NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Delandistrogene moxeparvovec for treating Duchenne muscular dystrophy in children 4 to 7 years ID3897

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of delandistrogene moxeparvovec within its marketing authorisation for treating Duchenne muscular dystrophy in children 4 to 7 years.

Background

Muscular dystrophies are a group of genetic disorders which cause muscle weakness and progressive disability. Duchenne muscular dystrophy (DMD) is the most common and progresses most rapidly. It is caused by the presence of different types of mutations on the X-chromosome in the gene for dystrophin, a protein that is important for maintaining normal muscle structure and function. The main types of mutation are deletions (where part of the gene is deleted), insertions (where an additional piece of DNA is inserted into the gene), duplications (when part of the gene is repeated) and point mutations (when a single letter in the DNA code is changed and alters the information needed to produce a protein). These changes cause muscle fragility that progressively leads to weakness and loss of walking ability during childhood and adolescence. DMD can either be inherited from a parent or can be the result of a random genetic mutation. Boys only have one X chromosome, and thus one single copy of the dystrophin gene, hence they have a much higher probability of developing DMD than girls. A very small number of girls develop DMD.

Initial symptoms of DMD usually present between the ages of 1 and 3 years and children with the disease may appear weaker than other children, and have difficulty walking, standing, or climbing stairs, and may have behavioural or learning difficulties. After the age of 12 most children will need to use a wheelchair. During adolescence, breathing muscles can weaken, causing shallow breathing and a less effective cough mechanism, which can lead to chest infections. Weakness of the heart muscle, called cardiomyopathy, occurs in almost all patients by the age of 18 years. The life expectancy of people with DMD depends on how quickly and intensely muscle weakness progresses and how it affects the patient's ability to breathe. The average lifespan is less than 30 years.

The incidence of DMD ranges from 1 in every 3,500 to 1 in 5,000 male live births. Each year, about 100 boys with DMD are born in the UK.1 Around 2,500 people in the UK have DMD.

NICE Highly Specialised Technology guidance 22 recommends ataluren for treating DMD resulting from a nonsense mutation in the dystrophin gene in people 2 years and over who can walk. Approximately 10% of patients with DMD carry a nonsense mutation in the dystrophin gene, equating to around 225 males aged over 2 years in England using current population size estimates.[2,3] The proportion of these people who are able to walk is unknown. Most other treatment options do not treat the

underlying cause of the disease and focus on alleviating symptoms and maintaining muscle strength. Increasing the time a patient is able to walk or delaying the loss of further muscle function are the major aims of many treatment options. Interventions may include the use of steroids (associated with several side effects) and physical aids (such as wheelchairs or leg braces), exercise, physiotherapy, and occasionally orthopaedic surgery. In addition, other supportive treatments such as dietetic advice, prevention and treatment of bone fragility and the management of complications of long-term steroid therapy are required. In the later stages of DMD, treatments to help improve breathing and increase oxygen levels may be needed if lung function becomes impaired.

The technology

Delandistrogene moxeparvovec (Elevidys, Roche) does not currently have a marketing authorisation in the UK for DMD. It has been studied in clinical trials compared with placebo in children aged 4 to 7 years with mutations between exon 18 and 58 and in another with mutations between exon 18 and 79.

Intervention(s)	Delandistrogene moxeparvovec
Population(s)	Children aged 4 to 7 years with Duchenne muscular dystrophy who are able to walk
Subgroups	If evidence allows the following subgroups will be considered: • mutation types
Comparators	• Established clinical management without delandistrogene moxeparvovec • Vamorolone (subject to NICE evaluation) For children with a nonsense mutation • Ataluren

Outcomes	The outcome measures to be considered include: • walking ability (ambulation) • muscle function • muscle strength • ability to undertake activities of daily living • bone function • cardiac function • concordance and optimisation of treatment • endocrine function • lung function • time to wheelchair • number of falls • time to scoliosis • upper body function • 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost comparison may be carried out. 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'. The availability and cost of biosimilar and generic products should 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 Highly Specialised Technologies Evaluations published:** Ataluren for treating Duchenne muscular dystrophy with a nonsense mutation in the dystrophin gene (2023) NICE Highly Specialised Technologies guidance 22.). **Related technology appraisals in development:** 'Fordadistrogene movaparvovec for treating Duchenne muscular dystrophy' NICE technology appraisal guidance [ID6133]. Publication date to be confirmed. Givinostat for treating Duchenne muscular dystrophy NICE technology appraisal guidance [ID6323]. Publication date to be confirmed. Vamorolone for treating Duchenne muscular dystrophy. NICE technology appraisal guidance [ID4024]. Expected publication date: 22 May 2024 **Related Guidelines:** Suspected neurological conditions: recognition and referral (2019) NICE guideline 127
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2023) Prescribed Specialised Services Manual(2023)

Questions for consultation

Where do you consider delandistrogene moxeparvovec will fit into the existing care pathway for Duchenne mascular dystrophy?

Would delandistrogene moxeparvovec be a candidate for managed access?

Do you consider that the use of delandistrogene moxeparvovec 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.

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 delandistrogene moxeparvovec 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. Duchenne muscular dystrophy (DMD) - Overview | Muscular Dystrophy UK. https://www.musculardystrophyuk.org/conditions/duchenne-muscular-dystrophy-dmd

2. Bladen CL et al. (2015) The TREAT-NMD DMD Global Database: analysis of more than 7,000 Duchenne muscular dystrophy mutations. Human Mutation: 36(4); 395–402

3. Office for National Statistics. Population estimates for the UK, England and Wales, Scotland and Northern Ireland: mid-2020. Accessed January 2022.