Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2877

nusinersen 12 mg solution for injection (Spinraza®)

Biogen Idec Ltd

07 August 2026

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission assessed under the orphan medicine process

nusinersen (Spinraza®) is accepted for restricted use within NHSScotland.

Indication under review: for the treatment of 5q Spinal Muscular Atrophy.

SMC restriction: for use in patients with pre-symptomatic 5q SMA

In a phase II single-arm study, 80% of pre-symptomatic patients with a genetic diagnosis of 5q Spinal Muscular Atrophy (SMA) who received treatment with nusinersen did not require respiratory intervention. Additionally, 92% of patients achieved the motor milestone of walking alone. Comparative evidence against risdiplam or onasemnogene abeparvovec is lacking.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Nusinersen is an antisense oligonucleotide treatment that modifies pre-messenger ribonucleic acid (pre-mRNA) splicing of the survival motor neuron 2 (SMN2) gene (which otherwise usually produces survival motor neuron [SMN] proteins that are defective and unstable). Translation of the modified pre-messenger RNA produces functional, full-length SMN protein.[1]

The recommended dose of nusinersen is 12 mg on days 0, 14, 28 and 63 by intrathecal injection, then once every 4 months thereafter. Treatment should be started as soon as possible after diagnosis. The need for continuation of nusinersen should be reviewed regularly and based on individual response to treatment.[1]

Nusinersen was previously assessed by SMC through the ultra-orphan framework and accepted for restricted use in NHSScotland for the treatment of 5q spinal muscular atrophy (SMA) in type 1 SMA (infantile-onset) and in symptomatic type 2 or type 3 SMA (later-onset) (SMC 1318/18, SMC2805).

1.2. Disease background

5q SMA is an inherited, autosomal recessive, neurodegenerative disorder resulting from deletions or mutation in the gene survival motor neuron 1 (SMN1) that codes for the SMN protein. This reduces levels of the SMN protein leading to a loss of spinal (and in more serious cases lower bulbar) motor neurons and progressive muscle weakness. A second, almost identical, SMN gene (SMN2) produces shorter and less functional SMN protein. Humans may have between 0 and 8 copies of the SMN2 gene. SMA is a clinical spectrum of disease with worsening disease severity and poorer prognosis being linked to having fewer SMN2 copies and a younger age of symptom onset. Most patients have a symptom free period after birth which differs depending on the individual and clinical subtype. SMA is classified into five clinical subtypes, type 0 , 1, 2, 3 and 4, according to age of onset and the patient's maximal functional status prior to degeneration. Most patients with two copies of the SMN2 gene are predicted to develop SMA type 1 and most with three copies of the SMN2 gene are expected to develop SMA type 2. Infants who are pre-symptomatic are identified through newborn screening which is now available in Scotland, or by targeted testing of related individuals.[2-7]

1.3. Company proposed position

The submitting company has requested that nusinersen is restricted for use in patients with pre-symptomatic 5q SMA. SMC advice is already available for SMA type 1, 2, and 3, as described above.

1.4. Treatment pathway and relevant comparators

Routine newborn screening for SMA has recently been introduced in Scotland and prior to this pre-symptomatic treatment has been limited.[7] There are currently two treatments available for pre-symptomatic 5q SMA in Scottish clinical practice. Risdiplam is an orally administered SMN2 pre-mRNA splicing modifier, which was accepted for use by SMC in 2022 in patients aged 2 months or older, with a clinical diagnosis of SMA type 1, type 2 or type 3 or with one to four SMN2

copies (SMC2401). It subsequently had a licence extension in 2023 to include use from birth and is available in NHSScotland through the inherited metabolic diseases medicines risk share agreement. Onasemnogene abeparvovec is a viral gene therapy administered by intravenous (IV) infusion. It was accepted for restricted use by SMC in 2021 including in pre-symptomatic patients with 5q SMA with a bi-allelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene, where patients are expected to develop SMA type 1 (SMC2311).[8-10] Risdiplam and onasemnogene abeparvovec may both be relevant comparators for pre-symptomatic SMA although clinical experts consulted by SMC indicated that nusinersen may not displace these treatments for most patients. The submitting company considered that onasemnogene abeparvovec was the relevant active comparator however, because of a lack of suitable data, the only comparator included in this submission was best supportive care (BSC).

1.5. Category for decision-making process

Eligibility for a PACE meeting

Nusinersen meets SMC orphan criteria.

2. Summary of Clinical Evidence

2.1. Evidence to support the positioning proposed by the submitting company

The NURTURE study provides evidence of the efficacy and safety for nusinersen in pre-symptomatic SMA.

Table 2.1. Overview of relevant study

Criteria	NURTURE[2, 11, 12]
Study design	Multicentre, open-label, single-arm phase II study
Eligible patients	• Aged ≤6 weeks at first dose with no clinical signs or symptoms strongly suggestive of SMA. • Genetic documentation of 5q SMA (homozygous gene deletion, mutation, or compound heterozygous mutation) with 2 or 3 copies of the SMN2 gene. • Ulnar compound muscle action potential amplitude ≥1 mV at baseline. • Absence of hypoxia. • Gestational age of 37 to 42 weeks for single births or 34 to 42 weeks for twins.
Treatments	Nusinersen 12 mg administered as an intrathecal injection by lumbar puncture. Four loading doses on days 1, 15, 29 and 64 followed by maintenance doses every 4 months (119 days) until day 2,801, for a total of 27 doses. Some infants received a 12 mg scaled equivalent dose before a protocol revision in March 2017.
Primary outcome	Time to death or respiratory intervention (invasive or non-invasive for ≥6 hours per day continuously for ≥7 days or tracheostomy).
Secondary outcomes	• Overall survival. • Attainment of motor milestones as assessed by WHO criteria. • Change from baseline in Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders. This is a 16-item, 64-point motor assessment developed to evaluate motor skills in infants with SMA type I, with higher scores indicating better motor function. • Change from baseline in Hammersmith Functional Motor Scale - Expanded. A 33-item, 66-point tool to assess motor function in children with SMA. It will be used to assess children aged ≥2 years with higher scores indicating better motor function. • Proportion of patients developing clinically manifested SMA as defined by: ○ Age-adjusted weight <5th percentile or decrease of ≥2 major weight growth

	curve percentiles (3rd, 5th, 10th, 25th, or 50th) or a percutaneous gastric tube placement for nutritional support.
Statistical analysis	Time to death or respiratory intervention, proportion of participants alive, proportion of participants achieving WHO motor milestones, proportion of participants developing clinically manifested SMA, and safety analyses were assessed in the intent-to-treat population which included all study participants who received ≥1 dose of nusinersen. All other efficacy analyses were assessed in interim efficacy sets that comprised all dosed patients who attended or had the opportunity to attend the targeted visit of the analysis (efficacy set).

Abbreviations: SMA = Spinal muscular atrophy; SMN2 = survival motor neuron 2; WHO = World Health Organization.

At the December 2024 data cut (final analysis) of the NURTURE study, the mean follow up was 7.72 years and 88% (22/25) of patients had received all 27 doses. The primary outcome of death or respiratory intervention was met by 20% (5/25) in the intention-to-treat population (ITT) population, all were in the 2 SMN2 copy cohort. The median time to death or respiratory intervention was not estimated due to too few events. The indication for ventilation was acute reversible infections in four patients. No patients required permanent ventilation or tracheostomy and there were no deaths. The WHO motor milestones achieved increased from baseline and were maintained at the last study visit.[11, 13, 14]

Table 2.2. Key efficacy results for NURTURE (data cut: December 2024).[11, 13-15]

	Nusinersen (n=25)	
	2 SMN2 copies (n= 15)	**3 SMN2 copies (n= 10)**
Primary outcome: Time to death or respiratory intervention		
Events, n (%)	5 (33%)	0
Deaths, n	0	0
Ventilatory support ≥ 6 hours per day ≥ 7 days, n (%)	5 (33%)	0
Selected WHO motor milestones achieved at last study visit		
Sitting without support	15 (100%)	10 (100%)
Standing alone	14 (93%)	10 (100%)
Walking alone	13 (87%)	10 (100%)
CHOP INTEND[a]		
Mean total score at baseline	47.0	51.9
Mean total score at last study visit	63.3	64
Hammersmith Functional Motor Scale – Expanded (HFMSE)[b]		
Mean score at first evaluable assessment	34.5	46.4
Mean score at last study visit	56.1	65.9

Abbreviations: CHOP INTEND = Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders; SMN2 = survival motor neuron 2; WHO = World Health Organization.
[a]The CHOP INTEND was assessed until a patient reached the maximum score of 64, after which it was not assessed.
[b]HFMSE has a maximum score of 66 and was measured in patients aged ≥ 2 years. Last study visit scores were reported in n=12 in 2 SMN2 and n=8 in 3 SMN2 groups.

Symptoms of SMA were observed in 48% of patients at 13 months of age, most (40%) were in the 2 SMN2 copy cohort, and in 28% of patients at 24 months of age (all with 2 SMN2 copies). The most common symptoms were weight <5th percentile, decrease of ≥2 major weight growth curve percentiles, or failure to achieve age-appropriate milestones. These patients continued to grow, gain weight and achieve milestones over time.[2, 11]

2.3 Indirect evidence to support clinical and cost-effectiveness comparisons

The submitting company conducted a matching adjusted indirect comparison (MAIC) between nusinersen and onasemnogene abeparvovec using data from the NURTURE and SPR1NT studies.[2, 16] The outcomes included the WHO motor milestones: stands with support before 18 months of age and walks alone before 18 months of age. Although the point estimates of the proportion difference favoured onasemnogene abeparvovec, there was no evidence of a difference between treatments as the 95% confidence intervals spanned 0. The results of this comparison have not been used in the cost-effectiveness analysis.

In the absence of direct evidence and limited indirect evidence versus relevant active comparators, the submitting company used the relative efficacy estimates of nusinersen versus a sham control from the ENDEAR (infantile-onset SMA) and CHERISH (later-onset SMA) studies to estimate BSC effectiveness in the cost-effectiveness analysis. The relative risk of decline was based on the proportions of patients that did not experience a motor milestone response. In ENDEAR, 49% (36/73) in the nusinersen group and 100% (37/37) in the sham control group did not have a motor milestone response. In CHERISH, 20% (13/66) and 5.9% (2/34) in the nusinersen and sham control groups respectively gained ≥1 WHO motor milestone. Longer term decline in attainment of WHO motor milestones was derived from a natural history study. [17-19] These results have been applied in the economic modelling.

3. Summary of Safety Evidence

Evidence from the NURTURE study supports the safety of nusinersen for the treatment of patients with pre-symptomatic 5q SMA; however, there are no comparative data. Published safety results are available from the December 2024 data cut with approximately 8 years of follow up. At this data cut, the median time on study was 7.92 years (range: 5.9 to 8.3) and the median number of doses was 27.[11, 14]

In the ITT study population (n=25), all patients had a treatment-emergent adverse event (AE), the proportions considered related or possibly related to study drug or lumbar puncture were 44% and 60% respectively. Serious adverse events (SAEs) occurred in 56% of patients; however, none were assessed as related to study treatment. No patients discontinued treatment due to an adverse event.[11]

The AEs assessed by the investigator as possibly related to study treatment included: hyperreflexia and protein urine present (8% each) alanine aminotransferase increased, aspartate aminotransferase increased, blood alkaline phosphatase increased, blood calcium increased, clonus, dermatitis allergic, eosinophil count increased, extensor plantar response, lymphocyte count increased, muscular weakness, musculoskeletal procedural complication, platelet count increased, post lumbar puncture syndrome, proteinuria, pyrexia, rash, tachycardia, and white blood cell count increased (4% each).[11, 14]

There were 48% of participants that experienced AEs considered by the investigator to be related to the lumbar puncture procedure. These included post lumbar puncture syndrome (24%), procedural pain (20%), and post procedural complication, musculoskeletal procedural

complication, post procedural swelling, procedural vomiting, and subdural hematoma (4% each). All lumbar puncture related AEs resolved.[11]

The most frequently reported SAEs reported in >4% of patients included pneumonia (20%), respiratory syncytial virus infection and choking (12% each), and respiratory syncytial virus bronchiolitis, upper respiratory tract infection, respiratory distress, respiratory failure, dehydration, pyrexia, and tonsillectomy (8% each). All SAEs resolved or were downgraded to AEs.[11]

The European regulator concluded that the safety profile of nusinersen in the NURTURE study was consistent with the known safety profile of nusinersen when given as a 12 mg dose and with previous clinical findings. No new safety concerns were identified.[11]

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- At the December 2024 data cut of the NURTURE study, after approximately 8 years of follow up, all patients were alive and 80% (20/25) did not require respiratory intervention (defined as invasive or non-invasive ventilation for ≥6 hours per day continuously for ≥7 days). There were also no patients that required a tracheostomy.[11, 13, 14]
- In the 2 SMN2 copy cohort, 87% achieved walking alone, 93% achieved standing alone and all were able to sit without support by the last study visit. These motor milestones were achieved by all patients in the 3 SMN2 copy cohort at the last study visit. There were no signs of halt or reversion of acquired milestones.[11, 13, 14]
- Regulators noted that nusinersen initiated in pre-symptomatic patients results in greater milestone acquisition compared with the natural history of the disease. They also considered that compared with studies of nusinersen in symptomatic patients, milestones were achieved earlier and the improvement was more sustained. Overall, they concluded that the use of nusinersen has a significant impact on the disease expression and prognosis in pre-symptomatic patients.[11]

4.2. Key uncertainties

- The key evidence for this submission is derived from NURTURE, a small, open-label, single-arm phase II study. Therefore, there is no direct evidence comparing nusinersen with risdiplam or onasemnogene abeparvovec, which are alternative treatments that are licensed for use in pre-symptomatic 5q SMA, and the relative efficacy and safety is uncertain. The submitting company attempted to conduct an unanchored MAIC for nusinersen versus onasemnogene abeparvovec in pre-symptomatic 5q SMA. However, they concluded that the unanchored design, differences between studies and small effective sample size, collectively introduced very high levels of bias and made it difficult to draw meaningful conclusions. They also noted that an indirect comparison of nusinersen versus risdiplam was not possible because of limited published data and differences in study design.
- The submitting company compared nusinersen with BSC in the cost-effectiveness analysis using a combination of efficacy estimates from the sham control arm from other pivotal nusinersen studies and natural history data.[17-19] However, these comparisons are uncertain

because of differences in study design, sample size, population and follow-up. The methodology used was unclear.

- The NURTURE study did not include pre-symptomatic patients who received short term nusinersen while waiting for treatment with onasemnogene abeparvovec. Therefore, there is limited evidence in this population for nusinersen as a bridging treatment to gene therapy. The NURTURE study also does not provide evidence for sequential treatment of nusinersen in patients who have previously received risdiplam or onasemnogene abeparvovec and may have experienced treatment failure or tolerability issues; studies assessing sequential treatment are ongoing.[20, 21]
- NURTURE included infants aged ≤6 weeks with SMA who had 2 or 3 copies of the SMN2 gene as these patients were most likely to develop SMA type 1 or 2.[2] There is no evidence of pre-symptomatic treatment with nusinersen in patients >6 weeks of age, or in those with >3 SMN2 copies who may be more likely to develop less severe SMA subtypes such as SMA type 3 or type 4.
- The most recent data cut (December 2024) of the NURTURE study provides evidence of nusinersen for the treatment in pre-symptomatic patients with SMA for up to approximately 8 years. However, SMA is a lifelong neurodegenerative condition and it is uncertain how longer term treatment with nusinersen, beyond 8 years and into adulthood, will affect the natural history of the disease. It is reassuring that patients in the NURTURE study retained acquired motor milestones and there was no evidence of halt or reversion.[2, 11]

4.3. Clinical expert input

Clinical experts consulted by SMC were mixed in their views about how nusinersen might fit into the treatment pathway. Overall, they considered it would be an additional treatment option for patients with pre-symptomatic 5q SMA.

4.4. Service implications

Clinical experts consulted by SMC generally considered the introduction of nusinersen for pre-symptomatic SMA may have service implications. Treatment will require hospital admission often administered under general anaesthetic because of the intrathecal route of administration. Preparation and delivery will require pharmacy aseptic resource, theatre time, a trained specialist doctor to administer and availability of several members of the multidisciplinary team in theatre including anaesthetists, theatre staff and a neuromuscular nurse specialist. These services may already be established as nusinersen is already available for symptomatic SMA.

5. Patient and clinician engagement (PACE)

A patient and clinician engagement (PACE) meeting with patient group representatives and clinical specialists was held to consider the added value of **nusinersen**, as an **orphan** medicine, in the context of treatments currently available in NHSScotland.

The key points expressed by the group were:

- 5q SMA is a severe neuromuscular condition that typically presents in infancy or early childhood and is life-limiting if left untreated. It exists across a spectrum of severity but is

characterised by irreversible loss of motor neurons leading to progressive muscle weakness affecting movement, breathing and swallowing, and resulting in lifelong disability. SMA places substantial emotional, physical and financial burdens on patients and families, with parents and carers often taking on extensive caregiving responsibilities.

- The rollout of newborn screening for 5q SMA is transforming care by enabling diagnosis and treatment before symptoms develop. Pre-symptomatic treatment has the potential to preserve neurological function, substantially improving quality of life. It may allow children to attend mainstream education and participate more fully in everyday activities with friends and family. Early treatment shifts the focus from survival alone to preserving independence and supporting the achievement of age-appropriate developmental milestones. Newborn screening may lead to a generation of children who may never experience the physical limitations that have historically been associated with SMA.
- By preventing or reducing disease progression, pre-symptomatic treatment may also lessen the need for complex care, specialised equipment and ongoing health and social care support. This could help reduce the physical, emotional and practical burden on families and carers, support more normal family life, and improve household wellbeing and financial security.
- There are currently two treatments available in Scotland for pre-symptomatic SMA: onasemnogene abeparvovec and risdiplam. Nusinersen would provide an additional treatment option, helping to ensure that treatment can be personalised to the individual. Access to all three treatments, which appear to show similar benefits, is essential to preserve patient and family choice and to enable treatment to start without delay.
- Nusinersen is unlikely to be the preferred first-line treatment for many patients with pre-symptomatic 5q SMA because it requires ongoing intrathecal administration, which is more invasive than alternative treatment options. However, it remains an important treatment option. It has an established safety profile, extensive long-term real-world evidence, and may be particularly valuable for patients who are not eligible for gene therapy or for whom other treatments are unsuitable or not well tolerated. While nusinersen requires periodic hospital visits, some families may find treatment every four months less burdensome than taking a daily oral medication. In addition, regular treatment visits may provide opportunities for ongoing clinical review, ensuring continued engagement with the healthcare team even when a child is clinically stable.

Additional Patient and Carer Involvement

We received a joint patient group submission from Muscular Dystrophy UK and Spinal Muscular Atrophy UK; both organisations are registered charities. Muscular Dystrophy UK has received 1.32% pharmaceutical company funding in the past two years, with none from the submitting company. Spinal Muscular Atrophy UK has received 17% pharmaceutical company funding in the past two years, including from the submitting company. Representatives from both organisations participated in the PACE meeting. The key points of their joint submission have been included in the full PACE statement considered by SMC.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

A summary of the submitted economic case is provided in Table 6.1.

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost-utility analysis, and an exploratory cost-minimisation analysis (CMA).
Time horizon	Lifetime – 100 years, with an assumed starting age of 6 weeks.
Population	The patients included in the economic modelling were infants with pre-symptomatic 5q SMA.
Comparators	Within the central analysis nusinersen plus BSC was compared with BSC alone. BSC comprised of a large number of non-pharmacological treatments including monitoring, dietary changes, physiotherapy and surgery. The costs of BSC were not included in the modelling. The cost outcomes for nusinersen, onasemnogene abeparvovec and risdiplam were compared within a CMA.
Model description	The submission used a Markov model which traced patient outcomes, in relation to physical functioning, across 5 health states. These health states were 'not sitting,' 'sitting without support,' 'standing with support,' 'walking independently' and 'permeant ventilation.' At baseline, the age of the cohort was less than 6 weeks and so all patients started the model in the 'not sitting' health state. Patients could transition out of 'not sitting' state as they aged and developed but also return to it due to the progression of SMA.
Clinical data	The main source of clinical evidence was the NURTURE study.[11, 13-15] This study informed state occupancy in the nusinersen arm across the first 96 months of the model, corresponding to the observation period. In the absence of comparative data, the submitting company estimated outcomes in the BSC arm over the first 15 months from the weighted data of patients receiving placebo in the ENDEAR and CHERISH studies.[17, 18] The submitting company judged that the data from ENDEAR (infantile-onset) would be most applicable to the pre-symptomatic sub-population with two copies of the SMN2 gene (Type 1 SMA), whilst CHERISH (later-onset) would be most applicable to the sub-population with three copies of SMN2 gene (Type 2 and 3 SMA). The weighting between SMA types in the BSC arm was based on the worldwide SMA distribution estimated by Calucho et al (2018).[22] Patients in the ENDEAR and CHERISH studies were older than those in the NURTURE study, meaning that their baseline mobility functioning did not represent a pre-symptomatic population. Therefore, adjustments were made to try and align baseline state occupancy with a younger, pre-symptomatic population.
Extrapolation	In the BSC arm, after the first 15 months, a per cycle probability of decline was applied, estimated from a retrospective cohort study of people with SMA from the Netherlands.[19] In the nusinersen arm, after the first 96 months, patients' status could also decline. That rate of decline was taken from the same source as the BSC arm but adjusted with a relative risk to account for the treatment effect of nusinersen. That relative risk was matched to the weighted relative risk of progression estimated between the nusinersen arms and the placebo arms in the ENDEAR and CHERISH studies. For patients receiving BSC, the rate of movement from the 'not sitting' state to the 'permanent ventilation' state was drawn from the literature.[23] Patients did not progress to the 'permanent ventilation' state if receiving nusinersen. No mortality events were observed in the NURTURE study. Instead the modelling matched mortality rates to those reported as part of a previous HTA submission for an SMA treatment.[24] Nusinersen was subject to a discontinuation rate. Upon discontinuation patient who had been receiving nusinersen would experience the same progression and mortality rates as BSC patients.
Quality of life	Utility values for patients were derived from a utility study originally conducted as part of a previous HTA submission[24] and used in several subsequent evaluations of SMA treatments.

	The values were 0.00 for 'permeant ventilation,' 0.19 for 'not sitting,' 0.60 for 'sitting without support,' 0.77 for 'standing with support' and 0.93 for 'walking independently'. These values were age-adjusted. In addition, the submitting company assumed that patients receiving nusinersen would have superior upper body functioning not otherwise captured by the health state utility value. The submitting company applied a 0.10 utility increment for all nusinersen patients.
Costs and resource use	The model included acquisition costs and administration costs for nusinersen. Additional costs included in the model accounted for medical tests, medical visits, hospitalisations, A&E attendance and social service costs.
PAS	A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. Under the PAS, a discount was offered on the list price. A PAS discount is in place for onasemnogene abeparvovec and risdiplam and these were included in the results used for decision-making by using estimates of the comparator PAS price.

6.2. Results

The base case analysis indicate nusinersen was dominant compared to BSC meaning it was estimated as resulting in lower costs and better health outcomes for patients. The scale of those health gains was estimated at 5.72 quality-adjusted life years (QALYs).

Disaggregated results showed that nusinersen incurred a large treatment cost, but savings across the 'permanent ventilation', 'not sitting' and 'sitting without support' states. QALY gains were from additional time spent in the 'standing with support' and 'walking independently' states.

Upon request the submitting company conducted a CMA comparing nusinersen against onasemnogene abeparvovec and risdiplam, assuming equal efficacy between all treatments. The results of that analysis cannot be presented due to the presence of confidential PAS discounts on all three treatments.

*Other data were also assessed but remain confidential.**

6.3. Sensitivity analyses

Within the base case, areas of uncertainty in the comparison with BSC were explored through one-way sensitivity analysis, probabilistic sensitivity analysis and scenario analysis. A selection of relevant scenarios is presented below.

Table 6.3: Scenario analysis results – Comparison of nusinersen plus BSC against BSC

	Parameter	Base case	Scenario	Incr. Costs (£)	Incr. QALYs	ICER (£/QALY)
	Base case			*CiC*	5.72	Dominant
1	Time horizon	100 years	50 years	*CiC*	5.71	Dominant
2			75 years	*CiC*	5.72	Dominant
3	Care giver utilities	Excluded	Included	*CiC*	8.58	Dominant
4	Nusinersen treatment utility increment	Include	Exclude	*CiC*	5.20	Dominant
5	Decline in health state for nusinersen patients	Included from 96 months (8 years)	Included from 180 months (15 years)	*CiC*	6.50	Dominant
6	Decline in health state for BSC patients	Drawn from natural history model	Rate from natural history model halved	*CiC*	6.28	Dominant
7			Rate from natural	*CiC*	5.14	Dominant

			history model doubled			
8	Lumbar puncture disutility	None	Disutility based on Lo et al (2021)[25]	*CiC*	4.91	Dominant

Abbreviations: CiC = commercial in confidence; Incr. = incremental; ICER = incremental cost-effectiveness ratio; QALYs =quality-adjusted life years

6.4. Key strengths

- The submitting company drew heavily from previous HTA submissions for SMA treatments, matching numerous inputs, assumptions and the model structure. This allowed for direct comparison with those submissions.
- The main comparator included in the economic analysis was BSC. This was identified as the most relevant comparator in the group of patients who are ineligible or intolerant to the other treatment options risdiplam or onasemnogene abeparvovec.

6.5. Key uncertainties

- Clinical experts consulted by SMC indicated that risdiplam and onasemnogene abeparvovec were used in Scotland, although sequencing in the pre-symptomatic population was unclear, and so these may be relevant comparators for some patients. The submitting company asserted that conducting a robust indirect comparison between the three treatment was infeasible. This was accepted as reasonable by the SMC, but led to uncertainty in the efficacy and cost-effectiveness between treatments. Upon request the company provided a CMA assuming that nusinersen, risdiplam and onasemnogene abeparvovec all had the same efficacy. That analysis also assumed no discontinuation of nusinersen or risdiplam, to align with the inability to discontinue onasemnogene abeparvovec, which is a one-off treatment. The results of that CMA cannot be reported due to the confidential PAS discounts for risdiplam and onasemnogene abeparvovec.
- The comparison to BSC across the first 15 months was done through a naive comparison with two other nusinersen studies – ENDEAR and CHERISH. Those studies were in different patient populations – infantile-onset and later-onset SMA – introducing heterogeneity issues. The differences in age of patients included in studies forced the submitting company to make changes to the proportion of patients achieving certain milestones at given times.
- In the base case, the company did not apply a disutility for the intrusive delivery of nusinersen through lumbar puncture. This was explored as a scenario (see Scenario 8, Table 6.3), where a reduction in incremental QALYs was observed. Nusinersen remained dominant.

7. Conclusion

The Committee considered the benefits of nusinersen in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and agreed that as nusinersen is an orphan medicine, SMC can accept greater uncertainty in the economic case.

After considering all the available evidence and the output from the PACE process, the Committee accepted nusinersen for restricted use in NHSScotland.

8. Guidelines and Protocols

N/A

9. Additional Information

9.1. Product availability date

30 May 2017

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per year (£)
nusinersen	**12 mg loading dose on days 0, 14, 28 and 63 followed by 12 mg maintenance dose every 4 months by intrathecal injection**	**Year 1 450,000 Subsequent years 225,000**

Costs from BNF online on 06/05/2026. Costs calculated using the full cost of vials assuming wastage. Costs do not take any patient access schemes into consideration.

10. Company Estimate of Eligible Population and Estimated Budget Impact

The submitting company estimated there would be 5 patients eligible for treatment with nusinersen in each year. The estimated uptake rate was 40% in years 1, 2 and 3. This resulted in 2 patients estimated to receive treatment in year 1 rising to 6 patients in year 3.

SMC is unable to publish the with-PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS. This template does not incorporate any PAS discounts associated with comparator medicines or PAS associated with medicines used in a combination regimen.

*Other data were also assessed but remain confidential.**

References

1. Electronic Medicines Compendium (EMC. Biogen Idec Ltd. Spinraza 12 mg solution for injection. Summary of product characteristics 2025 Mar 26 [cited; Available from: https://www.medicines.org.uk/emc/product/2715/smpc.
2. De Vivo DC, Bertini E, Swoboda KJ, Hwu WL, Crawford TO, Finkel RS*, et al.* Nusinersen initiated in infants during the presymptomatic stage of spinal muscular atrophy: Interim efficacy and safety results from the Phase 2 NURTURE study. Neuromuscul Disord. 2019;29(11):842-56. Epub 20190912.
3. Darras BT. Spinal muscular atrophies. Pediatr Clin North Am. 2015;62(3):743-66. Epub 20150411.
4. The European Medicines Agency (EMA) European Public Assessment Report. Nusinersen (Spinraza®). 13/09/2025 EMA/CHMP/379593/2025. https://www.ema.europa.eu/en/documents/variation-report/spinraza-h-c-004312-x-0038-epar-assessment-report_en.pdf.
5. Finkel RS, Benatar M. Pre-symptomatic spinal muscular atrophy: a proposed nosology. Brain. 2022;145(7):2247-9.
6. Spinal Muscular Atrophy UK. SMA Newborn Screening Test - Helping you decide. Last updated March 2026. Available at: https://smauk.org.uk/sma-newborn-screening-test-helping-you-decide/.
7. Scottish Government. New screening for rare condition in newborns. Published 23 March 2026. Available at: https://www.gov.scot/news/new-screening-for-rare-condition-in-newborns/.
8. Roche Products Limited. Risdiplam powder for oral solution (Evrysdi®) Summary of product characteristics. Electronic Medicines Compendium. https://www.medicines.org.uk/emc/product/12582/smpc Last updated: 17 December 2025.
9. Novartis Pharmaceuticals UK Ltd. Onasemnogene abeparvovec solution for infusion (Zolgensma®). Summary of product characteristics. Electronic Medicines Compendium. https://www.medicines.org.uk/emc/product/11572/smpc. Last updated: 06 June 2025.
10. National Services Scotland. List of medicines included in the ultra-orphan drugs risk share arrangement (February 2026). Available at: https://www.nss.nhs.scot/media/6532/nsd619-00305-medicines-included-in-ultra-orphan-drugs-risk-share-arrangement.pdf.
11. The European Medicines Agency (EMA). Assessment report for paediatric studies submitted according to Article 46 of the Regulation (EC) No 1901/2006. Nusinersen (Spinraza®). 21/08/25 EMADOC-1700519818-2209709. Available at: https://www.ema.europa.eu/en/documents/variation-report/spinraza-pam-0000279100-epar-assessment-report_en.pdf.
12. Crawford TO, Swoboda KJ, De Vivo DC, Bertini E, Hwu WL, Finkel RS*, et al.* Continued benefit of nusinersen initiated in the presymptomatic stage of spinal muscular atrophy: 5-year update of the NURTURE study. Muscle Nerve. 2023;68(2):157-70. Epub 20230706.
13. Kuntz Nl DVDCCTOKJFRSBEPJAHWLPAB. NURTURE study: long-term benefits of nusinersen in presymptomatic SMA over 8 years of follow-up. Cure SMA 2025 Annual SMA Research and Clinical Care Meeting; June 25-27, 2025; Anaheim, CA, USA.
14. Kuntz N, De Vivo D, Crawford T, Kirschner J, Finkel R, Bertini E*, et al.* 422PNURTURE study: long-term benefits of nusinersen in presymptomatic spinal muscular atrophy (SMA) over 8 years of Follow-up. Neuromuscular Disorders. 2025;53:105585.
15. BiogenLinc. Measures of Motor Function. Hammersmith Functional Motor Scale−Expanded (HFMSE). Last updated: February 2022. Available at: https://biogenlinc.co.uk/en/therapy-areas/sma/measures-of-motor-function/hfmse/.
16. Kevin A. Strauss MAF, Francesco Muntoni, Kayoko Saito, Jerry R. Mendell, Laurent Servais, Hugh J. McMillan, Richard S. Finkel, Kathryn J. Swoboda, Jennifer M. Kwon, Craig M. Zaidman, Claudia A. Chiriboga, Susan T. Iannaccone, Jena M. Krueger, Julie A. Parsons, Perry B. Shieh, Sarah

Kavanagh, Sitra Tauscher-Wisniewski, Bryan E. McGill & Thomas A. Macek Onasemnogene abeparvovec for presymptomatic infants with two copies of SMN2 at risk for spinal muscular atrophy type 1: the Phase III SPR1NT trial. Nature Medicine. 2022;28:1381-9.
17. Finkel RS, Mercuri E, Darras BT, Connolly AM, Kuntz NL, Kirschner J*, et al.* Nusinersen versus Sham Control in Infantile-Onset Spinal Muscular Atrophy. New England Journal of Medicine. 2017;377(18):1723-32.
18. Mercuri E, Darras BT, Chiriboga CA, Day JW, Campbell C, Connolly AM*, et al.* Nusinersen versus Sham Control in Later-Onset Spinal Muscular Atrophy. New England Journal of Medicine. 2018;378(7):625-35.
19. Wadman RI, Wijngaarde CA, Stam M, Bartels B, Otto LAM, Lemmink HH*, et al.* Muscle strength and motor function throughout life in a cross-sectional cohort of 180 patients with spinal muscular atrophy types 1c-4. Eur J Neurol. 2018;25(3):512-8. Epub 20180202.
20. ClinicalTrials.gov. A Study to Learn About the Effect of Higher Doses of Nusinersen (BIIB058) Given as Injections to Participants With Spinal Muscular Atrophy (SMA) Who Were Previously Treated With Risdiplam (ASCEND) (ASCEND). 2025 [cited 2025 Sep 29]; Available from: https://www.clinicaltrials.gov/study/NCT05067790.
21. ClinicalTrials.gov. A Study to Learn About the Effect of Nusinersen (BIIB058) Given as Injections to Children With Spinal Muscular Atrophy (SMA) Who Were Previously Treated With Onasemnogene Abeparvovec (RESPOND) (RESPOND). 2025 [cited 2025 Sep 29]; Available from: https://www.clinicaltrials.gov/study/NCT04488133.
22. Calucho M, Bernal S, Alías L, March F, Venceslá A, Rodríguez-Álvarez FJ*, et al.* Correlation between SMA type and SMN2 copy number revisited: An analysis of 625 unrelated Spanish patients and a compilation of 2834 reported cases. Neuromuscul Disord. 2018;28(3):208-15. Epub 2018/02/13.
23. Wijngaarde CA, Stam M, Otto LAM, van Eijk RPA, Cuppen I, Veldhoen ES*, et al.* Population-based analysis of survival in spinal muscular atrophy. Neurology. 2020;94(15):e1634-e44. Epub 2020/03/29.
24. National Institute for H, Care E. Onasemnogene abeparvovec for treating presymptomatic spinal muscular atrophy. Highly specialised technologies guidance. HST24. 2023 19 April. Report No.
25. Lo SH, Gorni K, Sutherland CS, Martí Y, Lloyd A, Paracha N. Preferences and Utilities for Treatment Attributes in Type 2 and Non-ambulatory Type 3 Spinal Muscular Atrophy in the United Kingdom. PharmacoEconomics. 2022;40(Suppl 1):91-102. Epub 20211018.

This assessment is based on data submitted by the applicant company up to and including 12 June 2026.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:*https://www.scottishmedicines.org.uk/about-us/policies-publications/

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC includes Scottish national contract prices in its decision-making. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document.

Patient Access Schemes (PAS): A PAS is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-

effective innovative medicines. The Patient Access Scheme Assessment Group (PASAG), established under the auspices of Public Services Delivery Scotland, reviews and advises NHS Scotland on the feasibility and acceptability on implementing proposed schemes. PASAG operates separately from SMC to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHS Scotland on the basis of a PAS that has been considered acceptable for implementation by PASAG, a set of guidance notes on the operation of the scheme will be circulated to health boards' Area Drugs and Therapeutics Committees prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.