



Luxturna (voretigene neparvovec-rzyl) Clinical Coverage Criteria

Description

Voretigene neparvovec-rzyl (Luxturna) is a gene therapy product approved by the United States (U.S.) Food and Drug Administration (FDA) for treatment of vision loss due to certain heritable retinal dystrophies with confirmed biallelic RPE65 mutation-associated retinal dystrophies. Specifically, this represents approximately 2% of cases of autosomal recessive retinitis pigmentosa (RP) and 8-16% of cases of Leber congenital amaurosis (LCA).

Policy

This Policy applies to the following Fallon Health products:

- Fallon Medicare Plus, Fallon Medicare Plus Central (Medicare Advantage)
- MassHealth ACO
- NaviCare HMO SNP (Dual Eligible Medicare Advantage and MassHealth)
- NaviCare SCO (MassHealth-only)
- PACE (Summit Eldercare PACE, Fallon Health Weinberg PACE)
- Community Care (Commercial/Exchange)

Luxturna (voretigene neparvovec-rzyl) requires prior authorization by a Fallon Health Medical Director, except as noted below, for MassHealth ACO members effective April 1, 2025. This prior authorization is separate from any prior authorization that may be required for the member's inpatient or outpatient encounter.

Effective April 1, 2025, MassHealth has transitioned the review and management of all APAD and APEC carve-out drugs, including Luxturna, to the MassHealth Drug Utilization Review (DUR) Program. Effective for dates of services on or after April 1, 2025, prior authorization requests for all APAD and APEC carve-out drugs, including Luxturna must be submitted to the DUR Program for review and approval prior to administration. **NOTE:** Only the prior authorization request for Luxturna and other APAD and APEC carve-out drugs will be reviewed by the MassHealth DUR Program, Fallon Health is still responsible for reviewing prior authorization requests for the member's inpatient or outpatient hospital encounter.

Fallon Health Clinical Coverage Criteria

Fallon Health Clinical Coverage Criteria for Luxturna apply to all products except for MassHealth ACO. For MassHealth ACO members, see MassHealth Variation below.

Luxturna is considered medically necessary when clinical documentation supporting all of the following criteria is submitted:

1. The member is at least 12 months but less than 65 years of age on the date of first administration.
2. The member has a clinical diagnosis of a biallelic RPE65 mutation-associated retinal dystrophy (e.g., Leber congenital amaurosis Type 2 (LCA2) and retinitis pigmentosa type 20 (RP20).
3. Genetic testing has confirmed the presence of biallelic RPE65-mediated inherited retinal dystrophy (homozygotes or compound heterozygotes). A copy of the genetic test results must be submitted.

4. Luxturna will be administered at a designated Ocular Gene Therapy Treatment Center (<https://mysparkgeneration.com/hcp-support.html>) and a retina specialist from the designated Ocular Gene Therapy Treatment Center has confirmed that the member has sufficient viable retinal cells as determined by non-invasive means, such as optical coherence tomography (OCT) and/or ophthalmoscopy. Documentation of one of the following is required:
 - a. An area of retina within the posterior pole of >100 µm thickness shown on OCT;
 - b. ≥ 3 disc areas of retina without atrophy or pigmentary degeneration within the posterior pole; or
 - c. Remaining visual field within 30 degrees of fixation as measured by a III4e isopter or equivalent.
5. Luxturna will be administered per FDA Prescribing Information Dosage and Administration:
 - a. The recommended dose of Luxturna for each eye is 1.5×10^{11} vector genomes (vg), administered by subretinal injection in a total volume of 0.3 mL.
 - b. Perform subretinal administration of Luxturna to each eye on separate days within a close interval, but no fewer than 6 days apart.
 - c. Recommend systemic oral corticosteroids equivalent to prednisone at 1 mg/kg/day (maximum of 40 mg/day) for a total of 7 days (starting 3 days before administration of Luxturna to the first eye) and followed by tapering the dose during the following 10 days. The same corticosteroid dosing regimen applies for the administration of Luxturna to the second eye. If the corticosteroid taper following Luxturna administration to the first eye is not complete three days prior to the planned Luxturna administration to the second eye, then the corticosteroid regimen for the second eye replaces the taper for the first eye
6. The member has not:
 - a. Used high-dose (>7500 retinol equivalent units [or >3300 IU] per day of vitamin A) retinoid compounds in the past 18 months; or
 - b. Had intraocular surgery in the past 6 months; or
 - c. Received any prior gene therapy for RPE65 mutation-associated retinal dystrophy.

Medicare Variation

None.

Medicare statutes and regulations do not have coverage criteria for Luxturna (voretigene neparvovec-rzyl). Medicare does not have an NCD for Luxturna (voretigene neparvovec-rzyl), however, Medicare has an NCD for Vitrectomy (80.11). Currently, there is supportive evidence for treatment with Luxturna in a subset of patients with clinical findings consistent with either retinitis pigmentosa or Leber congenital amaurosis for whom the biallelic RPE65 mutation is pathogenic. The ICD-10-CM classifies retinitis pigmentosa as H35.52 and Leber congenital amaurosis as H35.50. As vitrectomy surgery is required to inject Luxturna into the subretinal space, NCD 80.11, Vitrectomy, has been updated by CMS to accommodate H35.50 and H35.52 as indications (H35.54 is not among the indications supportive for vitrectomy in NCD 80.11). National Government Services, Inc., the Part A and B Medicare Administrative Contractor with jurisdiction in the Plan's service area does not have an LCD for Luxturna (Medicare Coverage Database search 04/19/2025). Coverage criteria for Luxturna are not fully established by Medicare, therefore the Plan's Clinical Coverage Criteria are applicable.

MassHealth Variation

Effective April 1, 2025, MassHealth will transition the review and management of all APAD and APEC carve-out drugs, including Luxturna, to the MassHealth Drug Utilization Review (DUR) Program. Effective for dates of services on or after April 1, 2025, all prior authorization requests for APAD and APEC carve-out drugs, including Luxturna must be submitted to the DUR Program for review and approval before administration. Only prior authorization requests for the APAD and APEC carve-out drugs themselves will be reviewed by the MassHealth DUR Program. Fallon Health will still be responsible for reviewing prior authorization requests for the member's inpatient or outpatient hospital encounter.

Additionally, also effective for dates of services on or after April 1, 2025, MassHealth will pay claims for APAD and APEC carve-out drugs for MassHealth ACO enrollees consistent with Sections 5.B.8.b and 5.C.9 of the current MassHealth Acute Hospital Request for Applications (Acute Hospital RFA) for in-state acute hospitals and regulations at 130 CMR 450.233(D) for out-of-state acute hospitals. Fallon Health will continue to pay claims for the member's inpatient or outpatient hospital encounter.

Refer to the following MassHealth Bulletins for additional information: MassHealth Managed Care Entity Bulletin 125 March 2025, MassHealth Acute Inpatient Hospital Bulletin 201 March 2025, and MassHealth Acute Outpatient Hospital Bulletin 41 March 2025, available at: <https://www.mass.gov/masshealth-provider-bulletins>.

The MassHealth Acute Hospital Carve-out Drugs List is available at: <https://masshealthdruglist.ehs.state.ma.us/MHDL/>.

Exclusions

- Use in infants less than 12 months of age is not recommended because of potential dilution or loss of Luxturna after administration due to active retinal cell proliferation occurring in this age group.
- The safety and efficacy of repeat administration of Luxturna has not been evaluated.

Summary of Evidence

Biallelic RPE65 mutation-associated retinal dystrophy is a serious and sight-threatening autosomal recessive genetic disorder. Clinical diagnoses that are caused by biallelic mutations in the RPE65 gene include Leber congenital amaurosis (LCA) Type 2 and retinitis pigmentosa (RP) type 20. Leber congenital amaurosis manifests in early life with severe vision impairment, whereas patients with retinitis pigmentosa undergo a gradual course of night blindness and visual field loss. There are approximately 1,000 to 3,000 patients with biallelic RPE65 mutation-associated retinal dystrophy in the United States.

On December 19, 2017, the U.S. Food & Drug Administration (FDA) approved Luxturna (Spark Therapeutics, Inc.), an adeno-associated virus vector-based gene therapy, for the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy.

On June 8, 2022, the FDA approved an update to the content of the Luxturna Package Insert to add chorioretinal atrophy to the Postmarketing Experience section of the Prescribing Information (Package Insert - Luxturna, Spark Therapeutics, Inc., Philadelphia, PA available at: <https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/luxturna>).

- Genetic testing is required to confirm the presence of pathogenic(s) variants in the RPE65 gene. By definition, pathogenic variant(s) must be present in both copies of the RPE65 gene to establish a diagnosis of biallelic RPE65-mediated inherited retinal dystrophy.
- Patients must have sufficient viable retinal cells as determined by non-invasive means, such as optical coherence tomography and/or ophthalmoscopy.
- 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 retinal cell's proliferation occurring in this age group.
- Gagne et al., 2022 reports the observation of perifoveal chorioretinal atrophy in a subset of patients who underwent subretinal injection of Luxturna for RPE65-mediated Leber congenital amaurosis. The authors recommend further study to isolate the factors that may predispose patients to this previously undescribed complication.

Luxturna works by delivering a normal copy of the RPE65 gene directly to retinal cells. These retinal cells then produce the normal protein that converts light to an electrical signal in the retina to restore a patient's vision loss. Luxturna uses a naturally occurring adeno-associated virus,

which has been modified using recombinant DNA techniques, as a vehicle to deliver the normal human RPE65 gene to the retinal cells to restore vision.

Luxturna is administered by subretinal injection to each eye on separate days within a close interval, but no fewer than 6 days apart. It is recommended that patients receive systemic oral corticosteroids equivalent to prednisone at 1 mg/kg/day (maximum of 40 mg/day) for a total of 7 days (starting 3 days before administration of Luxturna to the first eye) and followed by tapering the dose during the next 10 days. If the corticosteroid taper following Luxturna administration to the first eye is not complete three days prior to the planned Luxturna administration to the second eye, then the corticosteroid regimen for the second eye replaces the taper for the first eye (Package Insert. Luxturna, Spark Therapeutics, Inc., Philadelphia, PA. 2017).

U.S. Food & Drug Administration (FDA) approval of Luxturna on December 19, 2017, was based on the results of three clinical trials:

- NCT 00516477, a Phase 1, open label dose-escalation safety study in 12 children and adults, aged 8-44 years with RPE65-associated Leber's congenital amaurosis were given a subretinal injection of Luxturna in one eye. Results published by Maguire et al., 2009.
- NCT 01208389, a Phase 1 follow-on study in which the 12 participants from the Phase 1 study received Luxturna in the uninjected, contralateral eye. Improvements in functional vision have been sustained for 3 years—with observations ongoing Results published by Bennett et al., 2016.
- NCT 00999609, a Phase 3 safety and efficacy study in which 31 patients ranging in age from 4 to 44 years were randomized in a 2:1 ratio to either the Luxturna treatment group or the observational control group. One participant from each group withdrew after consent, before intervention, leaving an intent-to-treat population of 20 intervention and nine control participants. The participants were followed for one year for the primary efficacy endpoint of change in multi-luminance mobility testing (MLMT). A median MLMT score change of two (2) was observed in the Luxturna treatment group, while a median MLMT score change of zero (0) was observed in the control group, when using both eyes or the first-treated eye. An MLMT score change of two or greater is considered a clinically meaningful benefit for functional vision. No product-related serious adverse events or deleterious immune responses occurred. The FDA concluded that the submitted data provided sufficient evidence of effectiveness for patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy. This conclusion is based on improvement in functional vision, as determined by a significant difference in MLMT score change from Baseline to Year 1 between the Luxturna treatment and control groups, when using either both eyes ($p=0.0001$) or the first-treated eyes ($p=0.003$) (FDA, December 18, 2017, Summary Basis for Regulatory Action - Luxturna).

The durability of response is currently unknown given the recent FDA-approval of this therapy. Improvements in functional vision have been sustained through 3 years post-administration, with observation ongoing (Bennett et al., 2016). All participants enrolled in the Phase 1 and Phase 3 clinical studies for Luxturna are enrolled in a long-term observational study and will be followed for 15 years (NCT 03602820). To further evaluate the long-term safety, the manufacturer is also conducting a 5-year post-marketing observational study involving patients treated with Luxturna (NCT 03597399). Enrollment will start with the first patient treated following FDA approval and continue through March 31, 2020.

Luxturna may only be administered at Ocular Gene Therapy Treatment Centers designated by Spark Therapeutics: <https://luxturnahcp.com/about-luxturna/treatment-centers/>.

Analysis of Evidence (Rationale for Determination)

Based on the evidence from the Phase I and Phase III trials, voretigene neparvovec-rzyl has been found to clinically improve functional vision in patients with the biallelic mutations in the RPE65 gene in the inherited retinal degenerations, RP and LCA. In summary, Fallon Health considers a single treatment per eye, per lifetime of voretigene neparvovec-rzyl (Luxturna) medically reasonable and necessary for the treatment of beneficiaries with confirmed biallelic

RPE65 mutation-associated subtypes of RP or LCA, who otherwise meet all of the clinical criteria as outlined in this LCD.

Coding

The following codes are included below for informational purposes only; inclusion of a code does not constitute or imply coverage or reimbursement.

Effective for dates of service on and after January 1, 2019, HCPCS code J3398 should be used to report Luxturna along with the appropriate modifier (RT or LT) designating the recipient eye.

As noted in the FDA approved labeling, the recommended dose of Luxturna for each eye is 1.5 x 10¹¹ (150 billion) vector genomes, administered by subretinal injection in a total volume of 0.3 mL.² With the J code descriptor of 1 billion vector genomes, it is appropriate to indicate 150 units of J3398 on the claim form.

Effective January 1, 2024, outpatient hospitals and ambulatory surgical centers (ASCs) reimbursed under Medicare OPPS or ASC payment methodology should use 0810T to report the Luxturna administration procedure (Source: Medicare OPPS and ASC Final Rule CY 2024, CMS-1786-FC).

CPT/HCPCS Codes

Code	Description
0810T	Subretinal injection of a pharmacologic agent, including vitrectomy and 1 or more retinotomies
67036	Vitrectomy, mechanical, pars plana approach
67299	Unlisted procedure, posterior segment
J3398	Injection, voretigene neparvovec-rzyl, 1 billion vector genomes

ICD-10 Diagnosis Codes that Support Medical Necessity

ICD-10-CM	Description
H35.50	Unspecified hereditary retinal dystrophy
H35.52	Pigmentary retinal dystrophy

References

1. U.S. Food and Drug Administration (FDA). December 18, 2017, Summary Basis for Regulatory Action – Luxturna. Available at: <https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/luxturna>. Accessed June 18, 2021.
2. 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.
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6. Bennett J, Ashtari M, Wellman J, et al. AAV2 gene therapy readministration in three adults with congenital blindness. *Sci Transl Med*. 2012 Feb 8;4(120):120ra15.
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controlled, open-label, phase 3 trial. *Lancet*. 2017 Aug 26;390(10097):849-860. Erratum in: *Lancet*. 2017 Aug 26;390(10097):848.

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10. Sengillo JD, Justus S, Tsai YT, et al. Gene and cell-based therapies for inherited retinal disorders: An update. *Am J Med Genet C Semin Med Genet*. 2016 Dec;172(4):349-366.
11. Gao J, Hussain RM, Weng CY. Voretigene Neparvovec in Retinal Diseases: A Review of the Current Clinical Evidence. *Clin Ophthalmol*. 2020 Nov 13;14:3855-3869.
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13. MassHealth Drug List Table 72: Agents Not Otherwise Classified. Accessed 04/19/2025. Available at: <https://mhdl.pharmacy.services.conduent.com/MHDL/pubtheradetail.do?id=1976&drugId=7497>.
14. MassHealth Managed Care Entity Bulletin 42. September 2020. Updated MassHealth Acute Hospital Carve-Out Drugs Requirements. Available at: <https://www.mass.gov/masshealth-provider-bulletins>.
15. MassHealth Managed Care Entity Bulletin 125. March 2025. Cell and Gene Therapy Adjudicated Payment Amount per Discharge and Adjudicated Payment per Episode of Care Carve-Out. Available at: <https://www.mass.gov/masshealth-provider-bulletins>.
16. Gange WS, Sisk RA, Besirli CG, et al. Perifoveal Chorioretinal Atrophy after Subretinal Voretigene Neparvovec-rzyl for RPE65-Mediated Leber Congenital Amaurosis. *Ophthalmol Retina*. 2022 Jan;6(1):58-64.

Policy history

Origination date: 09/01/2021
Review(s)/Approval(s): Technology Assessment Committee: 06/22/2021 (policy origination), 01/24/2023 (updated Overview section to include information on chorioretinal atrophy, a previously undescribed complication of subretinal injection of Luxturna; updated references; clinical coverage criteria unchanged), 03/26/2024 (annual review; updated Policy section to indicate that Fallon Health Clinical Coverage Criteria are not applicable for MassHealth members; clinical coverage criteria unchanged; updated Coding section to inform providers that 340B stock may not be used for MassHealth ACO and NaviCare SCO members), 04/29/2025 (annual review; added new sections for Medicare Variation and MassHealth Variation; under Clinical Coverage Criteria, added 6.c. The member has not received any prior gene therapy for RPE65 mutation-associated retinal dystrophy; under Coding, removed MassHealth Acute Hospital Carve-Out Drugs List section, as it is no longer applicable. Effective 04/01/2025, MassHealth will transition the review and management of all APAD and APEC carve-out drugs to the MassHealth Drug Utilization Review Program; additionally, MassHealth will pay claims for these drugs for MassHealth ACO members).
Utilization Management Committee: 05/20/2025 (annual review; approved).

Instructions for Use

Fallon Health complies with CMS's national coverage determinations (NCDs), local coverage determinations (LCDs) of Medicare Contractors with jurisdiction for claims in the Plan's service area, and applicable Medicare statutes and regulations when making medical necessity determinations for Medicare Advantage members. When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, Fallon Health may

create internal coverage criteria under specific circumstances described at § 422.101(b)(6)(i) and (ii).

Fallon Health generally follows Medical Necessity Guidelines published by MassHealth when making medical necessity determinations for MassHealth members. In the absence of Medical Necessity Guidelines published by MassHealth, Fallon Health may create clinical coverage criteria in accordance with the definition of Medical Necessity in 130 CMR 450.204.

For plan members enrolled in NaviCare, Fallon Health first follows CMS's national coverage determinations (NCDs), local coverage determinations (LCDs) of Medicare Contractors with jurisdiction for claims in the Plan's service area, and applicable Medicare statutes and regulations when making medical necessity determinations. When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, or if the NaviCare member does not meet coverage criteria in applicable Medicare statutes, regulations, NCDs or LCDs, Fallon Health then follows Medical Necessity Guidelines published by MassHealth when making necessity determinations for NaviCare members.

Each PACE plan member is assigned to an Interdisciplinary Team. PACE provides participants with all the care and services covered by Medicare and Medicaid, as authorized by the interdisciplinary team, as well as additional medically necessary care and services not covered by Medicare and Medicaid. With the exception of emergency care and out-of-area urgently needed care, all care and services provided to PACE plan members must be authorized by the interdisciplinary team.

Not all services mentioned in this policy are covered for all products or employer groups. Coverage is based upon the terms of a member's particular benefit plan which may contain its own specific provisions for coverage and exclusions regardless of medical necessity. Please consult the product's Evidence of Coverage for exclusions or other benefit limitations applicable to this service or supply. If there is any discrepancy between this policy and a member's benefit plan, the provisions of the benefit plan will govern. However, applicable state mandates take precedence with respect to fully insured plans and self-funded non-ERISA (e.g., government, school boards, church) plans. Unless otherwise specifically excluded, federal mandates will apply to all plans.