Utilization Review Policy 191

POLICY: Ophthalmology – Gene Therapy – Luxturna Utilization Management Medical Policy
- Luxturna® (voretigene neparvovec-rzyl subretinal injection – Spark Therapeutics)

EFFECTIVE DATE: 1/1/2020
LAST REVISION DATE: 02/25/2026

COVERAGE CRITERIA FOR: All UCare Plans

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 dystrophies 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. Mutations 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* mutations; however, they are responsible for 0.8 to 1.5% of inherited retinal dystrophy cases.[3] In the US, the frequency of individuals with *RPE65* mutations was estimated to be 1:576,667, for a total of 563 individuals with such variants at any given time, or 7 new cases per year. An analysis of genotype data from 6 major world populations predicted that there are 16,620 individuals with biallelic *RPE65* mutations. 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.

POLICY STATEMENT

Prior Authorization is recommended for medical 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.

All reviews (approvals and denials) will be forwarded to the Medical Director for evaluation. Some clients have elected Embarc Benefit Protection. For these clients, the Medical Director will coordinate with eviCore to ensure the Embarc Benefit Protection portion of the review has been completed. If the Embarc Benefit Protection portion of the review has not been completed, the Medical Director will route to Embarc@eviCore.com prior to completing the review.

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, prescription claims records, prescription receipts, and/or other information. All documentation must include patient-specific identifying information.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Luxturna is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Biallelic Human Retinal Pigment Epithelial 65 kDa Protein (*RPE65*) Mutation-Associated Retinal Dystrophy.** Approve for a 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 **[documentation required]**; AND
   - **B)** Patient is ≥ 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 retreatment of eye(s) previously treated with Luxturna **[documentation required]**.

   Dosing. Approve the following dosing regimen (A and B):
   - **A)** One 1.5 x 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).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Luxturna is not recommended in the following situations:

1. **Retreatment of Previously Treated Eye(s)**. Luxturna is for one-time use in each eye. Repeat dosing in previously treated eye(s) is not approvable.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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/ijms22137207.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Policy Name Change:** The designation "Gene Therapy" was added to the policy title: Ophthalmology – Gene Therapy – Luxturna UM Medical Policy. No criteria changes.	02/22/2023
Annual Revision	No criteria changes.	02/28/2024
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/16/2024
Annual Revision	No criteria changes.	02/26/2025
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/15/2025
Annual Revision	**Policy Statement:** Approval duration was changed from 1 month (30 days) to 3 months (90 days). **Biallelic Human Retinal Pigment Epithelial 65 kDa Protein (*RPE65*) Mutation-Associated Retinal Dystrophy:** Removed "documentation required" for the age requirement.	02/25/2026