NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Omaveloxolone for treating Friedreich's ataxia in people 16 years and over

Final scope

Final remit/evaluation objective

To appraise the clinical and cost effectiveness of omaveloxolone within its marketing authorisation for treating Friedreich's ataxia in people 16 years and over.

Background

Friedreich's ataxia is a rare, inherited, progressive, multi-system neurodegenerative condition. Ataxia refers to disorders that affect co-ordination, balance and speech. Friedreich's ataxia is caused by mutations in the frataxin gene, leading to reduced production of the frataxin protein. Frataxin is involved in energy production and regulation of iron levels. A lack of frataxin in people with Friedreich's ataxia results in insufficient energy production, oxidative stress and iron accumulation in cell mitochondria (where energy is produced), as well as impaired activity of the regulatory protein Nrf2, leading to mitochondrial dysfunction and progressive neurodegeneration. The symptoms of Friedreich's ataxia usually start in childhood and differ depending on which parts of the body are affected. Neurodegeneration (damage of nerve cells) in the spinal cord, peripheral nerves and cerebellum cause the most common symptoms including poor balance and coordination, muscle weakness, loss of sensation, swallowing problems, and impaired speech. Other problems arise when cells are affected in the heart (causing cardiomyopathy) and pancreas (causing diabetes). People with Friedreich's ataxia may also develop problems with their hearing, eyesight, urinary tract and bowel, as well as orthopaedic conditions such as scoliosis. Symptoms worsen over time and most people need to use a wheelchair around 10 years after diagnosis[1]. Friedreich's ataxia sometimes starts later in life, which is associated with slower progression of neurological symptoms[2].

The prevalence of Friedreich's ataxia in England is estimated to be 1:56,695[3]. This would mean there are around 1,000 people in England with the condition. Men and women are equally affected. On average, people with Friedreich's ataxia live to around 39 years old, with cardiomyopathy the most common cause of death[5].

There are no NICE guidelines and no treatments that can slow the progression of Friedreich's ataxia. Current treatment is multidisciplinary and aims to manage symptoms[6]. Best supportive care includes pharmacological treatment and other interventions such as physiotherapy, occupational therapy and speech and language therapies to preserve muscle function. Pharmacological treatment for neurological symptoms can include botulinum toxin injections, baclofen, tizanidine, gabapentin, dantrolene sodium and benzodiazepines. Heart failure therapies including beta-blockers are often used to treat people with cardiomyopathy. Hypoglycaemic medications are also used in people who have diabetes arising from cell death in the pancreas. Other pharmacological and non-pharmacological treatments may be used for symptoms occurring in other parts of the body. Some symptoms, such as ataxia, currently have no treatment options available.

The technology

Omaveloxolone (Skyclarys, Biogen) does not currently have a marketing authorisation in the UK for treating Friedreich's ataxia in people 16 years and over. It has been studied in clinical trials alone compared with placebo in people aged 16 to 40 years old with a modified Friedreich's Ataxia Rating Scale (mFARS) score of between 20 and 80.

Intervention(s)	Omaveloxolone plus best supportive care
Population(s)	People with Friedreich's ataxia aged 16 years and over
Comparator	Best supportive care alone
Outcomes	The outcome measures to be considered include: • mobility • disease progression • neurological symptoms • cardiovascular events • upper limb coordination • fatigue • diabetes incidence • changes in visual acuity • changes in hearing • 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. 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:** None **Related technology appraisals in development:** None **Related NICE guidelines:** Suspected neurological conditions: recognition and referral. (updated 2023) NICE guideline 127. **Related NICE guidelines in development:** None **Related interventional procedures:** None **Related quality standards:** None
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2023) Manual for prescribed specialist services (2023/2024)

References

1. De Michele, G. et al (1996). Age of onset, sex, and cardiomyopathy as predictors of disability and survival in Friedreich's disease: a retrospective study on 119 patients. Neurology. 47(5):1260–4.

2. Ataxia UK. Friedreich's ataxia the facts. Accessed June 2024

3. Vankan, P. (2013). Prevalence gradients of Friedreich's Ataxia and R1b haplotype in Europe co-localize, suggesting a common Palaeolithic origin in the Franco-Cantabrian ice age refuge J. Neurochem 126 (1), 11–20.

4. Corben L.et al. (2022) Clinical Management Guidelines Writing Group. Clinical management guidelines for Friedreich ataxia: best practice in rare diseases. Orphanet J Rare Dis. 17(1):415.

5. Indelicato, E. et al (2023) Predictors of Survival in Friedreich's Ataxia: A Prospective Cohort Study. Movement Disorders. 39(3):510-518.