Luxturna® (Voretigene Neparvovec-Rzyl)

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➲ Instructions for Use

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Community Plan Policy

- Luxturna® (Voretigene Neparvovec-Rzyl)

Application

UnitedHealthcare Commercial

This Medical Drug Policy applies to UnitedHealthcare Commercial benefit plans.

UnitedHealthcare Individual Exchange

This Medical Drug Policy applies to Individual Exchange benefit plans.

Coverage Rationale

➲ See Benefit Considerations

Luxturna is proven and/or medically necessary for the treatment of inherited retinal dystrophies (IRD) caused by mutations in the retinal pigment epithelium-specific protein 65kDa (RPE65) gene in patients who meet all of the following criteria:

- Patient is greater than 12 months of age; **and**
- Diagnosis of a confirmed biallelic RPE65 mutation-associated retinal dystrophy [e.g., Leber's congenital amaurosis (LCA), Retinitis pigmentosa (RP), Early Onset Severe Retinal Dystrophy (EOSRD), etc.]; **and**
- Genetic testing documenting biallelic mutations of the RPE65 gene; **and**
- Sufficient viable retinal cells as determined by optical coherence tomography (OCT) confirming an area of retina within the posterior pole of > 100 µm thickness; **and**
- Prescribed and administered by ophthalmologist or retinal surgeon with experience providing sub-retinal injections; **and**
- Patient has not previously received Luxturna treatment in intended eye; **and**
- Provider does not request a planned inpatient admission for the sole purpose of administering Luxturna; **and**
- Authorization will be issued for no more than one treatment per lifetime per eye and for no longer than 45 days from approval

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and

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applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other policies and guidelines may apply.

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

Diagnosis Code	Description
H35.50	Unspecified hereditary retinal dystrophy
H35.52	Pigmentary retinal dystrophy
H35.54	Dystrophies primarily involving the retinal pigment epithelium

Background

Inherited retinal dystrophies (IRDs) are a group of rare, genetically heterogeneous disorders that cause progressive vision loss and blindness. More than 220 gene mutations have been associated with IRDs. Retinitis pigmentosa is the most common subtype and is characterized by progressive loss of peripheral vision and reduced light sensitivity. Leber congenital amaurosis (LCA), a severe early-onset form of IRD, is associated with rapid disease progression, nystagmus, and significant visual impairment beginning in infancy or early childhood. Mutations in at least 19 genes have been identified as causes of LCA.

Biallelic mutations in the RPE65 gene result in an inherited retinal dystrophy characterized by impaired retinal function, progressive vision loss, and eventual blindness. RPE65-associated disease may be clinically classified as Leber congenital amaurosis type 2, retinitis pigmentosa type 20, or other severe early-onset retinal dystrophies. The RPE65 gene encodes retinoid isomerohydrolase, an enzyme essential for the visual (retinoid) cycle. Deficiency of functional RPE65 disrupts the conversion of all-trans-retinol to 11-cis-retinal, a critical step required for phototransduction and normal vision.

Voretigene neparvovec (Luxturna) is an adeno-associated virus (AAV) vector-based gene therapy designed to deliver a functional copy of the RPE65 gene to retinal pigment epithelial cells. Expression of functional RPE65 restores retinoid isomerohydrolase activity, supports the visual cycle, and improves retinal function in patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy.

Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy.

Clinical Evidence

The efficacy of voretigene neparvovec in pediatric and adult patients with biallelic RPE65 mutation-associated retinal dystrophy was evaluated in an open-label, two-center, randomized trial. Of the 31 enrolled subjects, 21 subjects with confirmed biallelic RPE65 mutations were randomized in a 2:1 fashion to either the voretigene neparvovec group or control group and followed for one year. After completion of one year of observation, control subjects were allowed to crossover and receive voretigene neparvovec treatment. Enrollment criteria include the following: subjects had to be at least three years of age with confirmed biallelic RPE65 mutations, subjects had to have a visual acuity of worse than or equal to 20/60 (for both eyes) and/or visual field of less than 20 degrees in any meridian as measured by a GVF III4e isopter or equivalent (both eyes), subjects had to have sufficient viable retinal cells as determined by non-invasive means, such as OCT (defined as an area of retina within the posterior pole of > 100 microns thickness) or ophthalmoscopy, subjects had to have the ability to comprehend the MLMT, follow course instructions, and the capacity to successfully navigate the course, and subjects had to have a baseline score on the MLMT that would allow a measurable improvement to be observed. The pre-specified primary efficacy endpoint was the change from Baseline at Year 1 in multi-luminance mobility test (MLMT) performance using the bilateral testing condition of the intervention group compared to controls. A total of 29 subjects were randomized and received intervention, 20 to the intervention arm and 9 to control. Overall, 72% of all treated subjects (21 of 29) achieved the maximum possible MLMT improvement one-year post-administration,

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demonstrating significant improvement in functional vision at lower light levels. The benefits observed at one year in the original intervention group continued through at least two years post-administration, with observation ongoing.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

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 as determined by the treating physician(s). 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.

References

1. Luxturna [package insert]. Philadelphia, PA; Spark Therapeutics, Inc.; May 2022.
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 randomised, controlled, open-label, phase 3 trial. *Lancet.* 2017;390:849-60.

Policy History/Revision Information

Date	Summary of Changes

10/01/2026	**Template Update**
	• Transferred content to shared policy template that applies to both UnitedHealthcare Commercial and Individual Exchange benefit plans
	• Added *Application* section to indicate this policy applies to:
	  ○ UnitedHealthcare Commercial benefit plans
	  ○ Individual Exchange benefit plans
	Supporting Information
	• Updated *Background*, *Clinical Evidence*, and *References* sections to reflect the most current information
	• Removed *Documentation Requirements* section
	• Archived previous policy versions 2026D0063K and IEXD0063.08

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its policies and guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Benefit Drug Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

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