Wellmark Advantage Health Plan

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Effective Date: 04/14/2022

Luxturna™ (voretigene neparvovec-rzyl)

HCPCS: J3398

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indication
   b. Prescribed and administered by an ophthalmologist
   c. Patient is 12 months of age or older
   d. Documented biallelic RPE65 gene mutation
   e. Retinal thickness greater than 100 microns within the posterior pole
   f. Submission of baseline full field light sensitivity prior to approval and full field light sensitivity one year after administration as a follow-up to the prior approval request

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limit: Align with FDA recommended dosing
   b. Initial Authorization Period: 1 month with the allowance of only one dose per lifetime
   c. Renewal Criteria: Not applicable as no further authorization will be provided

***Note: Coverage may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- The RPE65 gene is expressed in the retinal pigment epithelium layer and encodes the RPE65 protien. The RPE65 protein is involved in a multi-step process called the visual cycle, which converts light entering the eye into electrical signals that are transmitted to the brain. When light hits photosensitive pigments in the retina, it changes 11-cis retinal, a form of vitamin A, to all-trans retinal. This conversion triggers a series of chemical reactions that create electrical signals that are transmitted to the brain enabling sight. The RPE65 protein then helps convert all-trans retinal back to 11-cis retinal so the visual cycle can begin again. Mutations in the RPE65 gene result in dysfunctional proteins, visual cycle disruption, and visual impairment that progresses to blindness.

- Luxterna 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 defined as retinal thickness

greater than> 100 microns within the posterior pole and determined by the treating physician. 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 proliferation of retinal cells occurring in this age group.

- The biallelic mutation of RPE65 is diagnosed with a genetic test. Results of one pathogenic variant in the homozygous state, or the same mutation on both alleles, confirm biallelic RPE65-mediated inherited retinal dystrophy. Compound heterozygousy is when there are two different pathogenic variants. Genetic testing showing compound heterozygousy in the trans configuration, with each allele having one pathogenic variant, confirms biallelic RPE65-mediated inherited retinal dystrophy. Results from genetic tests showing two different pathogenic variants in the cis configuration, where one allele has both variants and the other allele has none, rule out RPE65-mediated inherited retinal dystrophy. If a compound heterozygous state is detected, documentation of a trans configuration will be needed to confirm diagnosis.

- Safety and efficacy were established in an open-label, randomized trial of 31 pediatric and adult patients with biallelic RPE65 mutation-associated retinal dystrophy. Eligible patients had to be at least 3 years of age, have visual acuity less than 20/60 and/or visual field less than 20° in any meridian, and be within the mobility-testing passing range at baseline to allow for measurable improvement. Patients were randomized in a 2:1 ratio to either the intervention group, which received bilateral, sequential subretinal administration of voretigene neparvovec, or the control group. The primary endpoint was change in bilateral mobility testing. Secondary endpoints which were tested statistically in hierarchical order included: a change in full-field light sensitivity threshold testing, change in mobility test score for the first eye injected, and visual acuity testing. Mobility testing and full-field light sensitivity threshold testing were observed one year after the Luxturna injection and found to be significantly improved compared to the control group. The change in visual acuity noted after the first year was not significantly different between the control and Luxturna groups.

References:

1. Luxturna [prescribing information]. Philadelphia, PA: Spark Therapeutics, Inc.; December 2017.
2. Bennett J, Wellman JA, Marshall KA, et al. Safety and durability of effect of contralateral-eye administration of AAV2 gene therapy in patients with childhood-onset blindness caused by RPE65 mutations: a follow-on phase 1 trial. Lancet. 2016 Aug 13; 388 (10045): 661 - 72.
3. 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 randomized, controlled, open-label, phase 3 trial. Lancet. 2017 Aug 26; 390 (10097): 849 – 60.
4. Medlineplus.gov. RPE65 gene. 2020 Aug 18. Available at: https://medlineplus.gov/genetics/gene/rpe65/#synonyms. Accessed on February 4, 2021.
5. Chung DC, Bertelsen M, Lorenz B, et al. The natural history of inherited retinal dystrophy due to biallelic mutations in the RPE65 gene. Am J Ophthalmol. 2019 Mar; 199: 58 – 70.
6. Chung DC, McCague S, Yu ZF, et al. Novel mobility test to assess functional vision in patients with inherited retinal dystrophies. Clin Exp Ophthalmol. 2018 Apr; 46 (3): 247 – 59.

Policy History		
#	Date	Change Description
1.1	Effective Date: 04/14/2022	Annual review of criteria was performed, no changes were made.
1.0	Effective Date: 01/01/2022	Effective as of date on policy.

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*