NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Vamorolone for treating inflammation associated with Duchenne muscular dystrophy

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of vamorolone within its marketing authorisation for the treatment of inflammation associated with Duchenne muscular dystrophy.

Background

Muscular dystrophies are a group of genetic disorders which cause muscle weakness and progressive disability. Duchenne muscular dystrophy (DMD) is one of the most common and severe forms. DMD is caused by the presence of mutations on the X-chromosome in the gene for dystrophin, a protein that is important for maintaining normal muscle structure and function. These mutations 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, 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.

Initial symptoms of DMD usually present between the ages of 1 and 3 years and children with the disease may have difficulty walking, standing, or climbing stairs. Children with DMD may also have behavioural or learning disabilities. After the age of 12 most children will need to use a wheelchair as their muscles weaken and they lose the ability to walk. 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 18. The life expectancy of people with DMD depends on how quickly and intensely muscle weakness progresses and on how it affects the patient's ability to breathe. The average lifespan is less than 30 years.

The incidence of DMD is approximately 1 in 3600 – 5000 male live births.[1] Around 2500 people are affected by DMD in the UK.[2]

Most 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, leg braces or crutches), 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.

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NICE Highly Specialised Technology guidance 3 recommended ataluren within a managed access agreement, for treating DMD resulting from a nonsense mutation in the dystrophin gene in ambulatory people aged 5 years and older who can walk. NICE will review the recommendation at the end of the managed access period. Ataluren is the only therapy which treats the underlying cause of DMD.

The technology

Vamorolone (VBP15, Santhera), is a partial agonist of the glucocorticoid receptor. It inhibits the NFkB pathway reducing inflammation in people with DMD but does not activate GRE-mediated transcription, reducing possible side effects. Vamorolone is administered orally.

Vamorolone does not currently have a marketing authorisation in the UK for treating DMD. It has been studied in a number of phase II clinical trials in people with DMD. This includes a phase IIb trial comparing with a steroid (prednisolone) and placebo, in people aged between 4 and 7 years who were able to complete the time to stand test without assistance.

Intervention(s)	Vamorolone
Population(s)	People with Duchenne muscular dystrophy
Comparators	Established clinical management without vamorolone
Outcomes	The outcome measures to be considered include: • walking ability (ambulation) • muscle function • muscle strength • ability to undertake activities of daily living • cardiac function • lung function • time to wheelchair • number of falls • time to scoliosis • mortality • adverse effects of treatment • health-related quality of life (for patients and carers).

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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 Technology Appraisals:** Ataluren for treating Duchenne muscular dystrophy with a nonsense mutation in the dystrophin gene (2016) NICE highly specialised technologies guidance HST3 **Related appraisals in development:** Ataluren for treating Duchenne muscular dystrophy with a nonsense mutation in the dystrophin gene (review of HST3) [ID1642]. NICE highly specialised technologies guidance Eteplirsen for treating Duchenne muscular dystrophy [ID1003]. NICE highly specialised technologies guidance. Suspended appraisal. Idebenone for treating Duchenne muscular dystrophy ID1092. NICE highly specialised technologies guidance. Suspended appraisal. Drisapersen for the first-line treatment of Duchenne's muscular dystrophy [ID911]. NICE highly specialised technologies guidance. Suspended appraisal.

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	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 (2018/2019) NHS manual for prescribed specialist services (2018/2019)

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Questions for consultation

Where do you consider vamorolone will fit into the existing care pathway for DMD?

Which treatments are considered to be established clinical practice in the NHS for Duchenne muscular dystrophy?

Is ataluren a relevant comparator in the treatment of inflammation associated with DMD?

Should reduction in standard corticosteroid use be included as an outcome?

Would vamorolone be a candidate for managed access?

Do you consider that the use of vamorolone 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 vamorolone 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. We welcome comments on the appropriateness of appraising this topic through this 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).

NICE's health technology evaluations: the manual 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?

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- 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. Muscular dystrophy. Duchenne muscular dystrophy (DMD) – Overview. Available from: https://www.musculardystrophyuk.org/conditions/duchenne-muscular-dystrophy-dmd . Accessed: 8th August 2022.

2. Duchenne UK. About DMD – DMD in numbers. Available from: https://www.duchenneuk.org/about-duchenne-muscular-dystrophy/ Accessed: Accessed: 8th August 2022.

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