RECOMMENDATION ON VORETIGENE NEPARVOVEC IN THE TREATMENT OF INHERITED BIALLELIC RPE65 MUTATION-ASSOCIATED RETINAL DYSTROPHY

At its meeting of 7 November 2024, the Council for Choices in Health Care in Finland (COHERE Finland) adopted a recommendation on voretigene neparvovec in the treatment of inherited biallelic RPE65 mutation-associated retinal dystrophy.

Voretigene neparvovec is included in the national range of services for the treatment of inherited biallelic RPE65 mutation-associated retinal dystrophy in patients in whom the presence of sufficient viable retinal cells is confirmed, and who can benefit from the treatment based on individual evaluation. COHERE Finland also requires that the marketing authorisation holder and the buyer agree on a price substantially lower than the public wholesale price.

In COHERE Finland's opinion, gene therapy treatment that improves visual acuity is necessary in inherited retinal dystrophy for which no curative or disease-retarding treatment has been available to date. However, the research evidence involves uncertainty about the long-term efficacy of the treatment. Similarly, there is uncertainty about the significance of adverse effects, especially choroidal and retinal atrophy as a long-term effect.

The gene therapy product voretigene neparvovec is indicated for the treatment of adults and children with inherited biallelic RPE65 mutation-associated retinal dystrophy which has led to impaired vision. The patient must have sufficient viable retinal cells.

Inherited retinal dystrophy is caused by genetic defects. Progressive changes in the function of retinal cells lead to visual impairment. The recommendation pertains to inherited retinal dystrophy caused by biallelic mutation of the RPE65 gene. These mutations inhibit the production of functioning RPE65 protein in the body, which leads to the destruction of retinal sensory cells. Typical symptoms of inherited retinal dystrophy include impaired twilight vision, reduced visual acuity, tubular field of vision, and colour-vision deficiencies.

No curative or disease-retarding treatment has been previously available for inherited retinal dystrophy. In addition to impaired vision, the disease has a significant impact on a child's functional capacity and the lives of the child's family members.

Voretigene neparvovec is a gene therapy that enables the expression of 65 kDa (hRPE65) protein of the human retinal pigment epithelium in retinal pigment epithelial cells. Functional hRPE65 enables the light-stimulated retinal visual pigment regeneration process to be repaired on the

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retina. Voretigene neparvovec is administered subretinally as a single dose in both eyes under operating room conditions.

In the marketing authorisation study, the follow-up period for primary and secondary endpoints was three (delayed intervention) or four (initial intervention) years, during which gene therapy usually improved visual acuity and the retinal function compared to baseline. Adverse reactions related to the treatment and method of administration were observed in every patient. These included ocular, gastrointestinal and nervous system-related adverse events, most of which were mild and transient. Serious adverse events occurred in nine patients, including cataracts, increased intraocular pressure, and retinal detachment in one patient. In real-world studies, choroidal and retinal atrophy was observed, the cause of which is unclear but which does not appear to impair visual acuity.

When the immunosuppressive therapy prior to the administration of voretigene neparvovec and the medicine and dosage costs of the gene therapy are taken into account, the total costs per one patient receiving voretigene neparvovec in both eyes are EUR 652,000 at the public list price.

In COHERE Finland's opinion, the evidence of the efficacy available to date is clinically significant, although the long-term results involve uncertainty. According to the study, not all patients benefit from gene therapy. The only predictor of the efficacy is the number of viable retinal cells for the measurement of which no proper test is available. The attending physician is best at assessing the number of viable retinal cells in patients, and the assessment of suitability for gene therapy should be based on the structure and function of the retina.

The majority of the adverse events of the gene therapy were mild or moderate and did not appear to result in permanent adverse effects. Of the adverse events observed in real-world studies, the most notable is choroidal and retinal atrophy, which has progressed in patients over time. However, despite the atrophy, visual acuity has remained the same or improved in most patients.

This is a summary of a recommendation adopted by the Council for Choices in Health Care in Finland (COHERE Finland). The actual recommendation and the related background material are available in Finnish on the website of COHERE Finland under Valmiit suositukset.

The summary of the recommendation is also available in Swedish and English on the website.

The Council for Choices in Health Care in Finland (COHERE Finland) works in conjunction with the Ministry of Social Affairs and Health, and its task is to issue recommendations on services that should be included in the range of public health services. Further information about service choices in healthcare is available on the COHERE Finland website.

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