NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Intrathecal onasemnogene abeparvovec for treating spinal muscular atrophy ID6556

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of intrathecal onasemnogene abeparvovec within its marketing authorisation for treating spinal muscular atrophy.

Background

Spinal muscular atrophy (SMA) is a rare genetic disorder that causes muscle weakness and progressive loss of movement. It is most commonly caused by defects in the gene SMN1, which leads to degeneration of motor neurones in the spinal cord (this is termed '5q SMA'). The motor neurones most affected by this condition are those that allow walking, crawling, arm movement, head and neck movement, swallowing and breathing. SMA causes substantial disability, and may lead to increased mortality and reduced life expectancy. The most severe forms of SMA, if untreated, typically cause death before age 2 years. People with later-onset types of SMA usually live into adolescence or adulthood. SMA also 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.

SMA symptom severity varies substantially and is often grouped into SMA types based on the age of onset of symptoms and the best motor function the person obtained. The types of SMA decrease in severity from type 0, in which symptoms arise before birth and babies survive for only a few weeks, to type 4 (adult-onset) which is associated with mild motor impairment and a normal life span. Categorising people into types consistently at presentation is difficult due to the variable nature of the disease. Types 0 and 4 are rarely diagnosed and therefore there is little evidence for these types. In people with type 1 SMA, symptoms arise before 6 months and babies are unable to sit independently; babies with type 1 SMA have low muscle tone (hypotonia) and severe muscle weakness which affects movement, swallowing and breathing. In people with type 2 SMA, the onset of symptoms occurs at between 7 and 18 months, and people with this condition are often severely disabled and unable to walk unaided. People with type 3 SMA experience varying degrees of symptom severity with 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.[1]

SMA may also be diagnosed pre-symptomatically through genetic testing. The number of SMN2 gene copies, which encodes the SMN protein that can partially compensate for the loss of the SMN1 gene, is inversely related to the severity of SMA and can broadly predict the course of the disease[2]. However, at an individual level, accurate predictions cannot be made about the type or severity of SMA based on the SMN2 copy number alone.[3,4] Currently in England only a small number of people are identified pre-symptomatically where a sibling has been diagnosed with SMA but this may rise if newborn screening for SMA is implemented.

SMA affects an estimated 1 in 14,000 births worldwide and it is estimated that about 47 people were born with SMA in the UK in 2023, 60% with type 1 SMA.[1] Around 683-1,366 people currently have SMA in the UK.[1] Due to drug treatments which can improve the life expectancy of people with SMA, prevelance is expected to increase over time.

NICE highly specialised technology appraisal guidance 15 recommends intravenous onasemnogene abeparvovec as an option for treating 5q spinal muscular atrophy with a bi-allelic mutation in the SMN1 gene and a clinical diagnosis of type 1 SMA in babies, only if they are 6 months or younger, or they are aged 7 to 12 months, and their treatment is agreed by the national multidisciplinary team. NICE highly specialised technology appraisal guidance 24 partially updated the guidance to also recommend intravenous onasemnogene abeparvovec for treating pre-symptomatic 5q spinal muscular atrophy (SMA) with a biallelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene in babies aged 12 months and under.

Nusinersen and risdiplam are currently available through managed access agreements. NICE technology appraisal guidance 588 and 755 recommended these technologies within their respective marketing authorisations for people who have pre-symptomatic SMA, or SMA types 1, 2 or 3 only if the conditions of the managed access agreements are followed.

The technology

Intrathecal onasemnogene abeparvovec (OAV101 IT, Novartis Pharmaceuticals UK), does not currently have a marketing authorisation in the UK for treating 5q SMA. It has been studied in clinical trials for treating 5q SMA in people aged 2 - 17 years.

Onasemnogene abeparvovec as an intravenous infusion has a marketing authorisation in the UK for the treatment of

- people with 5q SMA with a bi-allelic mutation in the SMN1 gene and a clinical diagnosis of SMA Type 1, or
- people with 5q SMA with a bi-allelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene.

Intervention(s)	Onasemnogene abeparvovec (Intrathecal injection)
Population(s)	People with 5q spinal muscular atrophy
Subgroups	If the evidence allows the following subgroups will be considered: • Number of SMN2 gene copies • Functional status (non-sitter, sitter, walker) • SMA type • People who have had prior active treatment for SMA

Comparators	• Established clinical management, including
	  ○ Risdiplam (*subject to managed access review*)
	  ○ Nusinersen (*subject to managed access review)*
	  ○ Onasemnogene abeparvovec (intravenous infusion)
	  ○ Best supportive care

Outcomes	The outcome measures to be considered include: • motor function (including, where applicable, age-appropriate motor milestones such as sitting, standing, walking) • bulbar function (including, for example, swallowing and ability to communicate) • frequency and duration of hospitalisation • speech and communication • respiratory function • complications of spinal muscular atrophy (including, for example, scoliosis and muscle contractures) • need for non-invasive or invasive ventilation • stamina and fatigue • mortality • adverse effects of treatment • health-related quality of life (for patients and carers).
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.

Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related technology appraisals:** Risdiplam for treating spinal muscular atrophy (2023) NICE technology appraisal guidance 755. Nusinersen for treating spinal muscular atrophy (2023) NICE technology appraisal guidance 588. **Related highly specialised technology appraisals:** Onasemnogene abeparvovec for treating presymptomatic spinal muscular atrophy (2023) NICE Highly specialised technologies guidance 24. Review date not stated Onasemnogene abeparvovec for treating spinal muscular atrophy (2023) NICE Highly specialised technologies guidance 15. Review date not stated **Related technology appraisals in development:** Nusinersen and risdiplam for treating spinal muscular atrophy (review of TA588 and TA755). NICE technology appraisal guidance [ID6195] Publication date to be confirmed.

Questions for consultation

Where do you consider intrathecal onasemnogene abeparvovec will fit into the existing care pathway for SMA?

For people already on treatment, what may prompt switching to intrathecal onasemnogene abeparvovec?

Please select from the following, will intrathecal onasemnogene abeparvovec be:
A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):
For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would intrathecal onasemnogene abeparvovec be a candidate for managed access?

Do you consider that the use of intrathecal onasemnogene abeparvovec can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

Please indicate if any of the treatments in the scope are used in NHS practice differently than advised in their Summary of Product Characteristics. For example, if

the dose or dosing schedule for a treatment is different in clinical practice. If so, please indicate the reasons for different usage of the treatment(s) in NHS practice. If stakeholders consider this a relevant issue, please provide references for data on the efficacy of any treatments in the pathway used differently than advised in the Summary of Product Characteristics.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which intrathecal onasemnogene abeparvovec will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. SMA UK: What is 5q Spinal Muscular Atrophy? [online; accessed July 2025]

2. Calucho M Bernal S, Alías L et al. (2018) Correlation between SMA type and SMN2 copy number revisited: An analysis of 625 unrelated Spanish patients and a compilation of 2834 reported cases. Neuromuscular Disorders 28: 208-215

3. SMA UK: A Guide to the 2017 International Standards of Care for SMA. [online; accessed July 2025).

4. Mercuri E, Finkel RS, Muntoni F et al. (2018) Diagnosis and management of spinal muscular atrophy: Part 1: Recommendations for diagnosis, rehabilitation, orthopedic and nutritional care. Neuromuscular Disorders 28(2): 103-115