NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Idebenone for treating Duchenne muscular dystrophy

Final scope (post-referral)

Remit/appraisal objective

To appraise the clinical and cost effectiveness of idebenone within its marketing authorisation for treating Duchenne muscular dystrophy.

Background

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

Initial symptoms of Duchenne muscular dystrophy usually present between the ages of 1 and 3 years. Children with the disease may appear weaker than other children, 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. Continued weakening of breathing muscles results in disordered breathing during sleep, altered daytime mood, tiredness and frequent chest infections. Weakness of the heart muscle, called cardiomyopathy, occurs in almost all patients by the age of 18. The life expectancy of people with Duchenne muscular dystrophy depends on how quickly and intensely muscle weakness progresses and on how it affects the patient's ability to breathe. With medical care, most people with Duchenne muscular dystrophy die from heart or respiratory failure before or during their 30s.[1]

Boys only have one X-chromosome, and thus one single copy of the dystrophin gene, hence they have a much higher probability of developing Duchenne muscular dystrophy than girls. A very small number of girls develop Duchenne muscular dystrophy. The incidence of Duchenne muscular dystrophy is between 10.7 and 27.8 per 100,000 live born males.[2] In the UK, about 100 boys are born with Duchenne MD each year, and there are about 2,500 people living with the condition in the UK at any one time.[1]

In the ambulant population (people who are able to walk), increasing the time a patient is able to walk is one of the major aims of treatment. In the non-ambulant population, delaying the loss of further muscle function is one of the major aims of treatment. NICE highly specialised technology evaluation 3 recommends ataluren for treating Duchenne muscular dystrophy resulting from a nonsense mutation in the dystrophin gene in people aged 5 years and older who can walk. Current treatments mainly focus on alleviating symptoms and maintaining muscle strength. Interventions include physiotherapy, corticosteroids (associated with several side effects), vitamin D supplementation and physical aids (such as wheelchairs, leg braces or crutches), 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, cardiac management and treatments to help improve breathing and increase oxygen levels may be needed if lung function becomes impaired. Current respiratory support focusses on alleviating symptoms and improving breathing and can include assistive ventilation, non-invasive ventilation, cough assist machines and physiotherapy. Respiratory status also impacts the feasibility of orthopaedic surgery and is a major cause of morbidity and mortality.

The technology

Idebenone (Puldysa, Santhera Pharmaceuticals) is a synthetic short-chain benzoquinone analogue of co-enzyme Q10, a component of the respiratory chain. It aims to improve mitochondrial respiratory function and is an antioxidant. Idebenone is administered orally.

Idebenone does not currently have a marketing authorisation in the UK for treating Duchenne muscular dystrophy. It has been studied in clinical trials compared with placebo in people with Duchenne muscular dystrophy aged between 8 and 18 years. A key trial included mostly non-ambulatory (>90%) patients with declined respiratory function (that is, percent predicted peak expiratory flow ≤ 80%), and who were not taking concomitant corticosteroids.

Intervention(s)	Idebenone
Population(s)	People with Duchenne muscular dystrophy who have respiratory dysfunction and who are not taking concomitant glucocorticoids (including people previously treated with glucocorticoids)
Comparators	Established clinical management without idebenone

Outcomes	The outcome measures to be considered include: • pulmonary function (for example respiratory function parameters including lung capacity, time to assistive ventilation, frequency of chest infections and ability to cough) • change in hospital admissions due to respiratory issues • cardiac function • muscle strength and motor function (for example upper limb strength) • time to scoliosis • gastrointestinal functions (for example constipation) • ability to undertake activities of daily living (for example eating and using computers) • mortality • adverse effects of treatment • health-related quality of life (for people with DMD and their families/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 and NICE Pathways	Related Highly Specialised Technologies evaluations: Ataluren for treating Duchenne muscular dystrophy with a nonsense mutation in the dystrophin gene (July 2016) NICE Highly Specialised Technologies guidance HST3. Highly Specialised Technologies evaluations in development (including suspended appraisals): Drisapersen for the first-line treatment of Duchenne's muscular dystrophy [ID911] Suspended. Publication date to be confirmed.

	Eteplirsen for treating Duchenne muscular dystrophy [ID1003] Suspended. Publication date to be confirmed. Proposed Highly Specialised Technologies evaluation: Related Guidelines: Suspected neurological conditions: recognition and referral (2019). NICE guideline NG127. Muscle conditions (2019) NICE pathway
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) Chapter 11. Adult specialist neurosciences services, and Chapter 119. Specialist neuroscience services for children. Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1-2.

References

1 Muscular dystrophy (2019) NHS choices. Accessed November 2019.

2 Mah JK, Korngut L, Dykeman J, Day L, Pringsheim T, Jette N. (2014) A systematic review and meta-analysis on the epidemiology of Duchenne and Becker muscular dystrophy. Neuromuscular Disorders. 24(6):482-91.