NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

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

Draft scope

Draft 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 an inherited, progressive, multi-system neurodegenerative condition. It 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), leading to cell death. 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 and impaired speech. Other problems arise when cells are affected in different parts of the body such as the heart (causing cardiomyopathy) and pancreas (causing diabetes). 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 the UK is estimated to be between 1 in 20,000 to 1 in 54,000 people[3,4]. This would mean there are between around 3,400 and 1,300 people in the UK with the condition. However, the prevalence of Friedreich's ataxia has been found to be higher in Northern Ireland than the other UK countries, so the number of people with the condition in England is uncertain[5]. Men and women are equally affected. On average, people with Friedreich's ataxia live to around 36 years old, with cardiomyopathy the most common cause of death[1].

There are no NICE guidelines and no curative treatments for Friedreich's ataxia. Current treatment is multidisciplinary and aims to manage symptoms[6]. Physiotherapy, occupation therapy and speech and language therapies are used 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 betablockers 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.

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
Population(s)	People with Friedreich's ataxia aged 16 years and over
Subgroups	If the evidence allows the following subgroups will be considered. These include: • Time of onset (early vs. late onset)

Comparators	• Established clinical management without omaveloxolone, which may include (but not limited to):
	  ○ muscle relaxants (including botulinum toxin injections, baclofen, tizanidine, gabapentin, dantrolene sodium, benzodiazepines)
	  ○ hypoglycaemic medications
	  ○ heart failure therapies including betablockers and device implantation
	  ○ physiotherapy and speech and language therapists
	• Best supportive care

Outcomes	The outcome measures to be considered include: • mobility • neurological symptoms • cardiological outcomes • 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)

Questions for consultation

How is Friedreich's ataxia currently diagnosed in the NHS?

How is Friedreich's ataxia currently treated in the NHS? Are there existing clinical guidelines? What is established clinical management without omaveloxolone for this condition?

Where do you consider omaveloxolone will fit into the existing care pathway for the disease?

Would omaveloxolone be used in addition to (as an add on) or in place of current treatments for symptoms of the condition?

How should best supportive care be defined?

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom omaveloxolone is expected to be more clinically effective and cost effective or other groups that should be examined separately?

How is severity measured Friedreich's ataxia? How is severity linked to age of onset? Should time of onset Friedreich's ataxia be considered as a separate subgroup?

How many people in England and Wales aged over 16 have Friedreich's ataxia? Would omaveloxolone be suitable for everyone in this group?

Is there data to inform the prevalence of Friedreich's ataxia by region in England?

Please select from the following, will omaveloxolone be:

A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):

For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would omaveloxolone be a candidate for managed access?

Do you consider that the use of omaveloxolone 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 omaveloxolone 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. 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. Dürr. A., et al. (1996). Clinical and genetic abnormalities in patients with Friedreich's ataxia. N Engl J Med. 335(16):1169–1175.

4. European Medicines Agency (EMA). EU/3/18/2037: Orphan designation for the treatment of Friedreich's ataxia. 2018. Accessed June 2024.

5. 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.

6. 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.