Drug Coverage Policy

Effective Date.....07/15/2024
Coverage Policy Number.....IP0160
Policy Title..... Gene Therapy – Luxturna

Ophthalmology – Gene Therapy – Luxturna

- Luxturna® (voretigene neparvovec-rzyl subretinal injection – Spark Therapeutics)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

OVERVIEW
Luxturna, an adeno-associated virus vector-based gene therapy, is indicated for the treatment of confirmed **biallelic human retinal pigment epithelial 65 kDa protein (RPE65) mutation-associated retinal dystrophy**.[1] Patients must have viable retinal cells as determined by the treating physician(s).

Luxturna is made up of a live, non-replicating adeno-associated virus serotype 2 which has been genetically modified to express the human RPE65 gene.[1] Luxturna is designed to deliver a normal copy of the gene encoding RPE65 to cells of the retina in patients with reduced or absent levels of biologically active RPE65. Treatment with Luxturna is not recommended for patients younger than 12 months of age, because the retinal cells are still undergoing cell proliferation, and Luxturna would

potentially be diluted or lost during cell proliferation. The safety and effectiveness of Luxturna have not been established in geriatric patients. Clinical studies of Luxturna for this indication did not include patients ≥ 65 years of age.

Disease Overview
Inherited retinal dystrophies are a broad group of genetic retinal disorders that are associated with progressive visual dysfunction.[2] RPE65 mutation-associated retinal dystrophy is associated with numerous discrete gene mutations and affects 1,000 to 2,000 patients in the US. Mutations in the RPE65 gene lead to reduced or absent levels of RPE65 isomerohydrolase activity.[1] The absence of RPE65 leads to the accumulation of toxic precursors, damage to RPE-producing cells, and, over time, damage to photoreceptors, progressing to near total blindness in most patients.

Dosing Information
The recommended dose of Luxturna for each eye is 1.5×10^{11} vector genomes (vg) administered once per eye by subretinal injection.[1] After completing a vitrectomy (removal of the vitreous gel that fills the eye cavity) and under direct visualization, a small amount of Luxturna is injected slowly until an initial subretinal bleb is observed; the remaining volume is then injected slowly until the total 0.3 mL is delivered. Luxturna should be injected into each eye on separate days within a close interval, but no fewer than 6 days apart.

Documentation: **Documentation is required** for all of the criteria elements below. Documentation may include, but is not limited to chart notes, laboratory tests, claims records, and/or other information

Medical Necessity Criteria

Luxturna is considered medically necessary when the following criteria are met:

FDA-Approved Indication

1. **Biallelic Human Retinal Pigment Epithelial 65 kDa Protein (RPE65) Mutation-Associated Retinal Dystrophy.** Approve for one-time treatment course (i.e., a total of two injections, one injection in each eye) if the patient meets ALL of the following (A, B, C, D, and E):
   - **A)** Patient has a genetically-confirmed diagnosis of biallelic RPE65 mutation-associated retinal dystrophy; AND
   - **B)** Patient is ≥ 12 months of age and < 65 years of age; AND
   - **C)** Luxturna is administered by a retinal specialist; AND
   - **D)** Patient must have viable retinal cells as determined by the treating physician; AND
   - **E)** Patient is not receiving re-treatment of eye(s) previously treated with Luxturna.

   Dosing. Approve the following dosing regimen (A and B):
   - **A)** One 1.5×10^{11} vector genomes (vg) injection administered by subretinal injection into each eye; AND
   - **B)** The doses for the first eye and the second eye are separated by at least 6 days (i.e., injection of the second eye occurs 6 or more days after injection of the first eye).

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Re-treatment of previously treated eye(s).** Luxturna is for one time use in each eye. Repeat dosing in previously treated eye(s) is not approvable.

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J3398	Injection, voretigene neparvovec-rzyl, 1 billion vector genomes

References

1. Luxturna® subretinal injection [prescribing information]. Philadelphia, PA: Spark Therapeutics; May 2022.
2. FDA news release. FDA approves novel gene therapy to treat patients with a rare form of inherited vision loss. Published on: December 19, 2017. Page last updated: March 16, 2018. Available at: https://www.fda.gov/news-events/press-announcements/fda-approves-novel-gene-therapy-treat-patients-rare-form-inherited-vision-loss. Accessed on February 22, 2024.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Policy Name Change: Updated** Policy Name from "Voretigene Neparvovec-rzyl" to "Ophthalmology – Gene Therapy – Luxturna." **Biallelic Human Retinal Pigment Epithelial 65 kDa Protein (RPE65) Mutation-Associated Retinal Dystrophy: Removed** the requirement for the presence of sufficiently viable retinal cells determined by optical coherence tomography (OCT) and/or ophthalmoscopy, evidenced by either area of retina within the posterior pole of greater than 100 µm thickness per OCT, or at least 3 disc areas of retina without atrophy or pigmentary degeneration within the posterior pole, or remaining visual field within 30 degrees of fixation as measured by a III4e isopter or equivalent.	07/15/2024

The policy effective date is in force until updated or retired.