NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

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

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of intrathecal onasemnogene abeparvovec within its marketing authorisation for treating spinal muscular atrophy in people 2 years and over.

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 SMN1 gene, which is located on the 'q' arm of the chromosome 5 (this is termed '5q SMA'). It 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 causes substantial disability, and without treatment, usually leads to increased mortality and reduced life expectancy. 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 between people. Historically SMA has been grouped into types. The type is determined by a clinician at diagnosis. It is 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. If untreated, type 1 SMA typically leads to death before 2 years of age. 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 stand or walk unaided. Most people have weak breathing, chewing and swallowing muscles as well as weak upper limb movement and scoliosis. SMA type 2 may also shorten life expectancy. 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 and require support.[1] Life expectancy for SMA types 3 and 4 aligns with the general population. However, with the availability of disease modifying treatments (DMTs), SMA exists on a broad continuum, with overlap in symptoms and outcomes across the SMA types.

SMA may also be diagnosed pre-symptomatically through genetic testing. 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.

Genetic testing also determines the number of SMN2 gene copies. The SMN2 gene acts as a low-functioning back-up gene, which can partially compensate for the loss of the SMN1 gene. So the number of SMN2 gene copies 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]

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 2024, 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, prevalence 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. Additionally, NHS England provides funding for children with type 1 SMA who are over 12 months provided they weigh less than 21 kg.[5]

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 to <18 years.

Intervention(s)	Onasemnogene abeparvovec (Intrathecal injection)
Population(s)	People aged 2 years and over 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 • Age of symptom onset • Prior active treatment for SMA

Comparators	• Established clinical management, including (where eligible):
	  ○ 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 (2021, last updated 2023) NICE technology appraisal guidance 755. Nusinersen for treating spinal muscular atrophy (2019) 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. Onasemnogene abeparvovec for treating spinal muscular atrophy (2021, last updated 2023) NICE highly specialised technologies guidance 15. **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.

References

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

5. SMA UK: Who may access zolgensma treatment? [online; accessed November 2025]