NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Idebenone for treating visual impairment in Leber's hereditary optic neuropathy in people 12 years and over

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of idebenone within its marketing authorisation for treating visual impairment in Leber's hereditary optic neuropathy (LHON) in people aged 12 years and over.

Background

LHON is an inherited genetic condition, which causes rapid loss in vision. It is caused by alterations in the DNA of the mitochondria (structures in the cells responsible for metabolising carbohydrates and fatty acids into energy that the cells can use). These mutations increase the oxidative stress on retinal ganglion cells leading to cell damage and cell death. Retinal ganglion cells communicate visual information to the brain through fibres forming the optic nerve. When these cells are dead, they are unable to send signals to the brain, causing vision loss and blindness. The loss of vision is painless and initially occurs in 1 eye, with the other eye usually affected within 2 to 3 months.[1,2] The degree of vision loss varies but typically is severe enough to be registered as severely sight impaired. In some people, additional extraocular (non-vision related) symptoms may develop. This is referred to as 'LHON plus' and includes symptoms similar to multiple sclerosis, such as muscle weakness, poor coordination, and numbness.

The onset of the symptoms of LHON most commonly occurs in a person's late teens through to their early thirties, though vision loss can also appear in early childhood or late adulthood. LHON disproportionately affects men, because 50% of male carriers, but only 10% of female carriers, will develop the disease.[3]

Studies of LHON put the prevalence rate of vision loss caused by LHON at 3.22[4] or 3.65[5] per 100,000. The same studies put the prevalence rate of the mutations in mitochondrial DNA that cause LHON at 4.42[5] and 11.82[4] per 100,000. In 2018 it was estimated that 2,072 people have LHON in England.[6]

There are currently few treatment options for LHON, and significant improvements in vision are rare. There is currently no NICE guidance for LHON. Idebenone has a marketing authorisation in the UK for LHON. However, it is not currently commissioned for routine use in the NHS in England. Clinical management in England focuses on monitoring, psychological support and visual rehabilitation (for example, teaching people how to use aids for low vision), neuro-ophthalmologist visits and social care support.

The technology

Idebenone (Raxone, Chiesi Limited) is indicated for the treatment of visual impairment in adolescent and adult patients with LHON.

Intervention(s)	Idebenone
Population(s)	People aged 12 years and older with Leber's hereditary optic neuropathy.
Subgroups	If the evidence allows the subgroups of people with recent vision loss will be considered.
Comparators	• Established clinical management without idebenone including: - visual aids - occupational and low vision rehabilitation - lifestyle management (no smoking, reduced alcohol consumption, diet that includes fresh fruit and vegetables) • Lenadogene nolparvovec (subject to NICE evaluation)
Outcomes	The outcome measures to be considered include: • visual acuity • contrast sensitivity • retinal nerve fibre layer • macular thickness • immune response • visual field assessment • 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 of any managed access arrangement for the intervention will be taken into account. The cost effectiveness analysis should include consideration of the benefit in the best and worst seeing eye.

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 appraisal in development:** Lenadogene nolparvovec for treating Leber's hereditary optic neuropathy caused by the G11778A ND4 mitochondrial mutation. NICE technology appraisal guidance [ID1410] Publication date to be confirmed.
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2018) NHS manual for prescribed specialist services (2018/2019) NHS England (July 2020) Idebenone for treating people over 12 years of age with Leber's Hereditary Optic Neuropathy. Clinical Commissioning Policy. Reference 200401P

Questions for consultation

Where do you consider idebenone will fit into the existing care pathway for LHON?

Have all relevant comparators for idebenone been included in the scope? Which treatments are considered to be established clinical practice in the NHS for LHON in England?

Are the outcomes listed appropriate? Should outcomes related to the non-vision related symptoms of LHON be included?

Are there any subgroups of people in whom idebenone is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Would idebenone be a candidate for managed access?

Do you consider that the use of idebenone 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 idebenone is 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. Yu-Wai-Man P, Turnbull DM, Chinnery PF (2002) Leber hereditary optic neuropathy. Journal of Medical Genetics 39: 162–9

2. Harding AE, Sweeney MG, Govan GG, Riordan-Eva P (1995) Pedigree analysis in Leber hereditary optic neuropathy families with a pathogenic mtDNA mutation. American Journal of Human Genetics 57: 77–86

3. Brown MD, Wallace DC (1994). Spectrum of mitochondrial-DNA mutations in Leber's hereditary optic neuropathy. Clinical Neuroscience 2: 138–45

4. Yu-Wai-Man P, Griffiths PG, Brown DT et al. (2003). The epidemiology of Leber hereditary optic neuropathy in the North East of England. American Journal of Human Genetics 72(2): 333–9

5. Gorman GS, Schaefer AM, Ng Y, et al. (2015) Prevalence of nuclear and mitochondrial DNA mutations related to adult mitochondrial disease. Annals of Neurology 77(5): 753–759

6. Clinical Commissioning Policy: Idebenone for treating people over 12 years of age with Leber's Hereditary Optic Neuropathy. NHS England Reference: 200401P