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Policy Number: 066.000

Title: Coverage Determination Policy for Luxturna (voretigene neparvovec-rzyl)

Regions: ☒ **Texas** ☐ **Florida** ☐ **Indiana** ☐ **New Jersey** ☒ **New Mexico**

Impacted Areas:

- ☒ Network Management/Provider Services
- ☐ Member services
- ☐ Quality Management
- ☐ Credentialing
- ☐ IT
- ☐ Administration
- ☐ Compliance/delegation
- ☒ Utilization Management
- ☐ Case management
- ☐ Disease management
- ☒ Claims
- ☐ Human resources
- ☐ Finance
- ☒ Pharmacy
- ☐ ALL

Available LCD/NCD/LCA: None

Disclaimer:

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Table of Contents **Page**

Coverage Policy Number: 066.000

Line of Business: Medicare Part B

Policy Type: Prior Authorization

Coverage Determination:

Initial/New Requests

Luxturna (voretigene neparvovec-rzyl) 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:

A. Patient is greater than 12 months of age

B. 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.)

C. Genetic testing documenting biallelic mutations of the RPE65 gene

D. Sufficient viable retinal cells as determined by optical coherence tomography (OCT) confirming an area of retina within the posterior pole of > 100 µm thickness

E. Prescribed and administered by ophthalmologist or retinal surgeon with experience providing sub-retinal injections

F. Patient has not previously received RPE65 gene therapy in intended eye

Renewal/Continuation of Therapy Requests

NOTE: Luxturna is a one-time gene therapy for each eye.

FDA Approved Dose and Indication

FDA Approved Indication	FDA Approved Dose
Retinal dystrophy, In patients with viable retinal cells and confirmed biallelic RPE65 mutation	1.5×10^{11} vector genomes (vg), administered by subretinal injection in a total volume of 0.3 mL. Subretinal administration of Luxturna to each eye on separate days within a close interval, but no fewer than 6 days apart.

General Background

Luxturna is an adeno-associated virus vector-based gene therapy indicated for the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy. It is a one-time treatment for each eye.

RPE65 is a vital gene that is necessary for vitamin A metabolism in photoreceptor cells. Mutations in the RPE65 gene eventually leads to vision loss due to loss/death of RPE cells and degeneration of photoreceptors. Individuals with a RPE65 gene mutation may suffer from abnormalities in vision such as night blindness, loss of light sensitivity, loss of sharpness and clarity of vision, impaired dark adaptation, nystagmus, and eventually progress to complete blindness.

Leber's congenital amaurosis (LCA) and autosomal recessive retinitis pigmentosa (RP) are a group of inherited, early-onset, severe retinal dystrophies that cause substantial sight impairment in childhood. One of the causes of these conditions is mutations in the gene encoding RPE65.

LCA consists of a group of that cause severe vision loss in infancy. There are at least 19 different gene mutations that can be passed down and cause the spectrum of LCA. Diagnosis of LCA is confirmed by completion of an electroretinogram (ERG) that is used to measure the activity of the retina. LCA patients classically have a "flat" ERG, which suggests virtually no retinal function. Later, the retinas become damaged and show thinning, often with pigmentary changes, and the optic nerve heads become pale.

Similarly, retinitis pigmentosa (RP) comprises a complex group of inherited dystrophies characterized by progressive degeneration and dysfunction of the retina, primarily affecting photoreceptor and retinal pigment epithelial function. The retinal pigment epithelium (RPE) is the layer of the retina below the photoreceptors that plays a key role in the maintenance of the photoreceptor layer. RP may occur alone or as part of a syndrome and may be inherited as a dominant, recessive, or X-linked trait or occur sporadically.

Clinical Evidence

The efficacy of Luxturna in pediatric and adult patients with biallelic RPE65 mutation-associated retinal dystrophy was evaluated in an open-label, two-center, randomized trial (Study 2). Of the 31 enrolled subjects, 21 subjects were randomized to receive subretinal injection of Luxturna. One subject discontinued from the study prior to treatment. Ten subjects were randomized to the control (non-intervention) group. One subject in the control group withdrew consent and was discontinued from the study. The nine subjects who were randomized to the control group were crossed over to receive subretinal injection of Luxturna after one year of observation. The average age of the 31 randomized subjects was 15 years (range 4 to 44 years), including 64% pediatric subjects (n=20, age from 4 to 17 years) and 36% adults (n=11). The 31 randomized subjects included 13 males and 18 females. Sixty-eight percent (68%) of the subjects were White, 16% were Asian, 10% were American Indian or Alaska Native, and 6% were Black or African-American. Bilateral subretinal injections of Luxturna were administered sequentially in two separate surgical procedures with an interval of 6 to 18 days.

The efficacy of Luxturna was established on the basis of multi-luminance mobility testing (MLMT) score change from Baseline to Year 1. The MLMT was designed to measure changes in functional vision, as assessed by the ability of a subject to navigate a course accurately and at a reasonable pace at different levels of environmental illumination. The MLMT was assessed using both eyes and each eye separately at one or more of seven levels of illumination, ranging from 400 lux (corresponding to a brightly lit office) to 1 lux (corresponding to a moonless summer night). Each light level was assigned a score code ranging from 0 to 6. A higher score indicated that a subject was able to pass the MLMT at a lower light level. A score of -1 was assigned to subjects who could not pass MLMT at a light level of 400 lux. The MLMT of each subject was videotaped and assessed by independent graders. The MLMT score was determined by the lowest light level at which the subject was able to pass the MLMT. The MLMT score change was defined as the difference between the score at Baseline and the score at Year 1. A positive MLMT score change from Baseline to Year 1 visit indicated that the subject was able to complete the MLMT at a lower light level. Additional clinical outcomes were also evaluated, including full-field light sensitivity threshold (FST) testing, visual acuity, and visual fields.

HCPCS Code

HCPCS Code	J3398: voretigene neparvovec-rzyl, 1 billion vector genomes
Available Dosage Form (s)	Single dose vial with 0.5mL extractable volume and two vials of 1.7mL diluent. Luxturna contains 5 x 10^{12} vector genomes (vg) per mL and requires a 1:10 dilution prior to administration
Route of Administration	Subretinal injection by medical professional only

Acronyms

RPE65 = Retinal pigment epithelium-specific protein 65kDa

ERG = Electroretinogram

RPE = Retinal pigment epithelium

LCA = Leber's congenital amaurosis

RP = Retinitis pigmentosa

MLMT = Multi-luminance mobility testing

FST = Full-field light sensitivity

VG = Vector genomes

EOSRD = Early Onset Severe Retinal Dystrophy

OCT = Optical coherence tomography

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