stability on ongoing treatments such as risdiplam or nusinersen may prefer to continue with therapies that are familiar, adjustable and reversible, rather than switch to a permanent intervention whose lifetime effects remain unknown. For some, the irreversibility of gene therapy, and the fact that its effects cannot be modified or discontinued once delivered, adds to the psychological complexity of decision-making. Uncertainties about future pathways Another consideration relates to the future treatment pathway. At present, there is no clear clinical consensus on whether people would remain eligible for, or be able to return to, therapies such as risdiplam or nusinersen after receiving gene therapy. Although it is not known whether anyone would need to resume treatment after gene therapy, some individuals may still value the reassurance of an ongoing therapy that can be adjusted, monitored and continued over time. The possibility that they might feel gene therapy is not delivering the expected benefit, even if this cannot currently be predicted, may lead some people to prefer the security of maintaining their existing treatment rather than considering a permanent intervention with limited long-term data. Spinal Access Complications Many patients in this demographic have had spinal fusions with metal rods. Carers may fear that the procedure to deliver the drug will be traumatic, unsuccessful, or require Interventional Radiology (X-ray guidance), which adds a layer of procedural anxiety and radiation exposure. One time treatment: Because this is a one-time treatment, there is immense pressure for the injection to be perfect. The fear that the dose might not be distributed correctly due to severe scoliosis is a common concern.
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	AAV9 Antibodies: If a patient has naturally occurring antibodies to the AAV9 virus (often through common environmental exposure), they are currently ineligible for the treatment.
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Patient population

11. Are there any groups of patients who might benefit more or less from the technology than others? If so, please describe them and explain why.	<u>Benefit More</u> 1. People experiencing decline on current treatments Some patients currently on treatment find that their condition continues to slowly decline. For these individuals, the maintenance approach of their current medication may no longer be sufficient. A one-time gene therapy offers a different biological mechanism to target the root cause of the disease, providing a new opportunity for meaningful stabilisation when other options are losing efficacy. 2. Those unable to tolerate current treatments Some patients are currently untreated because they cannot tolerate the side effects of existing medications or the frequent, invasive procedures required to administer them. IT-Zolgensma i offers a viable path forward for those who have had to discontinue other therapies due to adverse reactions or delivery complications. 3. Heavier type 1 children There is a cohort of type1 children, many of whom live with complex needs, that were on the upper weight limit, or who were just over it, when IV Zolgensma became available. For these children the safety risks were considered too high. This was a very difficult time for the parents and families who felt like they had narrowly missed out on the opportunity of a one and done therapy. IT Zolgensma gives these children a second chance. <u>Benefit Less</u> 1. People with naturally occurring antibodies to the AAV9 virus Will not be able to receive gene therapy. 2, People with spinal fusions Spinal fusions could make intrathecal access difficult or impossible, especially if done a long time ago. Likelihood of success would have to be assessed on a case-by-case basis.
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Equality

12. Are there any potential equality issues that should be taken into account when considering this condition and the technology?	At present, access to gene therapy is limited to very young children living with SMA type 1, creating a clear inequality across the SMA community. Heavier type 1 children and children, teenagers and adults living with other types of SMA, many of whom have lived with the condition for many years, currently have no opportunity to benefit from gene therapy, and some also have limited or no access to existing treatments. This difference in eligibility creates inequity between those able to receive gene therapy and those who are not, despite comparable levels of unmet clinical need. Intrathecal gene therapy has the potential to reduce this inequality by extending a treatment option to the whole SMA community, enabling more people with SMA to access and, importantly, choose the treatment that is right for them.
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Other issues

13. Are there any other issues that you would like the committee to consider?	
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Key messages

14. In up to 5 bullet points, please summarise the key messages of your submission.	• Transformative Single-Dose Solution: Intrathecal onasemnogene abeparvovec is designed as a one-time administration that addresses the root cause of the disease. This removes the medicalisation of daily life and the anxiety associated with lifelong medication schedules. • Optimised Delivery for Heavier Patients: Delivering the therapy intrathecally bypasses the blood-brain barrier and allows for a smaller, concentrated dose. This makes gene therapy safer and more feasible for older or heavier patients who were ineligible for intravenous versions. • Addressing Health Inequality: Extending gene therapy to the whole spectrum of SMA, older children, teenagers, and adults reduces the current inequity where only very young infants have access to such technology. It ensures more people can choose the treatment that is right for them. • Stabilisation as a Critical Outcome: For older individuals, preventing further decline is a major clinical success that supports independence, mental wellbeing, and the ability to remain in education or employment. • Significant Unmet Need: While current treatments have improved lives, a specific group of patients remains with no viable options due to complex spines, intolerable side effects, or a lack of meaningful clinical benefit from existing therapies.
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Patient organisation submission

Intrathecal onasemnogene abeparvovec for treating spinal muscular atrophy in people 2 years and over [ID6556]