NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Highly Specialised Technologies Evaluation

Voretigene neparvovec for treating inherited retinal dystrophies caused by RPE65 gene mutations

Final scope

Remit/evaluation objective

To evaluate the benefits and costs of voretigene neparvovec within its marketing authorisation for treating inherited retinal dystrophies caused by RPE65 gene mutations for national commissioning by NHS England.

Background

Inherited retinal dystrophies are a group of eye diseases caused by gene mutations which result in the gradual degeneration of the light sensitive cells (photoreceptor cells) on the back of the eye (the retina). There are 2 main types of photoreceptor cells: rods and cones. Rods are found in the outer regions of the retina and are responsible for peripheral and night vision. Cones make up the central part of the retina (the macula) and are responsible for colour vision and perception of fine detail. Mutations in more than 200 different genes have been identified as the cause of inherited retinal dystrophies. Mutations in the 65 kDa retinal pigment epithelium (RPE65) gene primarily affect rods and are associated with 2 types of inherited retinal dystrophy: retinitis pigmentosa type 20 (RP20) and Leber's congenital amaurosis type 2 (LCA2). Over time, cone cells may also become damaged.

The symptoms of inherited retinal dystrophies caused by RPE65 gene mutations usually start in childhood. Initially people have problems seeing in dim light and lose their peripheral vision. As the disease progresses, central vision and colour vision are affected. It can lead to total blindness. LCA is the most severe form of inherited retinal dystrophy. The symptoms of LCA start at a younger age and the disease worsens more quickly; children with LCA have profound sight impairment either at birth or within the first year of life. Complications of inherited retinal dystrophies include cataracts and glaucoma.

Retinitis pigmentosa accounts for around half[1] of inherited retinal dystrophies and the prevalence is around 20 to 30 people per 100,000[2-6]. LCA is less common, affecting 2 to 3 people per 100,000[7]. Mutations in the RPE65 gene account for 2% of retinitis pigmentosa and 6 to 16% of LCA diagnoses[8,9]. Between approximately 100 and 200 people in England have inherited retinal dystrophies caused by RPE65 gene mutations.

There are no treatments available for inherited retinal dystrophies. Management focuses on monitoring, psychological support and visual rehabilitation, for example teaching people how to use aids for low vision.

Wearing sunglasses to protect the retina from ultraviolet light may help preserve vision.

The technology

Voretigene neparvovec (Luxturna, Novartis Pharmacueticals (UK)) is a gene therapy that treats specific forms of inherited retinal dystrophies caused by mutations in the RPE65 gene. It is administered by subretinal injection (that is, injected directly into the retina) by a surgeon.

Voretigene neparvovec has a positive opinion from the CHMP for treating people with vision loss due to inherited retinal dystrophy caused by confirmed biallelic RPE65 mutations and who have sufficient viable retinal cells. It has been studied in clinical trials, compared with no intervention, in both eyes in people aged 3 years and over with LCA due to RPE65 mutations.

Intervention(s)	Voretigene neparvovec
Population(s)	People with inherited retinal dystrophies caused by RPE65 gene mutations
Comparators	Best supportive care
Outcomes	The outcome measures to be considered include: • best corrected visual acuity (both eyes) • visual field • contrast sensitivity • photosensitivity • need for cataract surgery • adverse effects of treatment • health-related quality of life (for patients and carers).
Nature of the condition	• disease morbidity and patient clinical disability with current standard of care • impact of the disease on carer's quality of life • extent and nature of current treatment options

Clinical effectiveness	• overall magnitude of health benefits to patients and, when relevant, carers • heterogeneity of health benefits within the population • robustness of the current evidence and the contribution the guidance might make to strengthen it • treatment continuation rules (if relevant)
Value for money	• Cost effectiveness using incremental cost per quality-adjusted life year • Patient access schemes and other commercial agreements • The nature and extent of the resources needed to enable the new technology to be used
Impact of the technology beyond direct health benefits	• whether there are significant benefits other than health • whether a substantial proportion of the costs (savings) or benefits are incurred outside of the NHS and personal and social services • the potential for long-term benefits to the NHS of research and innovation • the impact of the technology on the overall delivery of the specialised service • staffing and infrastructure requirements, including training and planning for expertise
Other considerations	• Guidance will only be issued in accordance with the marketing authorisation • Cost effectiveness analysis should include consideration of the benefit in the best and worst seeing eye • Guidance will take into account any Managed Access Arrangements
Related NICE recommendations and NICE Pathways	**Related Interventional Procedures**: Insertion of a subretinal prosthesis system for retinitis pigmentosa (2015). NICE interventional procedures guidance 537. Insertion of an epiretinal prosthesis for retinitis pigmentosa (2015). NICE interventional procedures

	guidance 519. **Related NICE Pathways:** Retinal and macular conditions (2018) NICE pathway
Related National Policy	NHS England (2018) Manual for Prescribed Specialised Services 2018/19. (Chapters 12 and 120) NHS England (2017) Next steps on the five year forward view NHS England (2014) NHS Five year forward view Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 2,4 and 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

1 Daiger SP, Sullivan LS, Bowne SJ (2013) Genes and mutations causing retinitis pigmentosa. Clin Genet 84: 132–41.

2 Orphanet (2014) Retinitis pigmentosa. Accessed October 2018.

3 Bundey S and Crew SJ (1984) A study of retinitis pigmentosa in the City of Birmingham. J Med Genet 21: 417–20.

4 Haim M (2002) Epidemiology of retinitis pigmentosa in Denmark. Acta Ophthalmol Scand 80: 1–34.

5 Marlhens et al. (1998) Autosomal recessive retinal dystrophy associated with two novel mutations in the RPE65 gene. Eur J Hum Genet 6: 527–31

6 den Hollander et al. (2010) Lighting a candle in the dark: advances in genetics and gene therapy of recessive retinal dystrophies. J Clin Ivest 120: 3042–53.

7 Orphanet (2015) Leber congenital amaurosis. Accessed October 2018.

8 Cai X, Conley SM, Naash, MI (2009) RPE65: Role in the visual cycle, human retinal disease, and gene therapy. Opthalmic Genet 30: 57–62.

9 Cideciyan AV (2010) Leber Congenital Amaurosis due to *RPE65* Mutations and its Treatment with Gene Therapy. Prog Retin Eye Res 29: 398–427.