# 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)

Prior authorization by a Fallon Health Medical Director is required for Luxturna. This prior authorization is separate from any prior authorization that may be required for the member's inpatient or outpatient encounter.

**Medicare Advantage**
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).

Medicare does not have an NCD for Luxturna (voretigene neparvovec-rzyl). Medicare has an NCD for Vitrectomy (80.11). At this time, there is supportive evidence for Luxturna treatment 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 (MCD search 03/25/2024), therefore, the Plan's Clinical Coverage Criteria are applicable.

**MassHealth**
Fallon Health 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.

MassHealth has medical necessity criteria for Luxturna (voretigene neparvovec-rzyl), therefore, Fallon Health Clinical Coverage Criteria are not applicable for MassHealth members.

**NaviCare HMO SNP, NaviCare SCO**
For plan members enrolled in NaviCare, Fallon Health first follow's 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.

**PACE (Summit Eldercare PACE, Fallon Health Weinberg PACE)**
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.

## Fallon Health Clinical Coverage Criteria

Luxturna is considered medically necessary when medical record documentation confirms all of the following criteria are met:

1. The member is at least 12 months of age on 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 $1.5 \times 10^{11}$ 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.

## 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 report 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 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.
- 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 (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.

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.

## CPT/HCPCS Codes

| Code | Description |
|---|---|
| 67036 | Vitrectomy, mechanical, pars plana approach |
| C9770 | Vitrectomy, mechanical, pars plana approach, with subretinal injection of pharmacologic/biologic agent |
| J3398 | Injection, voretigene neparvovec-rzyl, 1 billion vector genomes |

### ICD-10 Diagnosis Codes

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

Modifiers (RT/LT) should be included on the same line as the CPT code to identify the eye to which administration of Luxturna occurred.

Outpatient hospitals and ambulatory surgical centers submitting claims for administering Luxturna for **Medicare and commercial plan members** should use HCPCS code C9770 effective January 1, 2021.

Outpatient hospitals and ambulatory surgical centers submitting claims for administering Luxturna **MassHealth ACO plan members** should use CPT code 67036. MassHealth does not recognize C HCPCS codes.

## MassHealth Acute Hospital Carve-Out Drugs List

Luxturna is on the MassHealth Acute Hospital Carve-out Drugs List. In accordance with **MassHealth Managed Care Entity Bulletin 42**, Fallon Health requires hospitals to take the following actions with respect to drugs and biologics on the MassHealth Acute Hospital Carve-Out List for MassHealth ACO plan members:

1. Drugs and biologics on the MassHealth Acute Hospital Carve-Out Drugs List require prior authorization. The hospital must obtain prior authorization for the drug or biologic from Fallon Health. This prior authorization is separate from any prior authorization that may be required for the member's inpatient or outpatient encounter.
2. A drug or biologic designated by MassHealth as a carve-out drug must not be included on the facility/institutional claim that the hospital submits for the plan member's inpatient or outpatient encounter.
3. The hospital must instead submit a separate claim for the carve-out drug on a facility/institutional claim form (i.e., UB-04). (In other words, the drug is the only item on the UB-04 claim.) The charge reported on the claim must be the "hospital's actual acquisition cost" for the drug.*
4. The claim for the carve-out drug must be reported with revenue code 0636 (Drugs requiring detailed coding), the HCPCS code for the drug, the National Drug Code (NDC) for the drug, and number of units of the carve-out drug administered to the member.
5. The hospital must also include the following as separate attachments to the claim:
    a. A statement of the hospital's actual acquisition cost of the carve-out drug (as defined below) used to treat the member; and
    b. A copy of the invoice(s) for the carve-out drug from the drug manufacturer, supplier, distributor, or other similar party or agent; and
    c. Other additional documentation that the Plan deems necessary to evidence the hospital's actual acquisition cost of the carve-out drug.

* For purposes of this requirement, the "hospital's actual acquisition cost" of the carve-out drug is

defined as follows:
"…*the hospital's invoice price for the drug, net of all on-or-off invoice reductions, discounts, rebates, charge backs and similar adjustments that the hospital has or will receive from the drug manufacturer or other party for the drug that was administered to the member including any efficacy, outcome, or performance-based guarantees (or similar arrangements), whether received pre-or post-payment*."

The MassHealth Acute Hospital Carve-out Drugs List is available at: https://masshealthdruglist.ehs.state.ma.us/MHDL/. This list may be updated from time to time.

Claims for Luxturna (J3398) for MassHealth ACO and NaviCare plan members must be submitted with the 11-digit NDC Code. When reporting an NDC, all of the following NDC information is required:

- NDC Qualifier (F4)
- NDC Unit of Measure Qualifier (F2, GR, ME, UN, ML)
- NDC quantity

## References


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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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## Policy history

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| 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). |