NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Onasemnogene abeparvovec for treating spinal muscular atrophy type 1

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of onasemnogene abeparvovec within its marketing authorisation for treating spinal muscular atrophy type 1.

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. 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 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 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.

It is estimated that about 78 people are born with SMA per year in the UK. There are currently between 650 and 1300 children and adults in the UK living with SMA; an upper limit of 2,500 has also been estimated. Around 60% of SMA in England is type 1.[1]

No active treatments are currently routinely available for SMA type 1, 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 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.

The technology

Onasemnogene abeparvovec (AVXS-101, AveXis) is a gene replacement therapy made of a virus 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 virus is expected to carry the gene into the nerve cells, enabling production of sufficient amounts of SMN. It is administered intravenously.

Onasemnogene abeparvovec does not currently have a marketing authorisation in the UK. It has been studied in single arm clinical trials in children less than 6 months of age with spinal muscular atrophy type 1.

Intervention(s)	Onasemnogene abeparvovec
Population(s)	Children with spinal muscular atrophy type 1
Comparators	• Best supportive care • Nusinersen (subject to ongoing NICE appraisal)
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. 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 and NICE Pathways	Nusinersen for treating spinal muscular atrophy. NICE technology appraisal [ID1069]. Publication expected November 2018
Related National Policy	NHS England, Manual for prescribed specialised services, 2017/18. Chapters 48, 119 and 134. Manual for prescribed specialised services 2017/18 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 https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf

Questions for consultation

How many people have SMA type 1 in England, and how many would be offered onasemnogene abeparvovec therapy?

How will people with type 1 SMA be identified for treatment with onasemnogene abeparvovec?

How is onasemnogene abeparvovec expected to be used in clinical practice? At what point in the treatment pathway would it be considered?

How should best supportive care be defined?

Have all relevant comparators for onasemnogene abeparvovec been included in the scope? Which treatments are considered to be established clinical practice in the NHS for spinal muscular atrophy? Is best supportive care be an appropriate comparator?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom onasemnogene abeparvovec is expected to be more clinically effective and cost effective or other groups that should be examined separately?

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 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.

Do you consider onasemnogene abeparvovec to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of onasemnogene abeparvovec can result in any potential significant and 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 Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. SMA Support UK (2018) http://www.smasupportuk.org.uk/spinal-muscular-atrophy-key-information Accessed August 2018.