POLICY: Ophthalmology – Luxturna™ (voretigene neparvovec-rzyl intraocular suspension for subretinal injection – Spark Therapeutics)

APPROVAL DATE: 02/20/2019

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 x 1011 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 fewer 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 x 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.

POLICY STATEMENT

This policy involves the use of Luxturna. Prior authorization is recommended for medical benefit coverage of Luxturna. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Dosing** for the diagnosis provided.

Because of the of the specialized skills required for evaluation and diagnosis of patients treated with Luxturna as well as the specialized training required for administration of Luxturna, approval requires Luxturna to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for one injection per eye. Note that a 1-month (30 days) approval duration is applied to allow for the one-time treatment of both eyes.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Luxturna is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Biallelic Human Retinal Pigment Epithelial 65 kDa Protein (RPE65) Mutation-Associated Retinal Dystrophy.** Approve for one-time treatment course (i.e., a total of two injections, one injection in each eye) if the patient meets the following criteria (A, B, C, and D):
   - **A)** According to the prescribing physician, the patient has a genetically-confirmed diagnosis of biallelic RPE65 mutation-associated retinal dystrophy; AND
   - **B)** Patient is ≥ 12 months of age; AND
   - **C)** Luxturna is administered by a retinal specialist; AND
   - **D)** Patient must have viable retinal cells as determined by the treating physician; AND
   - **E)** Patient is not receiving re-treatment of eye(s) previously treated with Luxturna.

   Dosing. Approve the following dosing regimen:
   - **A)** One 1.5 x 10^{11} vector genomes (vg) injection administered by subretinal injection into each eye; AND
   - **B)** The doses for the first eye and the second eye are separated by at least 6 days (i.e., injection of the second eye occurs 6 or more days after injection of the first eye).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Luxturna has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Re-treatment of previously treated eye(s)**. Luxturna is for one time use in each eye. Repeat dosing in previously treated eye(s) is not approvable.

2. Coverage is not recommended for circumstances *not* listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Luxturna™ subretinal injection [prescribing information]. Philadelphia, PA: Spark Therapeutics, Inc.; January 2018.
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: December 21, 2017. Available at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm589467.htm. Accessed on February 8, 2019.
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 8, 2019.

HISTORY

Type of Revision	Summary of Changes	Approval Date
New policy	New policy	02/07/2018
Selected revision	Removal of criteria regarding visual acuity and/or visual field, and removal of requirement for retinal thickness of ≥ 100 microns. Title of the policy changed to Ophthalmology – Luxturna.	02/28/2018
Annual revision	Criteria was revised to add "patient is not receiving re-treatment of eye(s) previously treated with Luxturna". "Re-treatment of previously treated eye(s)" was also added as a Condition Not Recommended for Approval. Previously, this was addressed in the Duration of Therapy section which is no longer included in the policy.	02/20/2019