NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Givinostat for treating Duchenne muscular dystrophy in people 6 years and over [ID6323]

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of givinostat within its marketing authorisation for treating Duchenne muscular dystrophy in people 6 years and over.

Background

Muscular dystrophies are a group of genetic conditions 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 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, so only have one single copy of the dystrophin gene. As a result, they have a much higher probability of developing DMD than girls. A very small number of girls develop DMD.

DMD can be diagnosed at birth, but initial symptoms of DMD usually present between the ages of 1 and 3 years. Children with the condition may appear weaker than other children, and have difficulty walking, standing, or climbing stairs. Children with DMD may also have behavioural or learning difficulties. After the age of 12 most children will need to use a wheelchair and at this stage may have difficulties with raising their arms above shoulder level. 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 people with DMD by the age of 18 years. Caregivers of people with DMD also have impacts to their overall quality of life that increase with DMD progression. This can include physical, emotional, and mental wellbeing, and impact employment status. The life expectancy of people with DMD depends on how quickly and intensely muscle weakness progresses and on how it affects the person's ability to breathe. The average lifespan is less than 30 years.[1]

The incidence of DMD ranges from 1 in every 3,500 to 1 in 5,000 male live births. Aproximately 100 boys with DMD are born in the UK each year and around 2,500 people are living with DMD in the UK.[2]

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 people 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.[3,4] The proportion of these people who are able to walk is unknown. Most other treatment options do not treat the underlying cause of the condition and focus on alleviating symptoms and maintaining muscle strength. Increasing the time a person with DMD 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, vitamin D, and occasionally orthopaedic surgery. In addition, other supportive treatments such as dietetic advice, councelling, 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.[5]

The technology

Givinostat (Duvyzat, ITF Pharma UK) does not currently have a marketing authorisation in the UK for DMD. It has been studied in clinical trials compared with placebo in ambulant males aged 6 years and over with DMD, and non-ambulant males aged 9 to 17 years of age with DMD.

Intervention(s)	Givinostat
Population(s)	People with Duchenne muscular dystrophy 6 years of age and older
Comparators	• Established clinical management without givinostat • Ataluren (For people aged 2 years and older with a nonsense mutation in the dystrophin gene and can walk [ambulatory])

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 in wheelchair • number of falls • time to scoliosis • lower body function • upper body function • mortality • adverse effects of treatment • health-related quality of life (people with DMD 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.
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 technology appraisals:**

	Ataluren for treating Duchenne muscular dystrophy with a nonsense mutation in the dystrophin gene (2023) NICE highly specialised technology guidance 22. **Related technology appraisals in development:** Vamorolone for treating Duchenne muscular dystrophy. NICE technology appraisal guidance [ID4024] Publication expected to be confirmed. Delandistrogene moxeparvovec for treating Duchenne muscular dystrophy in children 4 to 7 years. NICE technology appraisal guidance [ID3897] Publication date to be confirmed. Fordadistrogene movaparvovec for treating Duchenne muscular dystrophy. NICE technology appraisal guidance [ID6133] Publication date to be confirmed. **Related NICE 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 (2017) NHS Medicines for Children's Policy Department of Health and Social Care (2016) NHS outcomes framework 2016 to 2017 NHS Digital (2022) NHS Outcomes Framework England, March 2022 Annual Publication NHS England (2023) Manual for prescribed specialist services (2023/2024)

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. Muscular Dystrophy Association, Duchenne Muscular Dystrophy (DMD)
2. Muscular Dystrophy UK, Duchenne muscular dystrophy (DMD)
3. 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.
4. Office for National Statistics. Population estimates for the UK, England and Wales, Scotland and Northern Ireland: mid-2020.

5. Patient, Duchenne Muscular Dystrophy