



Drug Coverage Policy

Effective Date3/26/2026
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 where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. 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, including loss of vision.^{2,3} The combined prevalence of inherited retinal diseases is between 1:3,000 and 1:4,000.³ It is estimated there are over 2.5 million individuals affected by inherited retinal dystrophies worldwide. Variants in more than 270 different genes have been identified as the cause of inherited retinal dystrophies.² It is difficult to accurately estimate the prevalence of *RPE65* variants; however, *RPE65* variants are responsible for 0.8 to 1.5% of inherited retinal dystrophy cases.³ In the US, the frequency of individuals with *RPE65* variants was estimated to be 1:576,667, for a total of 563 individuals with such variants at any given time, or seven new cases per year. An analysis of genotype data from six major world populations predicted that there are 16,620 individuals with biallelic *RPE65* variants. Variants 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.

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Policy Statement

Prior Authorization is recommended for prescription benefit coverage of Luxturna. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Because of the specialized skills required for evaluation and diagnosis of patients treated with Luxturna as well as the specialized training required for administration of Luxturna, approval requires Luxturna to be administered by a retinal specialist. All approvals are provided for one injection per eye. Note: A 3-month (90 days) approval duration is applied to allow for the one-time treatment of both eyes.

Documentation: Documentation is required for use of Luxturna as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to chart notes, laboratory tests, claims records, prescription receipts and/or other information. All documentation must include patient-specific identifying information.

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

FDA-Approved Indication

1. Biallelic Human Retinal Pigment Epithelial 65 kDa Protein (RPE65) Variant-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, E and F):

- A. Patient has a genetically confirmed diagnosis of biallelic *RPE65* variant-associated retinal dystrophy **[documentation required]**; AND
- B. Patient is \geq 12 months of age and $<$ 65 years of age; AND
- C. Luxturna is administered by a retinal specialist **[documentation required]**; AND
- D. Patient must have viable retinal cells as determined by the treating physician **[documentation required]**; AND
- E. Patient is not receiving re-treatment of eye(s) previously treated with Luxturna **[documentation required]**.
- F. If criteria A through E are met, approve one dose of Luxturna (1.5 x 10¹¹ vector genomes [vg]) per eye (two doses per patient), to be administered by subretinal injection
Note: 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).

Dosing. Approve the following dosing regimen (A and B):

- A. One 1.5 x 10¹¹ 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).

Conditions Not Covered

Luxturna for any other use is considered not medically necessary 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

Note: 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. Sallum JMF, Kaur VP, Shaikh J, et al. Epidemiology of mutations in the 65-kDa retinal pigment epithelium (*RPE65*) gene-mediated inherited retinal dystrophies: a systematic literature review. *Adv. Ther.* 2022;39:1179-1198.
3. Aoun M, Passerini I, Chiurazzi P, et al. Inherited retinal diseases due to *RPE65* variants: from genetic diagnostic management to therapy. *Int J Mol Sci.* 2021;.22(13):7207. Doi: 10.3390/ijms2217207.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	<p>Policy Name Change: Updated Policy Name from "Voretigene Neparvovec-rzyl" to "Ophthalmology – Gene Therapy – Luxturna."</p> <p>Biallelic Human Retinal Pigment Epithelial 65 kDa Protein (<i>RPE65</i>) 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.</p>	07/15/2024
Annual Revision	No criteria changes.	3/20/2025
Annual Revision	<p>Policy Statement: Approval duration was changed from 1 month (30 days) to 3 months (90 days) to allow adequate time for prescribers and patients to schedule implant procedure.</p> <p>Biallelic Human Retinal Pigment Epithelial 65 kDa Protein (<i>RPE65</i>) Variant-Associated Retinal Dystrophy: "Variant" is used in place of "mutation". For the requirement that patient has a genetically confirmed diagnosis, the word "variant" replaced the word "mutation". Added a requirement that if all of the other requirements are met, one dose of Luxturna per eye will be approved. Added a Note that the doses for the first and second eye are separated by at least 6 days.</p>	3/26/2026

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

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