SUMMARY

Voretigene neparvovec

LUXTURNA 5 x 10^12 vector genomes/ml

concentrate and solvent for solution for injection

Reassessment at the request of the TC

Adopted by the Transparency Committee on 17 July 2024

Summary of opinion

Favourable opinion for reimbursement in "the treatment of adult and paediatric patients with vision loss due to inherited retinal dystrophy caused by confirmed biallelic *RPE65* mutations and who have sufficient viable retinal cells".

Transparency Committee's conclusions

Clinical Benefit

Clinical benefit according to the opinion of 3 April 2019:

- Inherited retinal dystrophies caused by biallelic *RPE65* mutations are rare, highly incapacitating diseases, with an early onset in children or young adults and leading to legal blindness. A distinction is made between severe forms (such as Leber congenital amaurosis) with a very early onset, from birth, with loss of visual acuity ranging from 1/10 to the total absence of light perception, associated with nystagmus and searching nystagmus, and slow-progressing forms often starting in adolescence or earlier, evolving towards visual field loss, initially peripheral and then central, and, finally, blindness.
- LUXTURNA 5 x 10^{12} vector genomes/mL concentrate and solvent for solution for injection is a curative treatment.
- The efficacy/adverse effects ratio is high.
- This is a first-line treatment in adult and paediatric patients with vision loss due to inherited retinal dystrophy caused by confirmed biallelic *RPE65* mutations (homozygous and compound heterozygous) and who have sufficient viable retinal cells.
- There are no therapeutic alternatives.

➔ **Public health benefit**

Considering:

- the seriousness of the disease, systematically progressing to blindness, with an onset either soon after birth (severe, fast-progressing forms), or later on in childhood or adolescence, with a slower progression of the disease,
- its extreme rarity,
- the unmet medical need,
- the response to the identified need in terms of improvement in functional visual acuity assessed using a Multi-Luminance Mobility Test (MLMT) compared to the absence of treatment, and maintenance of long-term efficacy (maximum follow-up of 6 years),
- despite the absence of robust evidence of the efficacy of voretigene neparvovec on quality of life,
- the impact on the organisation of care given its administration in hospital, in the surgical suite under controlled aseptic conditions, hospitalisation for a period of 24 hours, regular monitoring of patients in the short and long term, treatment limited to centers authorised to perform sub-retinal injections to treat retinal dystrophies, the need to perform a genetic test to make the diagnosis, with this impact being very low overall due to the rarity of the disease,

LUXTURNA (voretigene neparvovec) is likely to have an impact on public health.

Considering all of these elements, the Committee deems that the clinical benefit of LUXTURNA 5 x 10^{12} vector genomes/mL concentrate and solvent for solution for injection remains substantial in the MA indication.

Clinical Added Value

Considering:

- the unmet medical need in an incapacitating disease that progresses to blindness in the absence of other curative treatments,
- the quality of the evidence of the efficacy of LUXTURNA (voretigene neparvovec) in randomised, multicenter phase 3 study 301 versus the absence of treatment, and despite the open-label nature of the study,
- the relevance of the primary endpoint assessing the visual function of patients using a Multi-Luminance Mobility Test (MLMT) and the clinical relevance of the effect observed after 1 year of follow-up compared to the absence of treatment,
- long-term follow-up data from 3 studies (extension of study 301 with usable data for up to 6 years of follow-up, the PASS PERCEIVE study based on data from the international registry of 198 patients with follow-up for 1-2 years or 1 additional year for French patients and the LIGHT observational study in 12 patients with follow-up for ≥ 1 year) demonstrating the maintenance of clinical responses in mobility tests, full-field light sensitivity threshold (FST) testing using white light and visual field,
- a safety profile that is unchanged overall since the product was first marketed,

despite:

- the absence of robust evidence of an effect of LUXTURNA (voretigene neparvovec) on quality of life,

- the development in some patients included in the clinical studies (frequency unknown according to the SmPC) of progressive chorioretinal atrophy, which had little impact on assessment of the endpoints but in which the long-term progression needs to be evaluated,

the Committee deems that the clinical added value of LUXTURNA 5 x 10^{12} vector genomes/mL concentrate and solvent for solution for injection remains important (CAV II) in the management of adult and paediatric patients with vision loss due to inherited retinal dystrophy caused by confirmed biallelic *RPE65* mutations and who have sufficient viable retinal cells.