Luxturna™ (voretigene neparvovec-rzyl) – New orphan drug approval

- On December 19, 2017, the FDA approved Spark Therapeutics' Luxturna (voretigene neparvovec-rzyl), 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).
- Luxturna is the first directly administered gene therapy approved in the U.S. that targets a disease caused by mutations in a specific gene.
- Hereditary retinal dystrophies are a broad group of genetic retinal disorders that are associated with progressive visual dysfunction and are caused by mutations in any one of more than 220 different genes.
    - Biallelic RPE65 mutation-associated retinal dystrophy affects approximately 1,000 to 2,000 patients in the U.S.
- The RPE65 gene provides instructions for making an enzyme that is essential for normal vision. Mutations in the RPE65 gene lead to reduced or absent levels of RPE65 activity, blocking the visual cycle and resulting in impaired vision. Individuals with biallelic RPE65 mutation-associated retinal dystrophy experience progressive deterioration of vision over time. This loss of vision, often during childhood or adolescence, ultimately progresses to complete blindness.
- Luxturna works by delivering a normal copy of the RPE65 gene directly to retinal cells. These retinal cells then produce the normal protein that converts light to an electrical signal in the retina to restore patient's vision loss.
- The efficacy of Luxturna in patients with biallelic RPE65 mutation-associated retinal dystrophy was evaluated in an open-label, randomized trial of 31 subjects. The efficacy was established on the basis of multi-luminance mobility testing (MLMT) score change from baseline to year 1. An MLMT score change of ≥ 2 is considered a clinically meaningful benefit in functional vision.
    - The MLMT median (min, max) score change for bilateral eyes was significantly better for the Luxturna-treated patients [2 (0, 4)] vs. the control group [0 (-1, 2)]; p = 0.001.
    - The MLMT median (min, max) score change for the first-treated eye was significantly better for the Luxturna-treated patients [2 (0, 4)] vs. the control group [0 (-1, 1)]; p = 0.003.
- Warnings and precautions for Luxturna include endophthalmitis, permanent decline in visual acuity, retinal abnormalities, increased intraocular pressure, expansion of intraocular air bubbles, and cataract.
- The most common adverse reactions (≥ 5%) with Luxturna use were conjunctival hyperemia, cataract, increased intraocular pressure, retinal tear, dellen, macular hole, subretinal deposits, eye inflammation, eye irritation, eye pain, and maculopathy.
- The recommended dosage of Luxturna for each eye is 1.5×10^{11} vector genomes (vg), administered by subretinal injection in a total volume of 0.3 mL.
    - Luxturna should be administered in the surgical suite under controlled aseptic conditions by a surgeon experienced in performing intraocular surgery.

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- — Subretinal administration of Luxturna should be performed on each eye on separate days within a close interval, but no fewer than 6 days apart.
- — Use of systemic oral corticosteroids is recommended pre- and post-injection.

- Spark Therapeutics plans to launch Luxturna in the first quarter of 2018. Luxturna will be available as a single-dose vial containing a suspension of 5 x 10^{12} vg/mL, requiring a 1:10 dilution prior to administration.