Drug and Biologic Coverage Policy

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Coverage Policy Number 1809

Voretigene neparvovec

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Related Coverage Resources

Genetic Testing for Hereditary and Multifactorial Conditions
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INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for voretigene neparvovec-rzyl (Luxturna™).

Coverage Policy

Gene Therapy coverage varies across plans. Refer to the customer's benefit plan document for coverage details.

Voretigene neparvovec-rzyl) (Luxturna™) is considered medically necessary when ALL of the following criteria are met:

- Individual is at least 12 months of age and less than 65 years of age
- Treatment of vision loss due to inherited retinal dystrophy
- Documentation of confirmed biallelic RPE65 mutation (two confirmed pathogenic or likely pathogenic loss-of-function variants)
- Presence of sufficiently viable retinal cells as determined by optical coherence tomography (OCT) and/or ophthalmoscopy with ANY of the following:
  - Area of retina within the posterior pole of greater than 100 µm thickness per OCT
  - At least 3 disc areas of retina without atrophy or pigmentary degeneration within the posterior pole

    - Remaining visual field within 30 degrees of fixation as measured by a III4e isopter or equivalent
- No history of administration of voretigene neparvovec-rzyl in the same eye
- Prescribed by, or in consultation with, a retinal specialist

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Documentation: When documentation is required, the prescriber must provide written documentation supporting the trials of these other agents. Documentation may include, but is not limited to, chart notes, prescription claims records, and/or prescription receipts.

Authorization Duration

Authorization is for a single course of therapy (one injection per eye).

Conditions Not Covered

Luxturna (voretigene neparvovec-rzyl) is considered experimental, investigational or unproven for ANY other use including the following:

- Repeat administration in the same eye

Background

Overview

Luxturna, an adeno-associated virus vector-based gene therapy, is indicated for the treatment of patients with confirmed biallelic human retinal pigment epithelial 65 kDa protein (RPE65) mutation-associated retinal dystrophy.[1] Patients must have viable retinal cells as determined by the treating physician(s). Luxturna is made up of a live, non-replicating adeno-associated virus serotype 2 (AAV2) which has been genetically modified to express the human RPE65 gene. Luxturna is designed to deliver a normal copy of the gene encoding RPE65 to cells of the retina in patients with reduced or absent levels of biologically active RPE65.

The recommended dose of Luxturna for each eye is 1.5×10^{11} vector genomes (vg) administered once per eye by subretinal injection.[1] After completing a vitrectomy (removal of the vitreous gel that fills the eye cavity) and under direct visualization, a small amount of Luxturna is injected slowly until an initial subretinal bleb is observed; the remaining volume is then injected slowly until the total 0.3 mL is delivered. Luxturna should be injected into each eye on separate days within a close interval, but no less than 6 days apart. Luxturna is not recommended for patients < 12 months of age, because the retinal cells are still undergoing cell proliferation, and Luxturna would potentially be diluted or lost during cell proliferation. Luxturna is available as a single-dose vial containing 0.5 mL (extractable volume) of a 5×10^{12} vg/mL concentration of Luxturna, which requires a 1:10 dilution prior to administration with the supplied diluent.

Disease Overview

Inherited retinal dystrophies (IRDs) are a broad group of genetic retinal disorders that are associated with progressive visual dysfunction.[2] RPE65 mutation-associated retinal dystrophy is associated with at least 125 discrete gene mutations and affects 1,000 to 2,000 patients in the US.[2,3] Mutations in the RPE65 gene lead to reduced or absent levels of RPE65 isomerohydrolase activity.[1] The absence of RPE65 blocks the visual cycle. This leads to the accumulation of toxic precursors, damage to RPE-producing cells, and, over time, damage to photoreceptors, progressing to near total blindness in most patients. The deficiency in the RPE65 protein mainly affects rod photoreceptors that mediate peripheral vision and night vision.[3] The retinal anatomy is preserved for a relatively long period, and supplying the missing enzyme can result in restoration of the visual cycle and improvement in vision. Injection of Luxturna into the subretinal space results in transduction of some retinal pigment epithelial cells with a complementary deoxyribonucleic acid (cDNA) encoding normal human RPE65 protein, thereby providing the potential to restore the visual cycle.

Coding/ Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Covered when medically necessary when used to report voretigene neparvovec-rzyl (Luxturna™):

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

References

1. Luxturna™ subretinal injection [prescribing information]. Philadelphia, PA: Spark Therapeutics, Inc.; December 2019.
2. FDA news release. FDA approves novel gene therapy to treat patients with a rare form of inherited vision loss. Published on: December 19, 2017. Page last updated: March 16, 2018. Available at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm589467.htm. Accessed on February 17, 2020.
3. Spark Therapeutics. Luxturna™ (voretigene neparvovec). FDA Advisory Committee Briefing Document. Meeting of the Cellular, Tissue, and Gene Therapies Advisory Committee. Meeting date: October 12, 2017. Available at: https://www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/bloodvaccinesandotherbiologics/cellulartissueandgenetherapiesadvisorycommittee/ucm579300.pdf. Accessed on February 17, 2020.