NICE National Institute for Health and Care Excellence

Highly Specialised Technology

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

Onasemnogene abeparvovec for treating pre-symptomatic spinal muscular atrophy (MAA partial review of HST 15) [ID4051]

Thank you for agreeing to give us your organisation's views on this treatment 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 this treatment 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 20 pages.

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This form has 8 sections

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Section 1. About you

Table 1 Name, job, organisation

1. Your name	Portia Thorman and Robert Burley
2. Name of organisation	Spinal Muscular Atrophy UK (SMA UK) and Muscular Dystrophy UK (MDUK)
3. Job title or position	Advocacy Lead and Director of Care, Communications and Support
4a. Provide a brief description of the organisation. How many members does it have?	**Spinal Muscular Atrophy UK (SMA UK)** SMA UK is the charity that is working to ensure everyone affected by SMA has access to the best care, support and drug treatments; research continues to bring breakthroughs that improve people's quality of life. We are in touch with some 700 households in the UK with a child, young person or adult living with SMA. We estimate this to be over 60% of the total UK population. We are also in contact with more than 350 families who have been bereaved by SMA – the majority by SMA Type 1. SMA UK is accredited to the Information Standard. Our SMA-related information sheets are signposted by the NHS website. Our Research Correspondents (a clinical and a research doctor) report to the SMA community on the development of all drug treatments and clinical trials. We have regular contact with the SMA REACH UK clinical network – which includes clinicians who administer the nusinersen treatment programme and the clinical trials for onasemnogene abeparvovec. **Muscular Dystrophy UK**

	Muscular Dystrophy UK 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, including SMA. We have 450 individuals on our database with a personal interest in SMA. Muscular Dystrophy UK is here from the moment of diagnosis and beyond. We understand what it's like to live with muscular dystrophy and how it affects families and friends too. We're here with information, advice and practical and emotional support along with a network of local groups and an online community so that people living with a muscle-wasting condition can find someone to talk to. Muscular Dystrophy UK also funds pioneering research for better treatments to improve lives today and transform those of future generations. And we're pressing for better recognition of muscular dystrophy so that people get the best care and support and access to potential drugs much sooner.
4b. Has the organisation received any funding from the company/companies of the treatment 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 • **Novartis** - £7380 for consultancy inc. £400 expenses. - £66,732.83 to fund New Born Screening Alliance of which SMA UK are the accountable body. • Though not a direct comparator, we made our views on access to Risdiplam known publicly via our submissions and as patient experts to NICE and to the SMC consultations. • We are members of and form the secretariat for the UK SMA NBS Alliance https://smanewbornscreening.org.uk/ MDUK **Funding received from the manufacturers (Novartis/Novartis Gene Therapies EU LtD)** **26-Aug-21: £2,000.00; Sponsorship of MDUK's Muscles Matter Seminar Series 2021**

	30-Mar-22: £3,000.00 Support for MDUK's Neuromuscular Physiotherapist Conference 2022
4c. Do you have any direct or indirect links with, or funding from, the tobacco industry?	No
5. How did you gather information about the experiences of patients and carers to include in your submission?	In early 2018, in preparation for our submissions to NICE re: the appraisal of nusinersen treatment, SMA UK invited people in the SMA community to complete our on-line surveys. There were: • 128 returns describing **the health-related impacts of SMA** for 128 people living with SMA Types 1-3. Only two of these were from those whose children were affected by SMA Type 1 • 29 returns describing **the experiences of parents whose children had been treated with nusinersen**. The survey responses were integral to the patient group submissions as part of the evaluation of nusinersen. In July 2019 SMA UK and MDUK jointly conducted a survey asking people within the SMA community for their views on the possibility of the NHS funding onasemnogene abeparvovec (for ease referred to as Zolgensma™ in the survey and from now on in this submission). This was disseminated via the charities' (SMA UK, MDUK and TreatSMA) social media channels and SMA UK's monthly e-news. The questionnaire, information sheet and collation of all the 14 responses are in Appendices 1 – 3. This submission draws on: these surveys; the experience and knowledge of SMA UK Support Services Team as a result of its contact over many years with many families affected by SMA Type 1 andMDUK's Information and Support Team's experience. SMA UK and MDUK are also the secretariat for the UK SMA NBS Alliance which is advocating for SMA to be incorporated into the UK Newborn screening as soon as possible. Through the alliance we have heard anecdotal evidence on the benefits of treating pre-symptomatically and the impact on the child and the family when treatment is delayed until symptoms appear.

Commented [PT1]: To answer the MAA treatment experience questions, I put them out to the whats app group who were a great help.. That's a group of 31 families, 28 of which are zolgensma treated.

Section 2 Living with the condition and current treatment

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

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?	SMA is a complex, rare inherited neuromuscular condition that affects the lower motor-neurons in the spinal cord. It leads to the gradual loss of the ability to walk, crawl, move, breathe and swallow. It is a condition that requires complex medical support and is the leading genetic cause of death in infants. **SMA Type 1is the most severe form of SMA** with symptoms usually beginning between 0 and 6 months. Generally speaking, the earlier the onset of symptoms the more severe the condition. Babies are unable to sit without support and may be described as **'non-sitters'**. It's not possible to predict life expectancy accurately but for most children, without intervention for breathing difficulties, this has previously been estimated as less than two years[1]. Evidence suggests that since the International Standards of Care for SMA introduced more proactive management in 2007, children have been living longer[2]. Each child is affected differently, but in general, babies with SMA Type 1 are: • bright, alert and responsive; their intelligence isn't affected • able to smile and frown as their facial muscles aren't severely affected • often described as 'floppy' babies due to their low muscle tone (hypotonia) and severe muscle weakness • unable to support or lift their head due to their weak neck muscles • unable to sit unsupported and have difficulty rolling over • able to move their hands and fingers but have difficulty lifting their arms and legs They have: • breathing muscle weakness, which can cause a weak cry and difficulties with breathing and coughing • an increased chance of chest infections, which can be life-threatening

	• difficulty swallowing their saliva and other secretions, which may make them sound chesty or make them cough • difficulties feeding and gaining weight • an increased risk of fluids or food passing into their lungs (aspiration), which can cause choking and, potentially, chest infections or pneumonia which can quickly become life-threatening. Children receive care and support from a multidisciplinary healthcare team including specialists in: • hospital or community paediatric • respiratory care • physiotherapy • occupational therapy • dietetics • speech and language therapy • palliative care • general practice and community health care. This can feel overwhelming for the child and their family. **Positioning** is very important. If an infant is too upright or lies on anything that sags or is curved, their chest may concertina or 'hunch up' which makes it more difficult for them to take deeper breaths. During the day they need to have their position changed every hour or so. This helps to relieve pressure to ensure that their joints don't become stiff and gives them a change of view. Often their neck muscles are weak, and they may need a small neck roll to steady their neck in a more comfortable position and help with breathing. They may be provided with a collar to help and, if they're experiencing tightening of their muscles (contractures) and discomfort, they may have foot and hand splints. As children have a limited range of comfortable positions, they are at risk of developing pressure sores. **Spine, hips and bones** 60-90% of children with SMA Type 1 or 2 develop a scoliosis[2]. Children are monitored for this and if there are signs, they may be provided with a spinal brace to wear during the day to help them to sit and breathe more comfortably. It's common for children to have unstable hips which may affect one hip or both and will

need monitoring.They may be prescribed additional orthotics such as Ankle-Foot Orthosos (AFO's) and Knee-Ankle-Foot Orthosis (KAFO's) to reduce the impact of contractures.

Breathing

Weak breathing muscles are common resulting in 'insufficient' breathing which is a leading cause of health problems. To help their child, parents may have to manage:

- Chest physiotherapy to help with comfort and clearing secretions from their child's chest.
- Nebuliser to loosen secretions in the lungs.
- A suction machine to help remove their child's excess secretions.
- Medications that can break down the secretions (such as glycopyrrolate). These have to be used carefully as too high a dose can dry out the secretions too much, which then makes them harder to remove.
- Pain relief if their child is in pain or distress because of breathlessness
- Antibiotics which need to be prescribed quickly when their child is at risk of, or to treat, a chest infection.
- A mechanical insufflator – exsufflator machine (Cough assist) to help clear the secretions from their child's the lungs.
- Oxygen sometimes
- Non-invasive ventilation (NIV) (BiPAP) to help make their child's breathing easier. The SoC guidelines recommend really proactive use of NIV for all infants with symptoms of 'insufficient' breathing and that they start using it early before signs of breathing problems start.
- Short term invasive ventilation if their child has a medical emergency.
- A small number of children may have a tracheostomy

Feeding, nutrition and swallowing

Due to their muscle weakness, a child with SMA Type 1 may have difficulties with feeding and swallowing. Safe swallowing is one of the most important aspects of their care as children with a weak swallow are at risk of inhaling (aspirating) their feed which can cause choking and respiratory infections. Children often have a weak suck, and mealtimes take longer. Food may get stuck in their cheeks (pocketing) or they may find it hard to open their mouth due to muscle weakness. Infants will need a Video Fluoroscopic Swallow

	Study and to be monitored for the common problems of gastroesophageal reflux, constipation and vomiting. If swallowing becomes unsafe, or if a child isn't gaining enough weight, short-term options may include feeding through a n**asogastric (NG) or nasojejunal (NJ) tube.** A Gastrostomy **(PEG) tube** is a longer-term option. A **Nissen Fundoplication,** which helps to reduce any reflux, may be done at the same time. Diet has to be very carefully monitored and managed. **Day and Night Care** SMA can make children very sweaty with flushed faces and hot or cold hands. This can make it difficult to judge if their temperature is safe, creating anxiety for their parents. Thin, loose layers of clothing help maintain a comfortable temperature but changing clothing isn't easy, especially if their child is tired or uncomfortable. Parents need to avoid having to lie their child on their tummy due to breathing difficulties. Care is 24 hour 7 days a week.
7. What do carers experience when caring for someone with the condition?	**Impact on Families** The impact of a diagnosis of early onset SMA Type 1 on families is enormous. It often comes as a shock with parents expressing feelings of disbelief, confusion, anger and sadness. The 24 hour-a-day responsibility of caring for a child with complex medical needs that follows is physically, emotionally and psychologically exhausting: constant re-positioning and care, large amounts of medical equipment – many families having to adjust bedroom and living arrangements, the need for specialist car seats and buggies that aren't funded by the NHS, frequent hospital appointments and planned and emergency admissions, involvement of palliative and hospice care, caring for other children, the chronic grief and potential looming loss of their child. Parents describe sleep deprivation, often one will give up or cut back their paid work, social lives disappear. Caring for a child with SMA Type 1 also comes with significant financial implications due to the additional costs of living with a disability but also because family members may need to reduce their hours or stop working in order to meet the care needs of the child. Those that have other children and caring responsibilities can struggle to keep up. The impact ripples out to siblings, grandparents and other

Commented [PT2]: Is it worth putting in here a list of all the postural support equipment needed ? It certainly fills your house up!
Standing frame
Specialist supportive seating
Profiling bed
Bath chair
Toilet chair
Wet room/ specialist bath
Hoist

	relatives and friends, many of whom will try to help in some way, all of whom are also emotionally impacted. Parents whose children had, in early 2018, begun treatment with nusinersen and responded to our survey that year reflected: Before treatment; **"**he could not even grasp …. he was in intensive care on life support for every cold he got." "We were told to enjoy our time left with our child at point of diagnosis which was simply heart-breaking. Life as we knew it stopped. Numb with pain and filled with fear we were unable to work/sleep/deal with normal day to day life."
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.	The November 2017 international Standards of Care for SMA (SoC)2,3,4 outline what assessments and interventions families and adults should expect to find in any neuromuscular centre anywhere. This is the current core standard for treatment of SMA in England. Management interventions include: • Respiratory support, including chest physiotherapy, oral suctioning, medication to reduce secretions, cough assist and invasive and non-invasive ventilation; • Feeding support; • Help with managing constipation; • Physiotherapy and occupational therapy; • Treatment for spinal scoliosis, including a lycra suit, spinal brace or jacket and surgery.
9. Considering all treatments available to patients are there any unmet needs for patients with this condition?	There are currently three treatments for SMA available through managed access schemes in the UK – Spinraza, Risdiplam, and Zolgensma. However, Zolgensma is currently the only option for babies diagnosed pre-symptomatically. As such, it is imperative they continue to access this treatment as multiple

If yes please state what these are	studies have demonstrated that any damage cannot be reversed through treatments and that pre-symptomatic treatment is the sole way to provide the highest quality of life and reduce burden of care.

Section 3 Experience during the managed access agreement (MAA)

Table 3 Experience, advantages and disadvantages during the MAA

10. What are patients' and carers' experience of accessing and having the treatment? • Please refer to the MAA re-evaluation patient submission guide	There have been unavoidable inequalities to access to treatment across the UK as the treatment has rolled out across different treatment centres under the MAA. We have seen some examples of delays to access to treatment for some families due to poor communication channels. Communication between secondary and tertiary care centres is not always efficient, and at times, parents have felt 'out of the loop' in discussions about their child. There have also been cases where clinicians, including the NMDT, have changed their minds or added extra tests at the last minute without properly communicating their motives with the family which causes considerable distress.
11. What do patients and carers think are the advantages of the treatment? Please refer to the MAA re-evaluation patient submission guide	Feedback from our survey showed, 100% of respondents found the one off treatment beneficial and felt a strong improvement in their breathing (92.9%), improvement in motor milestones (78.6%) and noticed a positive impact on their quality of life (85.5%)
12. What do patients or carers think are the disadvantages of the treatment? Please refer to the MAA re-evaluation patient submission guide	No disadvantages were raised.

13. What place do you think this treatment has in future NHS treatment and care for the condition? Consider how this treatment has impacted patients and how it fits alongside other treatments and care pathway.	Despite being a rare disease, left untreated, SMA is the leading genetic cause of death in infants and toddlers. SMA involves the loss of nerve cells called motor neurons that control muscles. Once lost, motor neurons cannot be regenerated. 50-60% of children born with SMA can never sit up independently and without treatment, do not live beyond two years of age. There is no cure for SMA therefore being treated as early as possible is a key issue for babies born with SMA and their families. Being treated pre-symptomatically stops SMA in its tracks and this treatment is currently the only available option to do so.

Section 4 Patients views on assessments used during the MAA

Commented [MR3]: Portia, would you have anything to add here?

Table 4 Measurements, tests and assessments

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 the treatment?**	The outcome of any test or assessment on babies and young children will heavily depend on the mood of the child at the time. Many families living with SMA report that as a result of many blood tests and procedures, their children are very wary of medical professionals, this, often coupled with long journeys to specialist hospitals, can mean children regularly do not cooperate or show their best abilities within an assessment session. Tests and assessments are, of course, an integral part of assessing effectiveness of treatment but should always be looked at as a part of a bigger picture. Videos from everyday life, and discussions with parents and carers should be equally weighted as evidence of effectiveness.
15. Were there any tests or assessments that were difficult or unhelpful from a patient's or carer's perspective?	The requirement for a synacthen test in steroid management seems to vary across the country. Some treatment centres require it and others do a more basic blood cortisol test which does not require cannulation. The difference in approach has caused some anxiety within the tight-nit community. Any method that avoids cannulation would be the preferred approach . We have heard from several families that the AAV9 test was a very traumatic experience. Cannulation in SMA babies is very difficult. Some clinicians try multiple times to find a vein causing the patient and the family much distress. Other clinicians found they could get enough blood from a simple heel prick. There

	should be a low limit to the number of attempts to cannulate. If a heel prick is not considered appropriate, ultrasound guided cannulation by a vascular team should be used if possible.
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.	The MAA quantifiable tests and assessments currently only capture clinical data, measuring progress in motor function. Interviews focus on other clinical disciplines such as diet, respiratory and bulbar function. Emotional and psychological impact on the patient and their family are currently not captured. The psychological impact of diagnosis, treatment and care in SMA is enormous and should be captured as part of assessments going forward, with referrals being made if counselling or alternative treatment is considered appropriate.
17. What outcomes do you think have not been assessed or captured in the MAA data? Please tell us why	Progress in cognition and learning is not captured formally. Typically, SMA does not affect cognition, in many cases individuals living with SMA are exceptionally bright. However, with some cases of developmental and speech and language delay now emerging in the growing treated population, it is important that this is monitored with a more structured approach.

Section 5 Patient population

Table 5 Groups who may benefit and those who declined treatment

18. Are there any groups of patients who might benefit more or less from the treatment than others? If so, please describe them and explain why.	We understand from clinical evidence that, as with all the treatments being developed, the earlier the treatment the better the potential outcome, including for those who are pre-symptomatic. As such, there is a need to reconsider newborn screening for SMA.
19. Were there people who met the MAA eligibility criteria who decided not to start treatment? Please state if known the proportion of eligible patients who did not start the treatment and any reasons for this.	Not that we are aware of.

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.

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:

- Click or tap here to enter text.
- Click or tap here to enter text.
- Click or tap here to enter text.
- Click or tap here to enter text.
- Click or tap here to enter text.

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