Subject: Luxturna (Voretigene neparvovec-rzyl)

Background:
Voretigene neparvovec-rzyl (Luxturna) is a new adeno-associated virus vector-based gene therapy indicated for the treatment of biallelic *RPE65* mutation-associated retinal dystrophy, a category of disease that can include Retinitis Pigmentosa (RP) and Leber's congenital amaurosis type 2 (LCA2), both of which are associated with eventual complete loss of vision. The RPE65 protein, the product of the *RPE65* gene, supports and nourishes the retina by converting retinal pigments that have sensed light back into their light-sensitive form. Luxturna is an engineered virus that carries and infects the cells of its host with a normal copy of the *RPE65* gene.

Authorization:
Prior authorization is required for voretigene neparvovec-rzyl (Luxturna) requested by members enrolled in commercial (HMO, POS and PPO) products.

Policy and Coverage Criteria:

Initiation of Therapy:
Harvard Pilgrim Health Care (HPHC) considers voretigene neparvovec-rzyl (Luxturna) administration at a certified treatment facility as reasonable and medically necessary for the management of retinal dystrophy when medical record documentation confirms ALL of the following;

A. Member retinal dystrophy is due to mutation of both copies (biallelic mutation, not necessarily matching mutations) of the *RPE65* gene, as indicated by BOTH
   i. A form of retinal dystrophy associated with *RPE65* mutation, such as retinitis pigmentosa, fundus albipinctatus, or Leber's congenital amaurosis type 2, and
   ii. The presence of at least one mutation on each *RPE65* gene copy;
B. Member has viable retinal cells, as determined by a treating physician; and
C. Member is available to receive treatment at site according to recommended schedule and subsequent monitoring.

Note: Luxturna must be administered at a facility certified for the administration of Luxturna

Exclusions:
Harvard Pilgrim Health Care (HPHC) does not cover voretigene neparvovec-rzyl (Luxturna) when criteria above are not met.

Supporting Information:
The strongest research on the use of voretigene neparvovec-rzyl is a randomized, controlled, open-label clinical trial in twenty-nine participants with Leber's congenital amaurosis type 2 (LCA2), with the treatment group showing a significant improvement in multi-luminance mobility testing and full-field light sensitivity threshold testing that remained stable over the course of a year, compared to no or negligible improvement in the control group. No plausibly treatment-related serious adverse events or immune responses were recorded, although two participants experienced serious events related to a seizure disorder and an oral surgery complication. Earlier trials in participants with various RPE65-linked retinal dystrophy, while smaller and without controls, showed

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significant improvements in mobility and visual acuity that persisted to three years. Recorded treatment-related adverse events have largely been associated with the method of administration, subretinal injection, and the use of corticosteroids with treatment rather than Luxterna itself. The FDA approved Luxturna on the unanimous recommendation of its advisory committee in December 19, 2017, with an accelerated approval process being implemented due to the drug being granted priority review, breakthrough therapy, and orphan drug designations. Post-marketing observational studies are planned to establish the long-term safety and efficacy of the treatment.

Coding:

CPT® Code	Description
J3398	Injection, voretigene neparvovec-rzyl, 1 billion vector genomes

Approved by Medical Policy Committee: 1/2/2019
Approved by Clinical Policy Operational Committee: 7/18, 1/19
Policy Effective Date: 1/24/2019
Initiated: 7/18

References:

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