Clinical Policy: Voretigene neparvovec-rzyl (Luxturna)

Reference Number: PA.CP.PHAR.372
Effective Date:10/2018
Last Review Date: 01/2026

Description
Voretigene neparvovec-rzyl (Luxturna™) is an adeno-associated virus vector-based gene therapy.

FDA Approved Indication(s)
Luxturna is indicated for the treatment of patients with confirmed biallelic *RPE65* mutation-associated retinal dystrophy. Patients must have viable retinal cells as determined by the treating physician(s).

Policy/Criteria
Provider must submit documentation (including such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

All requests reviewed under this policy **require Precision Drug Action Committee (PDAC) Utilization Management Review**.

It is the policy of PA Health & Wellness® that Luxturna is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Retinal Dystrophy (must meet all)**:**

1. Diagnosis of retinal dystrophy, confirmed by genetic diagnosis of biallelic *RPE65* gene mutations;
2. Prescribed by or in consultation with an ophthalmologist;
3. Age ≥12 months;
4. Member has not previously been treated with Luxturna in the requested treatment eye(s);
5. Sufficient viable retinal cells as evidenced by both of the following (a and b):
   a. Retinal thickness on spectral domain optical coherence tomography (i.e., areas of retina with thickness measurements > 100 microns within the posterior pole);
   b. Fundus photography (i.e., presence of neural retina);
6. Member has not received intraocular surgery within prior 6 months;
7. Dose does not exceed 1.5×10^{11} vector genomes (vg) per eye.

Approval duration: 4 weeks (1 lifetime dose per eye)

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

II. Continued Therapy

A. Retinal Dystrophy (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.PHARM.01) applies;
2. Greater than 6 days but no more than 18 days have passed since treatment of the first eye;
3. Request is not for a repeat treatment of a previously treated eye (*see Appendix D*);
4. Dose does not exceed 1.5 x 10^{11} vg per eye.

Approval duration: 4 weeks (1 lifetime dose per eye)

B. Other diagnoses/indications:

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – PA.CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
FST: full-field stimulus testing
MLMT: multi-luminance mobility testing
RP: retinitis pigmentosa
VA: visual acuity
vg: vector genomes

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- No clinical data are available on repeat administration of Luxturna to treat an individual eye.
- Due to significant safety concerns associated with immunogenicity against the vector and/or expressed protein, treatment of the second eye should be within 18 days of treatment of the first eye, but no fewer than 6 days apart.
- Due to the safety concerns related to subretinal injection procedure, as well as lack of evidence of clinical benefit in patients with greater baseline visual function than specified in the criteria, only patients with significant vision loss in both eyes are candidates for treatment at this time.

- Patients who did not show any viable retinal cells were excluded from the clinical studies of Luxturna and may not benefit from treatment based on its mechanism of action. Viable retinal cells can be determined by the following:
  - Fundus photography documents the retina, the neurosensory tissue in our eyes through a specialized low power microscope with an attached camera.
  - Optical coherence tomography is a noninvasive imaging test that uses light waves to take cross-section pictures of the retina to visualize the retina's distinctive layers.
- Retinitis pigmentosa (RP) refers to a group of hereditary retinopathies or retinal dystrophies that affects about 2.5 million people worldwide. Mutations in human *RPE65* cause Leber congenital amaurosis and other forms of autosomal recessive RP, which are characterized by early-onset blindness. Leber congenital amaurosis occurs in 2 to 3 per 100,000 newborns and it is one of the most common causes of blindness in children.
- Significant vision loss as evidenced by visual acuity (VA) description:
  - Visual acuity of 20/60 or worse in both eyes:
    - Visual acuity can be measured by a Snellen eye test chart or a LogMAR chart.
    - The Snellen chart has optotypes arranged 5 by 5 on a grid to indicate the letter size. VA is determined by the line that the person can recognize, and if that line is twice as large as the reference standard (20/20), that person's Magnification Requirement (MAR) is 2x. If the MAR is 2x, the VA is 1/2 (20/40), and would need 2x the magnification. Similarly if the MAR is 3x, the VA is 1/3 (20/60), and would need 3x magnification.
    - The LogMAR chart comprises of rows of letters and is used to estimate a more accurate visual acuity than other more commonly used charts (e.g., the Snellen chart). Each letter in the LogMAR chart has a score value of 0.02 log units. Since there are 5 letters per line, the total score for a line on the LogMAR chart represents a change in 0.1 log units. The formula used in calculating the score is: [LogMAR VA = 0.1 + LogMAR value of the best line read – 0.02 X (number of letters read)]. Zero LogMAR indicates standard vision, while zero VA indicates blindness.
    - The World Health Organization established criteria for low vision using the LogMAR scale, which is defined as a best-corrected visual acuity worse than 0.5 LogMAR but equal or better than 1.3 LogMAR in the better eye. Blindness is defined as a best-corrected visual acuity worse than 1.3 LogMAR.
  - Visual field less than 20 degrees in any meridian:
    - Visual field is another distinct measurable function of the eye. It represents the visual area that is perceived simultaneously by a fixating eye.
    - The field of vision is that portion of space in which objects are visible at the same moment during steady fixation of gaze in one direction. The normal limits of the visual field consists of central vision, which includes the inner 30 degrees of vision and central fixation, and the peripheral visual field, which extends 100 degrees laterally, 60 degrees medially, 60 degrees upward, and 75 degrees downward.
    - Visual field can be measured by a **Goldmann Perimetry Test.**
      - Perimetry measures all areas of eyesight, including side, or peripheral, vision. Goldmann perimetry testing is the most widely used instrument for manual perimetry (meridian). It uses a specific background luminance and a bowl

with a specific radius with a dotted stimuli that is used to plot an isopter, which is denoted by:
  - Roman numerals = 0 to V (size)
  - Number = 1 to 5 (Luminance) use of filter
  - Alphabet = a to e use of filter
- Isopter: The line connecting all points in the visual field with the same threshold for a given test spot; boundary between area of visibility of the area of non-visibility for a particular stimulus.
- Expected findings for normal isopters for those under 50 years of age are:
  - Peripheral: I-4e
  - Intermediate: I-3e
  - Central: I-2e
- The visual field is considered abnormal if the threshold values are significantly brighter than the expected values.
- Patients with a visual field less than 20 degrees in any meridian as measured by a **III4e isopter or equivalent** in both eyes show significant vision loss for treatment with Luxturna.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Biallelic *RPE65* mutation-associated retinal dystrophy	1.5×10^{11} vg administered one time by subretinal injection in a total volume of 0.3 mL per eye	1.5×10^{11} vg/eye

VI. Product Availability

Single-dose vial: 5×10^{12} AAV2-hRPE65v2 vg/mL

VII. References

1. Luxturna Prescribing Information. Philadelphia, PA: Spark Therapeutics, Inc.; May 2022. Available at: https://www.fda.gov/media/109906/download?attachment.. Accessed November 7, 2025.
2. Russell S, Bennett J, Wellman JA, et al. Efficacy and safety of voretigene neparvovec (AAV2-hRPE65v2) in patients with *RPE65*-mediated inherited retinal dystrophy: a randomized, controlled, open-label, phase 3 trial. *Lancet*. 2017; 390:849-60. http://dx.doi.org/10.1016/
3. Dias MF, Joo K, Kemp JA, Fialho SL, da Silva Cunha A Jr, et al. Molecular genetics and emerging therapies for retinitis pigmentosa: Basic research and clinical perspectives. *Prog Retin Eye Res*. 2017; pii: S1350-9462:30052-6. doi: 10.1016/j.preteyeres.2017.10.004.
4. Kumaran N, Pennesi ME, Yang P, et al. Leber Congenital Amaurosis / Early-Onset Severe Retinal Dystrophy Overview. 2018 Oct 4 (Revised March 23, 2023). In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2021. Available at: https://www.ncbi.nlm.nih.gov/books/NBK531510/pdf/Bookshelf_NBK531510.pdf. Accessed November 7, 2025.
5. Evans JM. Standards for visual acuity. Intelligent Systems Division: National Institute for Standards and Technology. June 2006.

https://www.nist.gov/system/files/documents/el/isd/ks/Visual_Acuity_Standards_1.pdf. Accessed November 7, 2025.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

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

Reviews, Revisions, and Approvals	Date
Policy created	
1Q 2019 annual review: references reviewed and updated.	01/2019
1Q 2020 annual review; removed Leber congenital amaurosis LCA from diagnosis; removed baseline MLMT test requirement due to absence of available test sites; references reviewed and updated.	01/2020
1Q 2021 annual review: no significant changes; references reviewed and updated	01/2021
1Q 2022 annual review: no significant changes; references reviewed and updated.	01/2022
1Q 2023 annual review: change from 12 months to 3 years of age for diagnosis of retinal dystrophy; references reviewed and updated.	01/2023
1Q 2024 annual review: no significant changes; references reviewed and updated.	01/2024
1Q 2025 annual review: no significant changes; references reviewed and updated.	01/2025
1Q 2026 annual review: Updated language under Policy/Criteria to effectively redirect prior authorization reviews to Precision Drug Action Committee (PDAC) Utilization Management Review; removed FST testing requirement; references reviewed and updated.	01/2026