NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Nusinersen for treating spinal muscular atrophy

Final scope

Remit/appraisal objective

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

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 forms 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 4 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 1, in which symptoms arise before age 6 months, to type 4 (adult-onset). Babies with SMA type 1 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 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.

SMA affects an estimated 1 in 6,000 to 1 in 10,000 births worldwide,[1,2] and the incidence varies between different types of SMA. It is estimated that about 100 people are born with SMA per year in the UK, and there are currently between 1,200 and 2,500 children and adults in the UK living with SMA.[1,2]

There are currently no active treatments for SMA, and the condition is managed through multidisciplinary supportive care. Treatment usually follows guidelines from the International Standards of Care Committee for Spinal Muscular Atrophy. Supportive care strategies 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.

The technology

Nusinersen (Spinraza, Biogen) is a 2'-O-methoxyethyl antisense oligonucleotide which stimulates the survival motor neuron (SMN)-2 gene to increase SMN protein levels. It is administered by intrathecal injection.

Nusinersen has a marketing authorisation in the UK for treating 5q SMA. It has been studied in clinical trials compared with placebo (sham procedure) in infants and children with SMA.

Intervention(s)	Nusinersen
Population(s)	People with 5q spinal muscular atrophy
Comparators	Best supportive care
Outcomes	The outcome measures to be considered include: • motor function (including, where applicable, age-appropriate motor milestones) • 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.
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.

Other considerations	If the evidence allows, consideration will be given to subgroups based on severity of disease (including considerations such as age of SMA onset, SMA type and genotype [including *SMN2* copy number]) 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 and NICE Pathways	None
Related National Policy	NHS England, Manual for prescribed specialised services, 2017/18. Services 11, 48, 119 and 134. https://www.england.nhs.uk/wp-content/uploads/2017/10/prescribed-specialised-services-manual-2.pdf Department of Health. Rare diseases strategy; 2013 https://www.gov.uk/government/publications/rare-diseases-strategy NHS England, Standard contract for neurosciences: specialised neurology (adults), 2013/14. http://www.england.nhs.uk/wp-content/uploads/2013/06/d04-neurosci-spec-neuro.pdf 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/uploads/system/uploads/attachment_data/file/513157/NHSOF_at_a_glance.pdf

References

1. SMA Trust (2017) Spinal muscular atrophy – Key information. Accessed January 2018
2. SMA Support UK (2018) Summary information about SMA. Accessed January 2018.