



Nonprofit corporations and independent licensees
of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

P&T Date: 04/10/2025

Luxturna® (voretigene neparvovec-rzyl)

HCPCS: J3398

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

- A. Coverage of the requested drug is provided when all the following are met:
 - a. FDA approved indication
 - b. Prescribed and administered by an ophthalmologist
 - c. Patient is 12 months of age or older
 - d. Documented biallelic RPE65 gene mutation
 - e. Retinal thickness greater than 100 microns within the posterior pole
 - f. Submission of baseline full field light sensitivity prior to approval and full field light sensitivity one year after administration as a follow-up to the prior approval request
- B. Quantity Limitations, Authorization Period and Renewal Criteria
 - a. Quantity Limit: Align with FDA recommended dosing
 - b. Initial Authorization Period: 3 months with the allowance of only one dose per lifetime
 - c. Renewal Criteria: Not applicable as no further authorization will be provided

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at <http://www.cms.hhs.gov/>. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- The RPE65 gene is expressed in the retinal pigment epithelium layer and encodes the RPE65 protein. The RPE65 protein is involved in a multi-step process called the visual cycle, which converts light entering the eye into electrical signals that are transmitted to the brain. When light hits photosensitive pigments in the retina, it changes 11-cis retinal, a form of vitamin A, to all-trans retinal. This conversion triggers a series of chemical reactions that create electrical signals that are transmitted to the brain enabling sight. The RPE65 protein then helps convert all-trans retinal back to 11-cis retinal so the visual cycle can begin again. Mutations in the RPE65 gene result in dysfunctional proteins, visual cycle disruption, and visual impairment that progresses to blindness.

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

- Luxturna is an adeno-associated virus vector-based gene therapy indicated for the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy. Patients must have viable retinal cells defined as retinal thickness greater than 100 microns within the posterior pole and determined by the treating physician. Use in infants under 12 months of age is not recommended because of potential dilution or loss of Luxturna after administration due to the active proliferation of retinal cells occurring in this age group.
- The biallelic mutation of RPE65 is diagnosed with a genetic test. Results of one pathogenic variant in the homozygous state, or the same mutation on both alleles, confirm biallelic RPE65-mediated inherited retinal dystrophy. Compound heterozygosity is when there are two different pathogenic variants. Genetic testing showing compound heterozygosity in the trans configuration, with each allele having one pathogenic variant, confirms biallelic RPE65-mediated inherited retinal dystrophy. Results from genetic tests showing two different pathogenic variants in the cis configuration, where one allele has both variants and the other allele has none, rule out RPE65-mediated inherited retinal dystrophy. If a compound heterozygous state is detected, documentation of a trans configuration will be needed to confirm diagnosis.
- Safety and efficacy were established in an open-label, randomized trial of 31 pediatric and adult patients with biallelic RPE65 mutation-associated retinal dystrophy. Eligible patients had to be at least 3 years of age, have visual acuity less than 20/60 and/or visual field less than 20° in any meridian, and be within the mobility-testing passing range at baseline to allow for measurable improvement. Patients were randomized in a 2:1 ratio to either the intervention group, which received bilateral, sequential subretinal administration of voretigene neparvovec, or the control group. The primary endpoint was change in bilateral mobility testing. Secondary endpoints which were tested statistically in hierarchical order included: a change in full-field light sensitivity threshold testing, change in mobility test score for the first eye injected, and visual acuity testing. Mobility testing and full-field light sensitivity threshold testing were observed one year after the Luxturna injection and found to be significantly improved compared to the control group. The change in visual acuity noted after the first year was not significantly different between the control and Luxturna groups.

References:

1. Luxturna [prescribing information]. Philadelphia, PA: Spark Therapeutics, Inc.; May 2022.
2. Bennett J, Wellman JA, Marshall KA, et al. Safety and durability of effect of contralateral-eye administration of AAV2 gene therapy in patients with childhood-onset blindness caused by RPE65 mutations: a follow-on phase 1 trial. *Lancet*. 2016 Aug 13; 388 (10045): 661 - 72.
3. 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 Aug 26; 390 (10097): 849 – 60.
4. Medlineplus.gov. RPE65 gene. 2020 Aug 18. Available at: <https://medlineplus.gov/genetics/gene/rpe65/#synonyms>. Accessed on February 4, 2021.
5. Chung DC, Bertelsen M, Lorenz B, et al. The natural history of inherited retinal dystrophy due to biallelic mutations in the RPE65 gene. *Am J Ophthalmol*. 2019 Mar; 199: 58 – 70.
6. Chung DC, McCague S, Yu ZF, et al. Novel mobility test to assess functional vision in patients with inherited retinal dystrophies. *Clin Exp Ophthalmol*. 2018 Apr; 46 (3): 247 – 59.

Policy History												
#	Date	Change Description										
2.2	Effective Date: 04/10/2025	Annual review of criteria was performed, no changes were made										
2.1	Effective Date: 04/11/2024	Annual review of criteria was performed, no changes were made										
2.0	Effective Date: 04/06/2023	Updated approval length to 3 months										
1.9	Effective Date: 04/14/2022	Annual review of criteria was performed, no changes were made.										
1.8	Effective Date: 04/08/2021	Annual review of criteria was performed, no changes were made										
1.7	Effective Date: 04/16/2020	Annual review of criteria was performed, no changes were made										
1.6	Effective Date: 05/09/2019	Annual review of criteria was performed, no changes were made										
1.5	Effective Date: 08/07/2018	UM medical management system update for BCNA and MAPPO <table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	Yes	BCNA	Yes
Line of Business	PA Required in Medical Management System (Yes/No)											
BCBS	Yes											
BCN	Yes											
MAPPO	Yes											
BCNA	Yes											
1.4	Effective Date: 05/03/2018	New drug review, updated background and indication, preliminary criteria updated by removing restrictions based on visual acuity/visual fields as well as adding necessity to submit full field light sensitivity at base line and after one year										
1.3	Effective Date: 02/08/2018	Update to Preliminary Criteria										
1.2	Effective Date: 02/01/2018	UM medical management system update for BCN and BCBS <table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	No	BCNA	No
Line of Business	PA Required in Medical Management System (Yes/No)											
BCBS	Yes											
BCN	Yes											
MAPPO	No											
BCNA	No											
1.1	Effective Date: 12/07/2017	Update to Preliminary Criteria										
1.0	Effective Date: 02/09/2017	Preliminary Criteria										

* The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or <http://dailymed.nlm.nih.gov/dailymed/index.cfm>.

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

**Blue Cross Blue Shield/Blue Care Network of Michigan Medication
Authorization Request Form
Luxturna™ (Voretigene neparvovec-rzyl) HCPCS CODE: J3398**



This form is to be used by participating physicians to obtain coverage for Luxturna. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

Nonprofit corporations and independent licensees
of the Blue Cross and Blue Shield Association

PATIENT INFORMATION

PHYSICIAN INFORMATION

Name	Name
ID Number	Specialty
D.O.B. <input type="checkbox"/> Male <input type="checkbox"/> Female	Address
Diagnosis	City /State/Zip
Drug Name <input type="checkbox"/> Luxturna	Phone/Fax: P: () - F: () -
Dose and Quantity	NPI
Directions	Contact Person
Date of Service(s)	Contact Person Phone / Ext.

STEP 1: DISEASE STATE INFORMATION

- Please provide the NPI number for the place of administration: _____
- Please provide the estimated date of injection: _____
- Has patient previously received Luxturna? ☐ Yes ☐ No
- Is biallelic RPE65 gene mutation present? ☐ Yes (**Must attach test results**) ☐ No
- Retinal Thickness (posterior pole) OS: _____ OD: _____
- Has a full-field light sensitivity threshold test (FST) been performed? ☐ Yes (**Must attach test results**) ☐ No

Chart notes are required for the processing of all requests. Please add any other supporting medical information necessary for our review (required)

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

☐ Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name	Physician Signature	Date
Step 2: Checklist	<input type="checkbox"/> Form Filled Out <input type="checkbox"/> Attach Genetic Testing Results	<input type="checkbox"/> Attach Chart Notes
Step 3: Submit	By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979	By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320

Confidentiality notice: This transmission contains confidential information belonging to the sender that is legally privileged. This information is intended only for use of the individual or entity named above. The authorized recipient of this information is prohibited from disclosing this information to any other party. If you are not the intended recipient, you are hereby notified that any disclosure, copying, distribution or action taken in reliance on the contents of this document is strictly prohibited. If you have received this in error, please notify the sender to arrange for the return of this document.