NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Highly Specialised Technologies Evaluation

Onasemnogene abeparvovec for treating spinal muscular atrophy

Final scope

Remit/evaluation objective

To evaluate the benefits and costs of onasemnogene abeparvovec within its marketing authorisation for treating spinal muscular atrophy for national commissioning by NHS England.

Background

Spinal muscular atrophy, or 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 types of SMA typically cause death before age 2 years, although 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 is a heterogeneous condition, which is often grouped into 5 main types, based on the age of onset of symptoms and how much motor function the person has. 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. Types 0 and 4 are rarely diagnosed. In SMA type 1, symptoms arise before age 6 months and babies are unable to sit independently; babies with SMA have low muscle tone (hypotonia) and severe muscle weakness which affects movement, swallowing and breathing. In type 2 SMA, the onset of symptoms is between age 7 and 18 months, 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.

It is estimated that approximately 1 in 10,000 people are born with SMA,[1] suggesting that about 65 people are born with SMA per year in England. Approximately 60% of all new diagnoses of SMA are SMA type 1.[1] Estimates range from 680 to 2,500 for the current number of children and adults in the UK living with a type of SMA, but the exact number is uncertain.[1]

No active treatments are currently routinely available for SMA and the condition is managed through multidisciplinary supportive care. Treatment usually follows guidelines from the International Conference on the Standard of Care for Spinal Muscular Atrophy.[2,3] Supportive care strategies do not affect disease progression but aim to minimise the impact of disability, address complications and improve quality of life. These may involve respiratory, gastroenterology, and orthopaedic care, as well as nutritional support, physiotherapy, assistive technologies, occupational therapy and social care.

At present, nusinersen (Spinraza) is the only active treatment available for treating SMA. Nusinersen is administered by intrathecal injection and is currently recommended for pre-symptomatic SMA or SMA types 1, 2 or 3 if the conditions in the managed access agreement are followed. However, as nusinersen is available via a managed access agreement, its use is not considered to be embedded in NHS clinical practice because its availability to patients is contingent on further evidence generation and re-appraisal by NICE. Additionally, the significant uncertainties identified prevented NICE's committee from making a positive recommendation during its appraisal, so it cannot be considered to be routinely commissioned. Therefore, for the purposes of this highly specialised technology evaluation, nusinersen will not be considered as a comparator.

The technology

Onasemnogene abeparvovec (Zolgensma, AveXis) is a single-use gene replacement therapy made of a viral 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 to carry the gene into the nerve cells, enabling production of sufficient amounts of SMN. It is administered intravenously. Treatment with onasemnogene abeparvovec is expected to be used exclusively in the context of a highly specialised service.

Onasemnogene abeparvovec has a marketing authorisation in the UK and is indicated for the treatment of people with 5q spinal muscular atrophy (SMA) with a bi-allelic mutation in the SMN1 gene and a clinical diagnosis of SMA Type 1, or 5q SMA with a bi-allelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene.

Intervention(s)	Onasemnogene abeparvovec
Population(s)	People with: • 5q spinal muscular atrophy (SMA) with a bi-allelic mutation in the SMN1 gene and a clinical diagnosis of SMA Type 1, or • 5q SMA with a bi-allelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene

Comparators	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) • 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 • mortality • adverse effects of treatment • health-related quality of life (for patients and carers).
Nature of the condition	• disease morbidity and patient clinical disability with current standard of care • impact of the disease on carer's quality of life • extent and nature of current treatment options
Clinical Effectiveness	• overall magnitude of health benefits to patients and, when relevant, carers • heterogeneity of health benefits within the population • robustness of the current evidence and the contribution the guidance might make to strengthen it • treatment continuation rules (if relevant)
Value for Money	• Cost effectiveness using incremental cost per quality-adjusted life year • Patient access schemes and other commercial agreements • The nature and extent of the resources needed to enable the new technology to be used

Impact of the technology beyond direct health benefits	• whether there are significant benefits other than health • whether a substantial proportion of the costs (savings) or benefits are incurred outside of the NHS and personal and social services • the potential for long-term benefits to the NHS of research and innovation • the impact of the technology on the overall delivery of the specialised service • staffing and infrastructure requirements, including training and planning for expertise.
Other considerations	• Guidance will only be issued in accordance with the marketing authorisation. • If evidence allows, consideration may be given to a subgroup of people with pre-symptomatic disease. • Guidance will take into account any Managed Access Arrangements.
Related NICE recommendations and NICE Pathways	Nusinersen for treating spinal muscular atrophy (2019). NICE technology appraisal 588. Review date July 2024.
Related National Policy	NHS England, Manual for prescribed specialised services, 2018/19. Chapters 48, 119 and 134. Manual for Prescribed Specialised Services 2018/19 NHS England (2018) Clinical Commissioning Policy Statement: Nusinersen for genetically confirmed Spinal Muscular Atrophy (SMA) type 1 for eligible patients under the Expanded Access Programme (EAP). Reference: 170038P Department of Health and Social Care (2018) The UK Strategy for Rare Diseases. Second Progress Report from the UK Rare Diseases Policy Board Department of Health (2016) The UK Strategy for Rare Diseases. Rare Diseases implementation plan for England NHS England (2018) National Programmes of Care and Clinical Reference Groups: E04. Paediatric Neurosciences

	NHS England (2013) 2013/14 NHS standard contract for paediatric neurosciences- neurodisability. Reference: E09/S/c NHS England (2013) 2013/14 NHS Standard Contract for Diagnostic Service for Rare Neuromuscular Disorders (all ages). D04/S/a Department of Health, National service framework for long term conditions, 2005 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/198114/National_Service_Framework_for_Long_Term_Conditions.pdf Department of Health, The NHS Outcomes Framework 2016/17, 2016. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/513157/NHSOF_at_a_glance.pdf

References

1. Spinal Muscular Atrophy UK (2018) https://smauk.org.uk/what-is-spinal-muscular-atrophy Accessed April 2020 2019.
2. Mercuri E 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.
3. Finkel RS et al. (2018) Diagnosis and management of spinal muscular atrophy: Part 2: Pulmonary and acute care; medications, supplements and immunizations; other organ systems; and ethics. Neuromuscular Disorders, 28(3): 197–207.