National Institute for Health and Care Excellence

Highly Specialised Technologies

ID1473 Onasemnogene abeparvovec for treating spinal muscular atrophy type 1

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit

Section	Consultee/ Commentator	Comments [sic]	Action
Appropriateness	AveXis	AveXis agree that onasemnogene abeparvovec should be referred to NICE for appraisal, given the unmet need for spinal muscular atrophy type 1. However, AveXis believes that the appraisal is more suited to the highly specialised technology (HST) route rather than the single technology appraisal (STA) route, for the following reasons: **1.** The target patient group for the technology in its licensed indication is so small that **treatment will usually be concentrated in very few centres in the NHS;** We agree with the NICE scope which estimates that 78 patients are born per year with SMA (all types). SMA Type 1 is the most common form, representing 45-60% of cases (Ogino et al., 2004; Arnold et al., 2015 [1]) Assuming the upper estimate of 60% SMA type 1, this translates to a maximum of 47 babies born in the UK per year.	Comment noted. Following extensive discussion, it was agreed that this topic is appropriate for consideration as a highly specialised technologies (HST) evaluation.

Section	Consultee/ Commentator	Comments [sic]	Action
		- Ogino S, Wilson RB, Gold B. New insights on the evolution of the *SMN1* and *SMN2* region: simulation and meta-analysis for allele and haplotype frequency calculations. *Eur J Hum Genet* 2004;12:1015–23. - Arnold W., Kassar D., and Kissel J. Spinal muscular atrophy: Diagnosis and management in a new therapeutic era. *Muscle Nerve* 2015;51:157–167. There is a narrow time window in which to intervene as the treatment is intended for very young infants who are recently diagnosed (incident SMA type 1 population only) Treatment optimally should be initiated as early as possible following diagnosis. Unfortunately, there is considerable delay before diagnosis, particularly in the absence of SMA new born screening in the UK. Therefore, it is expected that many infants who would otherwise have been eligible for treatment with onasemnogene abeparvovec may not be identified early enough to be suitable candidates for this therapy. These infants will require highly specialised centres to manage the resulting care decisions 2. The target patient group is distinct for clinical reasons SMA type 1 is a very clearly defined target patient group. SMA is conventionally classified into 4 phenotypes based on the age of onset and highest motor function achieved. SMA Type 1 is	

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		defined by: an age of onset before 6 months; failure to ever achieve a sitting position. Life expectancy is usually less than 2 years. Diagnosis of SMA Type 1 needs to be confirmed by genetic testing. The clinical studies were and are being conducted in symptomatic SMA Type 1 patients with 2 copies of survival motor neuron 2 gene (SMN2) 3. The condition is chronic and severely disabling; The prognosis of Type 1 SMA patients with 2 copies of SMN2 is particularly dire; these patients show signs of the disease soon after birth (<6 months of age), never gain the ability to sit due to severe progressive weakness. Typically they do not survive past 2 years of age without significant mechanical, ventilatory and nutritional support. (Tisdale et al.,2015 [2] Arnold et al., 2015 [1]) - Tisdale S, Pellizzoni L. Disease mechanisms and therapeutic approaches in spinal muscular atrophy. J Neurosci. 2015 Jun 10;35(23):8691-700. doi: 10.1523/JNEUROSCI.0417-15.2015. Review. The MHRA has recently designated AVXS101 a Promising Innovative Medicine (PIM) which is only granted to life-threatening or seriously debilitating conditions with high unmet need.	

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		4. The technology is expected to be used exclusively in the context of a highly specialised service; Treatment can only be administered in a very restricted number of highly specialised centres, maybe 2-3 centres at most due to: - the unique nature of the manufacturing process and the need to tailor the dose for each individual patient; - the need for a secure supply chain; - institutions must be prepared to handle a genetic therapy; - treating physicians must have expertise in the management of SMA Type 1and the administration of this treatment 5. The technology is likely to have a very high acquisition cost; Given the significant clinical outcomes with a one-time IV administration with potentially life long benefit, very small number of the incident SMA type 1 patients potentially eligible for this therapy, the rarity and severity of the disease, significant unmet need despite the availability of a chronic treatment (nusinersen), as well as the complex and innovative nature of this gene replacement therapy, it is expected that onasemnogene abeparvovec will have a very high acquisition cost. 6. The technology has the potential for life long use;	

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		This is one of the first ever gene replacement therapies where clinical effectiveness is anticipated to be maintained for the lifetime of the patient. 7. The need for national commissioning of the technology is significant As stated above the treatment is to be tailored to the patient and delivered in very few highly specialised centres (2 or maybe 3), national commissioning and oversight will be essential, for instance coordinated by the Paediatric Neurosciences Clinical Reference Group.	
	Spinal Muscular Atrophy UK	*Would it be appropriate to refer this topic to NICE for appraisal?* Yes	Comment noted. No action required.
	Muscular Dystrophy UK	Yes – this is the first gene therapy for SMA Type 1. The therapy has the potential to mark a step change in the treatment of patients with this condition.	Comment noted. No action required.
	Genetic Alliance UK	Spinal muscular atrophy (SMA) is a rare condition causing debilitilitating symptoms and frequently death in infancy. There is currently no routinely available treatment which addresses underlying cause of SMA, and this significant unmet need has been recognised by the European Medicines Agency who have granted the medicine entry to the PRIME scheme a programme that promotes accelerated market authorisation (MA) assessment on the basis that a medicine targets significant unmet health need. As such, it is appropriate for the medicine to be considered by NICE.	Comment noted. This evaluation will consider the technology for treating spinal muscular atrophy type 1, within its marketing authorisation. Following extensive discussion, it was agreed that this topic is appropriate for

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		However, it is not yet clear what the indication of the marketing authorisation for treatment is likely to be, as the MA application has not yet been submitted. Onasemnogene abeparvovec is being studied in patients with types 1, 2 and 3 of SMA, including presymptomatic patients. The medicine appears to be being scoped on the assumption that the licensed indication will match the first pivotal trial of the medicine (STR1VE), which studied the treatment in patients with SMA type 1 who were less than six months of age at the time of gene therapy, and who had one or two copies of the SMN2 backup gene. It is estimated that about 40-50 babies are born with SMA type 1 per year, and slightly more than 25 children with type 1 alive in the UK at any time. These patients numbers, as well as the still relatively novel curative intent of a gene therapy, mean that the HST evaluation process is more appropriate for this treatment than the Single Technology Appraisal process.	consideration as a highly specialised technologies (HST) evaluation.
	Biogen Idec Ltd.	Yes, onasemnogene abeparvovec should be appraised by NICE via the same route as nusinersen is being appraised.	Comment noted. Following extensive discussion, it was agreed that this topic is appropriate for consideration as a highly specialised technologies (HST) evaluation.
	Royal College of Pathologists	With a prevalence of approximately 1/10,000 and a carrier frequency of around 1/50 (roughly half as frequent as cystic fibrosis), the Spinal Muscular Atrophies (SMAs) are among the most frequent autosomal recessive heredity disorders. Most cases of SMA1result from homozygous gene-deletion events and patients typically have a life expectancy of < 2years. As a single dose gene replacement therapy, AVXS-101 aims to target the root cause of	Comment noted.

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		symptoms by enabling nerve cells to produce sufficient amounts of SMN protein. It would therefore be appropriate to refer this topic to NICE for appraisal.	
	Treat SMA	No comments	Noted.
Wording	AveXis	We agree with the remit as it specifies Type 1 To appraise the clinical and cost effectiveness of onasemnogene abeparvovec within its marketing authorisation for treating spinal muscular atrophy Type 1	Comment noted. No action required.
	Spinal Muscular Atrophy UK	*Does the wording of the remit reflect the issue(s) of clinical and cost effectiveness about this technology or technologies that NICE should consider?* Yes	Comment noted. No action required.
	Muscular Dystrophy UK	*Does the wording of the remit reflect the issue(s) of clinical and cost effectiveness about this technology or technologies that NICE should consider?* Yes	Comment noted. No action required.
	Genetic Alliance UK	This is the standard wording.	Comment noted. No action required.
	Biogen Idec Ltd.	N/A	Comment noted. No action required.
	Treat SMA	"To appraise the clinical and cost effectiveness of onasemnogene abeparvovec within its marketing authorisation for treating spinal muscular atrophy."	Comment noted. This evaluation will consider the technology for

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			treating spinal muscular atrophy type 1, within its marketing authorisation.
Timing Issues	AveXis	As a rare, fatal and rapidly progressing neurological disease, SMA type 1 is the leading genetic cause of death in infants. Onasemnogene abeparvovec results in unprecedented clinical outcomes for infants and reduced burden for patients and caregivers and the health care system. No disease modifying treatments are currently routinely available for SMA type 1 in England and Wales. If approved, it is anticipated that onasemnogene abeparvovec will be the first one-time treatment, administered as soon as possible after diagnosis is confirmed. NICE appraisal of onasemnogene abeparvovec should be prioritised to ensure availability to potential patients as early as possible.	Comment noted. NICE aims to provide draft guidance to the NHS within 6 months from the date when the marketing authorisation for a technology is granted. NICE has scheduled this topic into its work programme.
	Spinal Muscular Atrophy UK	**Very urgent.** Infants with SMA Type 1 have been able to access nusinersen via the Expanded Access Programme. This is due to close at the end of October and, unless a Managed Access Agreement (MAA) is secured, newly diagnosed infants will no longer have access to this treatment. Even if there is an MAA for nusinersen, if this new 'one off' treatment offers equal or better potential for quality of life, parents and clinicians need to have the choice to access it. The length of time the appraisal process for nusinersen in England has taken has created immense distress for families in the SMA community. We urge NICE not to allow this to happen with this treatment	Comment noted. NICE aims to provide draft guidance to the NHS within 6 months from the date when the marketing authorisation for a technology is granted. NICE has scheduled this topic into its work programme.
	Muscular Dystrophy UK	The proposed appraisal is very urgent as the treatment has the potential to increase survival and improve the functional outcomes of infants with SMA	Comment noted. NICE aims to provide draft

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		Type 1, especially as there is currently no approved treatment for SMA available on the NHS.	guidance to the NHS within 6 months from the date when the marketing authorisation for a technology is granted. NICE has scheduled this topic into its work programme.
	Genetic Alliance UK	We understand that the marketing authorisation application has not yet been submitted. However, currently there are no routinely available treatments for the condition and significant unmet need. SMA is the most common genetic cause of infant mortality in the UK. The evaluation is of particular urgency due to the speed at which the condition progresses particularly in SMA type 1, with only months from onset of symptoms to likely death. Early evidence also suggests that early treatment significantly improves outcomes. For this reason it is important that the evalutaion process be started now so that patients in England are able to access the treatment as soon as possible after a license is granted.	Comment noted. NICE aims to provide draft guidance to the NHS within 6 months from the date when the marketing authorisation for a technology is granted. NICE has scheduled this topic into its work programme.
	Biogen Idec Ltd.	N/A	Noted
	Treat SMA	As of this writing, NHS does not offer any pharmacological treatment to the population covered by this technology	Comment noted. No action required.
Additional comments on the draft remit	Biogen Idec Ltd.	Although no active treatments are currently routinely available, approximately 90% of prevalent SMA type I patients are on an expanded access programme for nusinersen where Biogen is providing the treatment free of charge pending the outcome of the NICE technology appraisal [ID1069]	Comment noted. No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	AveXis	It is incorrect to suggest that the target population is all prevalent patients with Type 1. It is also incorrect if it is implied that 60% of prevalent patients (2,500) are Type 1. Patients with SMA Type 1 do not survive beyond 2 years without intensive support and hence the proportion of prevalent patients that are Type 1 is very small. We agree with the NICE scope which estimates that 78 patients are born per year with SMA. SMA Type 1 is the most common form representing 45-60% of cases (Ogino et al., 2004: Arnold et al 2015) Assuming the upper estimate of 60% SMA type 1 this translates to 47 babies in the UK as a whole. There is a narrow time window in which to intervene as the treatment is intended for very young infants who are very recently diagnosed (incident SMA type 1 population only). Suggest the background should focus on SMA type 1 as this is the subject of this appraisal. Make it clear that it is SMA Type 1 that typically causes death before age 2 years Delete the following: In type 2 SMA, the onset of symptoms is between 7 and 18 months of age, and people with this condition are often severely disabled and unable to walk unaided. Type 3 SMA is a heterogeneous condition, with a varying degree of muscle weakness appearing between age 18 months and 18 years; most people with type 3 SMA can walk or sit unaided at some point, but many lose mobility over time.	Comment noted. The background section has been updated based on consultation comments and discussion at the scoping workshop. This section of the scope is intended to provide a brief summary of the disease and how it is managed, and is not designed to be exhaustive.
	Spinal Muscular Atrophy UK	We suggest that this could be clearer and more accurate, as follows: • Refer throughout to **5q SMA.** This is the most common **form** of SMA and includes **Types** 1, 2, 3 and 4 • First paragraph might more accurately read:	Comments noted. The background section has been updated based on consultation comments and discussion at the

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		'Its most common form, 5q SMA, which includes childhood onset SMA Types 1, 2, 3 and adult onset Type 4, is caused by defects in the gene SMN1, which leads to degeneration of motor neurones in the spinal cord. The motor neurones most affected by this condition are those that allow walking, crawling, arm movement, head and neck movement, swallowing and breathing. SMA Type 1, the most severe of the childhood onset types of 5q SMA typically cause death before age 2 years. It has substantial effects on families and carers, including the impact of caring for the patient, the need for specialist equipment and ongoing emotional, financial and social impacts' **We suggest that, given this treatment is only for SMA Type 1, it may not be relevant to talk about the other types of 5q SMA.** If it is considered relevant, we suggest these descriptions may more accurately continue as follows: • 'SMA Type 2 may shorten life expectancy while life expectancy for SMA Types 3 and 4 is normal.' Also suggest that Type 2 and 3 descriptions should read: • 'In SMA Type 2 the onset of symptoms is between 7 and 18 months of age. People with this condition are often severely disabled **and are unable to stand without support. They are never able to walk unaided.'** • 'Most people with Type 3 SMA **can walk at some point,** but many lose mobility over time.'	scoping workshop. This section of the scope is intended to provide a brief summary of the disease and how it is managed, and is not designed to be exhaustive.

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		• **Treatment usually follows guidelines agreed by international experts. These have been most recently documented in the Standards of Care for SMA (November 2017).** (note there is no committee as such) References for this (which you may want at the end of the document?) are: • Mercuri E, et al. **Diagnosis and management of spinal muscular atrophy: Part 1: recommendations for diagnosis, rehabilitation, orthopedic and nutritional care**. Neuromuscul Disord. 2018 Feb;28(2):103-115. doi:10.1016/j.nmd.2017.11.005. Epub 2017 Nov 23. http://smasupportuk.org.uk/international-standards-of-care-for-sma (Accessed 29 August 2019) • Finkel RS et al. **Diagnosis and management of spinal muscular atrophy: Part 2: Pulmonary and acute care; medications, supplements and immunizations; other organ systems; and ethics.** Neuromuscul Disord. 2018 Mar;28(3):197-207. doi: 10.1016/j.nmd.2017.11.004. Epub 2017 Nov 23. http://smasupportuk.org.uk/international-standards-of-care-for-sma (Accessed 29 August 2019) We note the remit references our website as the source of population stats – thank you. Just to say we updated all our information sheets in September so the actual link to this information is now: http://smasupportuk.org.uk/what-is-spinal-muscular-atrophy . Just a small note of concern, that the remit quotes SMA Support UK as the source of the statistics, rather than pinpointing the information sheet / link which identifies these two publications as the source of the incidence and prevalence of 5q SMA data:	

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		• Verhaart IEC, Robertson A, Wilson IJ, Aartsma-Rus A, Cameron S, Jones CC, Cook SF, Lochmüller H (2017) **Prevalence, incidence and carrier frequency of 5q–linked spinal muscular atrophy –a literature review**. *Orphanet J Rare Dis* 12: 124. • Verhaart IEC, Robertson A, Leary R, McMacken G, König K, Kirschner J, Jones CC, Cook SF, Lochmüller H. (2017) **A multi-source approach to determine SMA incidence and research ready population.** *J Neruol* 264: 1465-1473. And these as the source of the England & Wakes population statistics: • Office of National Statistics (2018) '**Births in England and Wales: 2017'.** Available at: • www.ons.gov.uk/peoplepopulationandcommunity/births deathsandmarriages/livebirths/bulletins/birthsummarytables englandandwales/2017 (Accessed:26 August 2018) • Office for National Statistics '**Overview of the UK Population: July 2018.'** Available at www.ons.gov.uk/peoplepopulationandcommunity/population andmigration/populationestimates/bulletins/annualmidyear populationestimates/mid2017#main-points (accessed 26 August 2018) Would readers need to know this so that they can confirm / dispute what has been said?	

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	Muscular Dystrophy UK	No comment	Noted.
	Biogen Idec Ltd.	The wording is broadly accurate except: around 60% of incident cases are type 1 SMA, the prevalent percentage of type I SMA is significantly lower (approximately <10%).	Comment noted. The background section has been updated based on consultation comments and discussion at the scoping workshop.
	Treat SMA	The SMA classification is incorrect. The currently used classification is based exclusively on the highest achieved motor function ("non-sitters", "sitters", "walkers") irrespective of the time of onset of symptoms. For example, it is common to observe early symptoms of the disease in weak sitters (type 2) well before 6 months of age. Similarly, subclinical symptoms (e.g., decrease in ulnar CMAP) may be present in pre-symptomatic non-sitters.	Comment noted. This section of the scope is intended to provide a brief summary of the disease and how it is managed, and is not designed to be exhaustive. Further details of SMA classification may be considered during the evaluation.
The technology/ intervention	AveXis	It is incorrect to say that a virus is injected. Wording suggested to make it clearer that a vector is injected and NOT a virus: "Onasemnogene abeparvovec is a one time gene replacement therapy made of a viral capsid shell (vector) that has been modified to contain the primary gene for the human survival motor neuron (SMN) protein, which is lacking or mutated in people with SMA. When injected the vector is expected	Comment noted. The technology section of the scope has been updated based on consultation comments and discussion at the scoping workshop.

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		to carry the gene into the nerve cells, enabling production of sufficient amounts of SMN. It is administered intravenously as a single one time infusion.	
	Spinal Muscular Atrophy UK	Yes, as far as we are aware	Comment noted. No action required.
	Muscular Dystrophy UK	No comment	Noted.
	Genetic Alliance UK	As mentioned above, we understand that onasemnogene abeparvovec is also being studied in symtomatic patients with types 2 and 3 of SMA, as well as presymptomatic patients with types 1, 2 and 3.	Comment noted. The technology section of the scope has been updated based on consultation comments and discussion at the scoping workshop. This evaluation will consider the technology for treating spinal muscular atrophy type 1, within its marketing authorisation.
	Biogen Idec Ltd	N/A	Noted
	Treat SMA	The technology description is incorrect. Correctly, the technology has been studied in single-arm clinical trials in children less than 9 (nine) months at enrollment. Two trial participants were 7 and 8 months old respectively at enrollment.	Comment noted. The technology section of the scope has been updated based on consultation comments

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			and discussion at the scoping workshop.
Population	AveXis	To reflect the expected label the population should be: indicated for a single treatment of spinal muscular atrophy (SMA) Type 1.	Comment noted. No action required.
	Spinal Muscular Atrophy UK	We understand this is the correct population for this intravenous treatment which is not possible for children diagnosed later with SMA Type 2 or 3.	Comment noted.
	Muscular Dystrophy UK	No comment	Noted.
	Genetic Alliance UK	As mentioned above, it is estimated that about 40-50 babies are born with SMA type 1 per year. Our members SMA UK estimate that there are about 25 children with type 1 alive in the UK at any time, though due to increasing life expectancies, this number may need to be revised upward slightly. It should also be considered that if nusinersen increases the life expectancy of affected children as has been seen in the clinical trials, this will also increase these numbers. The treatment is also being studied in presymptomatic babies, and it may be appropriate to consider infants treated symptomatic and presymptomatic separately.	Comment noted. If evidence allows, and included within the marketing authorisation, consideration may be given to people with presymptomatic SMA.
	Biogen Idec Ltd	Yes, however consideration should be given to subgroups including: - age of symptom onset - disease duration at time of drug dosing - baseline CHOP-INTEND scores - Anti AAV9 antibody titre	Comment noted. If evidence allows, and included within the marketing authorisation, consideration may be given to people with presymptomatic SMA.

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	Treat SMA	The population is inappropriately defined. (1) There is inconsistency between the population in which the proposed technology was studied and the population defined in the remit. Whilst the initial study protocol defined the studied population on the basis of ages at symptom onset (< 6 months) and at screening (< 9 months), the draft remit proposes to define the target population based on functional status ("type 1", i.e., non-sitters). Neither the clinical and nor the background data support the proposition that all of the studied patients would be unable to sit unsupported if left untreated. In particular, the functional status of the patients no. E.06 and E.10 was not inconsistent with natural history of weak sitters (SMA type 2a) prior to treatment. Given that safety considerations will anyway restrict the use of the technology to patients within a specified body weight bracket, and in view of the well-known ambiguity and arbitrarity of SMA classification, we propose that the words “type 1” are omitted from the remit. (2) Given the molecular and physiological mechanism of SMA, the population should also include pre-symptomatic infants – in this subpopulation the technology is highly likely to be able to entirely prevent appearance of any symptoms of spinal muscular atrophy. Thus, its pre-symptomatic use will, in alll likelihood, be associated with higher cost effectiveness.	Comment noted. This evaluation will consider the technology for treating spinal muscular atrophy type 1, within its marketing authorisation. If evidence allows, and included within the marketing authorisation, consideration may be given to people with presymptomatic SMA.
Comparators	AveXis	Best supportive care Nusinersen (subject to ongoing NICE appraisal)	Comments noted. No action required.
	Spinal Muscular Atrophy UK	If nusinersen is recommended for funding by NHS England we suggest that: • Nusinersen alone is not the ‘best alternative care’ comparator.	Comments noted. The components of best supportive care may be considered during the

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		In most cases, the 'best alternative care' comparator would be: • Nusinersen in conjunction with adherence to supportive care as outlined in the internationally agreed standards of care for SMA (November 2017) However, a family may not wish to embark on long-term intrathecally administered nusinersen treatment, or there may be a clinical reason why nusinersen is not recommended for a particular child. In this case, the 'best alternative care' comparator would be: • Adherence to supportive care as outlined in the internationally agreed standards of care for SMA (November 2017)	evaluation. No action required.
	Muscular Dystrophy UK	If Nusinersen was approved, it would be an appropriate comparator.	Comments noted. No action required.
	Biogen Idec Ltd	Nusinersen is currently being appraised by NICE as per its marketing authorisation. No final recommendation as to its funding has yet been made but the clinical consultation has identified patients in which nusinersen may not be appropriate and therefore best supportive care would be the comparator including: - type 1a patients - type 1 patients with permanent ventilation at baseline - type 1 patients where intrathecal administration is not technically feasible There may also be an element of caregiver choice. In all cases best supportive care is the only alternative option and therefore should be considered as a comparator for this appraisal.	Comments noted. No action required.

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	Treat SMA	Comparators should include: - Nusinersen (also in the pre-symptomatic group) - Best supportive care - Palliative care	Comment noted. No action required.
Outcomes	AveXis	The outcome measures should also include: • motor function (including, where applicable, age-appropriate motor milestones sitting, standing, walking) • bulbar function (swallowing, talking)	Comment noted. The outcomes have been updated based on consultation comments and discussion at the scoping workshop.
	Spinal Muscular Atrophy UK	This appears to be a comprehensive list. We strongly suggest, however, that health-related quality of life should be of both the patient and parent / carers / family. Due to their children's care or needs, parents/carers of children with SMA Type 1 often struggle with lack of sleep, emotional distress and mental health challenges. The impact on siblings and grandparents can also be significant, affecting their emotional / mental health quality of life.	Comment noted. The outcomes have been updated based on consultation comments and discussion at the scoping workshop.
	Muscular Dystrophy UK	We would also argue that the benefit and improved quality of life to carers/families should also be included to appropriately capture the benefit to patients.	Comment noted. The outcomes have been updated based on consultation comments and discussion at the scoping workshop.

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	Genetic Alliance UK	The outcomes listed are appropriate, however stamina and fatigue are less relevant (and measurable) in patients with type 1 than in less severe subtypes of SMA.	Comment noted. The outcomes have been updated based on consultation comments and discussion at the scoping workshop.
	Biogen Idec Ltd	Yes the stated outcomes should capture the most important health related benefits. Other considerations could include: - bulbar function - speech/communication - weight over/under gain - pain - fracture frequency - frequency of infections - rate of overall SMA related adverse events	Comment noted. The outcomes have been updated based on consultation comments and discussion at the scoping workshop.
	Treat SMA	Additional patient-relevant outcomes that could be taken into consideration include: - the level of impairment of the swallowing function - the number, length and frequency of hospitalisations (esp. due to respiratory disfunction) - the development of SMA symptoms (in case of pre-symptomatic treatment	Comment noted. The outcomes have been updated based on consultation comments and discussion at the scoping workshop.
Economic analysis	AveXis	In the STA process, NICE compares interventions by calculating the incremental cost effectiveness ratio (ICER). In general, interventions with an ICER of less than £20,000 per QALY gained are considered to be cost	Comment noted. Following extensive discussion, it was agreed that this topic is

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		effective. This does not take into account wider societal benefits, and the rarity of disease which tends to result in higher drug acquisition costs. AveXis considers that the cost effectiveness threshold generally used by NICE within STAs would not be appropriate to assess onasemnogene abeparvovec given (i) the rarity of the disease and the consequent limited evidence base, both with and without onasemnogene abeparvovec treatment, and (ii) important benefits provided will not be captured by the quality adjusted life years measure of health benefit (e.g. benefit to carers, among others). AveXis requests NICE to reconsider its proposal to assess onasemnogene abeparvovec under the STA programme and rather assess it under the HST programme.	appropriate for consideration as a highly specialised technologies (HST) evaluation.
	Spinal Muscular Atrophy UK	Please see comments in answer to questions posed in the Innovation section	Comment noted.
	Muscular Dystrophy UK	Given the potential long-term benefits, the analysis may want to consider differential discounting for costs and benefits.	Comment noted.
	Biogen Idec Ltd	Biogen believe a cost comparison methodology is inappropriate for this technology because: - The marketing authorisation for nusinersen is for 5q SMA whereas the expected marketing authorisation (as per the draft scope) is type I SMA - Onasemnogene abeparvovec will not be similar in clinical efficacy or resource use to best supportive care - The trials of onasemnogene abeparvovec and nusinersen (ENDEAR) are not directly comparable due to: o differing baseline characteristics	Comment noted. No action required.

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		○ different outcomes measured ○ single arm vs. sham-controlled ○ sample size ○ duration Therefore, any indirect comparison conducted between these treatments will be associated with significant uncertainty. - New data is expected to emerge for nusinersen in the coming year(s) - There will be significant long-term uncertainty around both effectiveness and safety even if comparative efficacy is established Given the that nusinersen and onasemnogene are very different technologies then they may be offered to significantly different patient populations	
	Treat SMA	Care should be taken to use appropriate time horizon when evaluating cost of comparators: - median survival of around 1 year with natural history - median survival in the range of 5 years (0–adulthood) with best supportive care - both RCT and real-world data on nusinersen effects Additionally, care should be taken to assess costs and burden of care based on reliable UK data.	Comment noted. No action required.
Equality and Diversity	AveXis	None	Noted.
	Spinal Muscular Atrophy UK	We understand from Avexis and clinicians that, if access is agreed, due to the specialist nature of the treatment and method of delivery, it would be likely to	Comment noted. Access to specialist centres is not an

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		be limited to the two treatment Centres currently engaged in related clinical trials. It would be important to ensure that all families with a child meeting the treatment criteria have equal access, no matter where they live. To ensure this, assistance with travel and accommodation for those needing it would be essential.	equality issue that can be considered by the committee in highly specialised technologies guidance. No action required.
	Muscular Dystrophy UK	No comment	Noted.
	Biogen Idec Ltd	N/A	No action required.
	Treat SMA	The use of the concept of gross "SMA type" as a deciding factor in accessing this life-saving technology might be challenged as inadaequately justified and thus discriminatory towards those with a specific type of disability. Using a hard criterion of age or body weight seems more appropriate and fair.	Comment noted. This evaluation will consider the technology for treating spinal muscular atrophy type 1, within its marketing authorisation. If appropriate, the committee may give consideration to the impact of disability on its methods and considerations during the evaluation.
Other considerations	AveXis	None.	Noted.
	Muscular Dystrophy UK	The physical, psychological and financial benefits of this treatment to carers/families should be considered in the appraisal.	Comment noted.

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	Biogen Idec Ltd	N/A	No action required.
	Royal College of Pathologists	SMA is both a clinically and genetically heterogeneous group of neuromuscular disorders and therefore inclusion criteria should include definition of genetic diagnostic criteria.	Comments noted. Diagnosis of SMA is not within the scope of this evaluation.
	Treat SMA	No comments	Noted.
Innovation	AveXis	Onasemnogene abeparvovec is a highly innovative technology. It is one of the first ever gene replacement therapies with unprecedented results: "..extended survival, improved motor function, and increased scores on the CHOP intend scale to levels that had not previously been observed in this disease" (Mendell et al. 2017[3]) - Mendell et al N Engl J Med 2017;377:1713-1722 This has been recognised by key bodies. The EMA granted onasemnogene abeparvovec priority medicine (PRIME) status on 26 January 2017 and an Orphan status on 19 June 2015 for treatment of SMA patient. The MHRA designated onasemnogene abeparvovec a Promising Innovative Medicine (PIM) on 25 September 2018. AveXis considers that the use of the onasemnogene abeparvovec will result in important benefits provided will not be captured by the quality adjusted life years measure of health benefit (e.g. benefit to carers, among others).	Comment noted. The innovative nature of the technology will be considered by the evaluation committee based on evidence presented to it. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
	Spinal Muscular Atrophy UK	**Do you consider onasemnogene abeparvovec to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?** A 'one-off' intravenous treatment leading to improvements in the outcomes listed would be a step-change in the treatment and management of the condition. To quote Professor Kevin Talbot DPhil FRCP, Head of the Division of Clinical Neurology, Nuffield Department of Clinical Neurosciences, University of Oxford, this gene therapy, 'is a remarkable development and a historic landmark' The treatment uses harmless, genetically-engineered viruses to increase SMN protein levels and in late 2017, received "Breakthrough Therapy" status in the USA to facilitate its development. It is most definitely innovative in its approach endeavouring to address the fundamental cause of 5q SMA Type 1. **Do you consider that the use of onasemnogene abeparvovec can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?** We note the significant difficulties there have been with the economic analysis for nusinersen and that the NICE committee's consultation paper (August 2018) raised concerns that identifying robust utility values in babies and young children is exceptionally challenging. We draw attention to the flaws the measures present as summarised by **Griebsch, I *et al*. Quality-Adjusted Life-Years Lack Quality in Pediatric Care:**	Comment noted. The innovative nature of the technology will be considered by the evaluation committee based on evidence presented to it. The Guide to the methods of technology appraisal and Interim process and methods of the highly specialised technologies programme specify that reference-case economic analyses should include all direct health benefits (for patients and, when relevant, carers) and to costs incurred by the NHS and Personal Social Services; consideration will also be given to impacts of the technology beyond direct health benefits

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		A Critical Review of Published Cost-Utility Studies in Child Health Pediatrics May 2005, VOLUME 115 / ISSUE 5 : • Children undergo dramatic changes in growth and function (e.g., mobility, self-care) at different rates, difficulties may arise to attribute improvements to health care interventions rather than to normal development. There is no methodologic guidance about how this should or even might be dealt with. • All current generic measures (with the exception of the Health Utility Index Mark 2) are derived from adult populations, and additional attributes that are particularly relevant to child health, including, for example, autonomy, body image, cognitive skills, and family relationships, may not be captured by these measures. Furthermore, no generic instrument for children and infants **younger than 5 years** is available. • Children, particularly young children do not have the cognitive ability to comprehend and complete valuation or even measurement tasks. The implication is that, for very young children, some form of proxy inevitably will be used for measurement tasks, whether this be the clinician or the parent. Although parents may be perceived by economists as the more appropriate source of measurement and/or valuation, the potential for interaction between the utility function of the parent and the proxy (their child) for whom he or she is making the measurement/valuation may lead researchers to choose to use clinician judgment to avoid this problem. The issues with this are that: clinicians only see and record a 'snapshot' which may not truly represent the changes taking place and impact on daily living for both child and parents; measurement tools are insufficiently subtle and limited in their measurements. This last point is confirmed in many studies that show this, for example, Srikrishna S, *et al.* (2009) **Is there a discrepancy between patient and**	(including non-health benefits, costs outside the NHS and PSS, and others). If appropriate, the committee may give consideration to the challenges associated with measuring and valuing health-related quality of life in the population under consideration.

Section	Consultee/ Commentator	Comments [sic]	Action
		physician quality of life assessment? Neurourol Urodyn. 2009;28(3):179-82. doi: 10.1002/nau.20634. The NICE nusinersen committee (August 2018) further concluded that quantifying carer -related disutilities was extremely difficult. We are concerned that an economic analysis should cover all direct health and personal health and social services costs including: • **mental health:** • **equipment costs and housing adaptations**: • **emergency hospital stays, surgery and clinic time:** • **continuing health care (CHC) cost:** Though we accept that, due to the length of time the treatment has been trialled, there will be uncertainty as to future long-term outcomes for those treated with this gene therapy, the evidence to date clearly indicates that these wider costs will potentially reduce significantly. We consider it vital that this potential is adequately reflected in the ICER. We are also concerned that any model needs to reflect that the health impact is not only on **one** carer but also on the many e.g. grandparents often play a key role. Also, that due to the 'carer burden' of caring for someone with SMA, that it impacts on other caring responsibilities of the carer e.g. a parent who is unable to care for a sick or elderly relative such that their care needs fall to health and personal social services. However much effort is made to adjust the ICERs to better reflect evidence and address shortcomings, we suggest that NICE's economic	

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		analysis remains fundamentally flawed as it does not reflect the much wider impact in the 'real world' of the costs of the condition and potential benefits of treatment. From our perspective there needs to be a much more holistic approach as only then can the ICERs really begin to reflect the true potential value of this and any treatment. As examples of this 'real world' wider impact of 5q SMA, there are: • **education costs**: requiring Teaching Assistants, school adaptations • **work costs:** carers (parents and grandparents) who have to give up work to care for their child, and in the long term the child – loss of potential productivity and contribution to the economy through work / taxes • **health and social care costs borne by families:** interventions and support paid for by health and social services and included in NICE's model are insufficient for families to manage and are 'topped up' either formally or informally by the family e.g. care hours • **many equipment and housing adaptation costs are borne by families** **In summary: we strongly suggest that NICE adopts an economic analysis that includes:** • **all these 'real-world' costs that are currently not included in their model** • **all aspects of the health and personal health and social services required to support a child with SMA Type 1 and their family** • **the impact of SMA affecting more than one carer.**	

Section	Consultee/ Commentator	Comments [sic]	Action
		Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits. Avexis Clinical Trial data will in due course also include Phase 3 trial results STRIVE1-EU.	
	Muscular Dystrophy UK	This is the first gene therapy for patients with SMA which has the potential to be a step change in the management of the condition. The QALY does not appropriately capture the benefits to patients. There is incomplete understanding from health care professionals of the huge burden of disease an the implication for parents and carers of children with SMA type 1. Mothers (more often than fathers) will need to turn their child in bed 6-8 times per night, every night of the year. This brings challenges in terms of the mental and personal health, employment, and wellbeing of the wider family that we do not feel are captured by the QALY calculation. Whilst the immediate family is affected the most, the issue will affect nearly everybody who is in contact with the family and has a very wide overall impact.	Comment noted. The innovative nature of the technology will be considered by the appraisal committee based on evidence presented to it. The Guide to the methods of technology appraisal and Interim process and methods of the highly specialised technologies programme specify that reference-case economic analyses should include all direct health benefits (for patients and, when relevant, carers) and to costs incurred by the NHS and Personal Social Services; consideration will also be given to impacts of

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			the technology beyond direct health benefits (including non-health benefits, costs outside the NHS and PSS, and others). No action required.
	Genetic Alliance UK	Yes. As yet very few gene therapies have been licensed in the EU, and this treatment also represents a stepchange in the management of the condition, as the first single administration potentially curative treatment for the condition.	Comment noted. The innovative nature of the technology will be considered by the appraisal committee based on evidence presented to it. No action required.
	Biogen Idec Ltd	N/A	Noted.
	Treat SMA	This is an innovative technology which has a significant potential to bring about meaningful improvement in health-related benefit.	Comment noted. The innovative nature of the technology will be considered by the appraisal committee based on evidence presented to it. No action required.

Section	Consultee/ Commentator	Comments [sic]	Action
Questions for consultation	AveXis	**How many people have SMA type 1 in England, and how many would be offered onasemnogene abeparvovec therapy?** We agree with the NICE scope which estimates that 78 patients are born per year with SMA. SMA Type 1 is the most common form representing 45-60% of cases (Ogino et al., 2004; Arnold et al., 2015[4]) Assuming the upper estimate of 60% SMA type 1 this translates to a maximum of 47 babies in the UK (42 in England and Wales) would be eligible for treatment within the licensed indication and willing and able to be treated in time. In practice only a subset of these patients will be treated within the time window for administration due to delay in diagnosis. - Ogino S, Wilson RB, Gold B. New insights on the evolution of the *SMN1* and *SMN2* region: simulation and meta-analysis for allele and haplotype frequency calculations. *Eur J Hum Genet* 2004;12:1015–23. - Arnold W., Kassar D., and Kissel J. Spinal muscular atrophy: Diagnosis and management in a new therapeutic era. *Muscle Nerve* 2015;51:157–167. **How will people with type 1 SMA be identified for treatment with onasemnogene abeparvovec?** • In the absence of a new born screening programme (and there is not a national programme in the UK at present) the majority of infants will only come to clinical attention when they develop symptoms and if SMA is suspected this will need to be confirmed with genetic testing. In very few cases it is possible that where it is known that SMA runs in	Comments noted. No further action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		the family an infant may be tested shortly after birth which could be prior to symptom onset. **How is onasemnogene abeparvovec expected to be used in clinical practice?** • Treatment (a one-time single IV infusion) should be administered as early as possible, after the diagnosis of SMA Type 1 is confirmed – **At what point in the treatment pathway would it be considered?** There is a narrow window in which to intervene as the treatment is intended for infants who are recently diagnosed (incident SMA type 1 population only). • Treatment optimally should be initiated as early as possible following diagnosis. **How should best supportive care be defined?** In 2007, an International Conference on the Standard of Care for SMA published a consensus statement on SMA standard of care that has been widely used throughout the world (Wang et al. 2007). These standards remain key guidelines for doctors and families in the UK (SMA Support UK 2017, NHS 2018, NHS Health Education England 2018). An update on standards of care recommendations for SMA was published in 2017 (Finkel et al. 2018, Mercuri et al. 2018). Prior to 2017, there was no approved disease-modifying therapy for patients with SMA in the European Union (EU). Treatment options were limited to nutritional, pulmonary, and orthopaedic care (Schroth 2009, Arnold et al. 2015, García-Salido A. et al. 2015).	

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		The Jennifer Trust for Spinal Muscular Atrophy (JTSMA) reviewed and published in 2010 the interpretation of the consensus document, with specific relevance to the management of infants with severe form of Type 1 SMA in the UK (Appendix 1: Multidisciplinary Care for Infants with Severe Type 1 SMA (JTSMA)) (Wang et al. 2007, Roper H. et al. 2010). **Have all relevant comparators for onasemnogene abeparvovec been included in the scope?** Yes. **Which treatments are considered to be established clinical practice in the NHS for spinal muscular atrophy?** Currently best supportive can be considered as clinical practice for SMA Type 1. **Is best supportive care an appropriate comparator?** Yes **Are the outcomes listed appropriate?** Yes – see additions above. **Are there any subgroups of people in whom onasemnogene abeparvovec is expected to be more clinically effective and cost effective or other groups that should be examined separately?**	

Section	Consultee/ Commentator	Comments [sic]	Action
		Within the proposed label there are no subgroups of people with SMA Type 1 in whom onasemnogene abeparvovec is expected to be more clinically effective and cost effective. **Do you consider onasemnogene abeparvovec to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?** Yes – see above in the section titled "Innovation". It is a transformational treatment **Do you consider that the use of onasemnogene abeparvovec can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation**? • Important benefits provided by onasemnogene abeparvovec will not be captured by the quality adjusted life years measure of health benefit (e.g. benefit to carers among others). **Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.**	
	Spinal Muscular Atrophy UK	**How many people have SMA type 1 in England, and how many would be offered onasemnogene abeparvovec therapy?**	Comments noted. No further actions required. Following extensive discussion, it was agreed that this topic is appropriate for

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		Population statistics (see references above and England & Wales live births 2017 = 679,106), suggest that the incidence of SMA Type 1 in England and Wales = 60% x 68 = **41 infants born with SMA Type 1 each year.** We assume that potentially all these infants would be offered this therapy though it may not be clinically indicated for a very few extremely weak infants with SMA Type 0. If nusinersen is at this stage being funded by NHS England for infants with SMA Type 1, this may be an alternative choice. Both treatments would be offered in combination with best supportive care as outlined in the SoC with a further alternative of best supportive care only. **How will people with type 1 SMA be identified for treatment with onasemnogene abeparvovec?** Infants may be diagnosed in hospital shortly after birth, following admission with a respiratory crisis or in the community following concerns of muscle weakness reported / observed by parents / health visitor / community nurse / GP. Diagnosis can be quickly confirmed via an SMN1 gene deletion blood test which is usually available within 2 – 4 weeks. Given the clinical trial findings are strongly indicating that the earlier the intervention the better the potential outcome, it is essential that this path to diagnosis is as rapid as possible. Any health practitioner potentially making this diagnosis must be both aware of and able to offer a rapid path to this treatment. Communication and referral paths from the community, neuromuscular centres and specialist treatment centres must be first rate and seamless. A diagnosis of SMA Type 1 is devastating for parents and families who often describe their shock, numbness, disbelief and emotional turmoil. It is a hugely	consideration as a highly specialised technologies (HST) evaluation.

Section	Consultee/ Commentator	Comments [sic]	Action
		difficult time for them to make any decisions and yet the timing of any potential drug treatment may well be critical. Not only would they have to decide on whether to agree to a drug treatment, they would now potentially be having to decide which of two options to choose. It is essential that these options are discussed fully and carefully with them by clinical experts, that expectations are appropriately managed and that they are supported emotionally and practically during this time and that this support continues **How is onasemnogene abeparvovec expected to be used in clinical practice? At what point in the treatment pathway would it be considered?** We understand the earlier the intervention the better the potential outcomes and that therefore treatment should be considered and delivered as soon after diagnosis as is practically possible. **Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators? Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?** The NICE committee appraisal of nusinersen has already compiled significant data on the impact of SMA Type 1 on families and data on the clinical effectiveness of nusinersen. It has already explored current economic models and deliberated over their limitations. It will be aware of new data on nusinersen via 'real-world' studies of those enrolled in the global EAP for SMA Type 1 and any new reports by Biogen of further clinical trial /other data following licencing in other countries. NICE will be aware of other ongoing trials being conducted by Biogen and Novartis/Avexis.	

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		To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly. Both Great Ormond Street Hospital (GOSH) and the John Walton Muscular Dystrophy Centre for Research in Newcastle will be delivering the Phase 3 trial of the therapy. There should therefore be no practical barrier to the administration and delivery of the treatment. SMA REACH is already mapping outcomes of the natural history of children with 5q SMA and the outcomes for children with SMA Type 1 treated with nusinersen. The infrastructure is therefore there for the monitoring of outcomes with this therapy. Outcomes that have every day clinical meaning and don't create an extra burden for clinicians need to be recorded. Administrative support / funding for this needs to be in place and, we understand, is underway. There need to be easy ways for parents to report the impact treatment has on their child and their health-related quality of life. We understand there are already significant developments for this via the global TREAT-NMD SMA Patient Registries, which include the UK SMA Patient Registry. Work to streamline the interface between SMA REACH and other SMA Patient Registries needs to continue such that outcomes for nusinersen, this treatment and any future treatments are captured and can be compared via one database. Clinicians will need to have available clear accessible user-friendly information about the treatment options that families will face. They will need to be given time to deliver this information and to either provide or set up appropriate ongoing support.	

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		Patient groups will also need this information so that, when asked, they can support parents / families with accurate information about treatment and processes which enable parents / families to make their own very personal and individual choices. **NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).** We strongly urge NICE to appraise this technology via the HST route as it meets the criteria for this route, namely: • Clinical trial evidence suggests that there is likely to be significant benefit to patients in terms of efficacy and administration. This is a 'one off' intravenous treatment • Though the price will be high, due to its being 'one off' the price will be known • There is appropriate clinical trial evidence, such as would enable evaluation. This is either available or anticipated to be available in the near future • The timing is right. There has not yet been an application to EMA, but we understand this is imminent. NICE has already collected a significant amount of evidence of the impact of SMA and the urgent need for treatment and is aware of economic models and their limitations. There is therefore a huge inroad already into the information required for this appraisal. This should allow NICE to include a plan for an HST of this	

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		treatment in its workload timeline now and publish timely guidance within six months of the marketing authorisation • Given the information available, the relevant clinical question(s) could be addressed by the application of the highly specialised technologies evaluation methodology **Additionally:** • The target patient group for the technology in its licensed indication is of an absolute maximum of 40 children a year. The numbers are so small and the technology so specialised that it will be concentrated in very few centres in the NHS – likely to be only the two named above • The target patient group is distinct for clinical reasons: though there is some blurring between types of SMA as there is a continuum of severity, we understand this intravenous treatment has to be delivered by age 6 months. Only children with SMA Type 1 show symptoms and are diagnosed by this age • The condition is chronic and severely disabling – this is clearly evidenced and well known to NICE via the EAP for SMA Type 1 and its nusinersen appraisal • The technology is expected to be used exclusively in the context of a highly specialised service: though the prevalence of all Types of 5q SMA exceeds the 'usual' 500 limit for specialised services, in view of the population incidence, services for SMA Type 1 would meet this criterion • The technology is likely to have a very high acquisition cost • The technology has the potential for life long impact • The need for national commissioning of the technology is significant.	
	Biogen Idec Ltd	**How many people have SMA type 1 in England, and how many would be offered onasemnogene abeparvovec therapy?**	Comments noted. No further actions required.

Section	Consultee/ Commentator	Comments [sic]	Action
		Biogen believe there are approximately 80-90 patients in England with SMA type I (approximately 90% of these are receiving nusinersen through the expanded access programme). Biogen are unable to comment on how many patients would be offered onasemnogene abeparvovec in clinical practice **How should best supportive care be defined?** The international treatment guidelines for patients with SMA include a two-part updated consensus statement by the International Standard of Care Committee (SCC) of the topics covered in the previous recommendations. Part 1 provides an update on diagnosis, rehabilitation, orthopaedic and spinal management in SMA, whereas part 2 discusses the pulmonary management, acute care, other organ involvement, ethical issues, medications, and the impact of new treatments for SMA. These guidelines are currently followed by treatment centres in England: - Mercuri E, Finkel RS, Muntoni F, Wirth B, Montes J, Main M, et al. Diagnosis and management of spinal muscular atrophy: part 1: recommendations for diagnosis, rehabilitation, orthopedic and nutritional care. Neuromuscul Disord. 2017 Dec; - Finkel RS, Mercuri E, Meyer OH, Simonds AK, Schroth MK, Graham RJ, et al. Diagnosis and management of Spinal Muscular Atrophy: Part 2: pulmonary and acute care; medications, supplements and immunizations; other organ systems; and ethics. Neuromuscul Disord. 2017 Dec	Following extensive discussion, it was agreed that this topic is appropriate for consideration as a highly specialised technologies (HST) evaluation.

Section	Consultee/ Commentator	Comments [sic]	Action
		NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process? Biogen believe onasemnogene abeparvovec should be appraised through the same process as deemed appropriate by NICE for nusinersen.	
	Treat SMA	The technology and its expected use in clinical practice suggest that it should be evaluated through the Highly Specialised Technologies route	Comment noted. Following extensive discussion, it was agreed that this topic is appropriate for consideration as a highly specialised technologies (HST) evaluation.
Additional comments on the draft scope	Muscular Dystrophy UK	The potential of this treatment for this patient group underlines the urgent need to put in place a newborn screening programme for SMA, complete with a corresponding pathway to ensure patients and their families are adequately supported at every stage of the screening and diagnosis journey. We would argue that this treatment meets all the criteria to be appraised through the Highly Specialised Technology Programme. Particularly in regards to criteria 4, it is likely that the treatment will be used exclusively in the context of a highly specialised service delivered in just 1 or 2 centres in England.	Comments noted. Diagnosis of SMA and newborn screening are not within the scope of this appraisal. Following extensive discussion, it was agreed that this topic is appropriate for consideration as a highly specialised

Section	Consultee/ Commentator	Comments [sic]	Action
			technologies (HST) evaluation.
	Biogen Idec Ltd	N/A	No action required.

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

Association of British Neurologists
Department of Health and Social Care