WIKIPEDIA
The Free Encyclopedia

Voretigene neparvovec

Voretigene neparvovec, sold under the brand name **Luxturna**, is a gene therapy medication for the treatment of Leber congenital amaurosis.[4]

Leber's congenital amaurosis, or biallelic RPE65-mediated inherited retinal disease, is an inherited disorder causing progressive blindness. Voretigene is the first treatment available for this condition.[7] The gene therapy is not a cure for the condition, but substantially improves vision in those treated.[8] It is given as a subretinal injection.

Voretigene neparvovec was approved for medical use in the United States in December 2017,[9] Australia in August 2020[10] and in Canada, in October 2020.[11] It is the first *in vivo* gene therapy approved by the US Food and Drug Administration (FDA).[12]

Medical uses

Voretigene neparvovec is indicated for the treatment of people with vision loss due to inherited retinal dystrophy caused by confirmed biallelic RPE65 mutations and who have sufficient viable retinal cells.[6]

Chemistry and production

Voretigene neparvovec is an AAV2 vector containing human RPE65 cDNA with a modified Kozak sequence. The virus is grown in HEK 293 cells and purified for administration.[13]

Voretigene neparvovec

Gene therapy	
Target gene	RPE65
Vector	Adeno-associated virus serotype 2
Nucleic acid type	DNA
Clinical data	
Trade names	Luxturna
Other names	voretigene neparvovec-rzyl
AHFS/ Drugs.com	Professional Drug Facts (https://www.drugs.com/ppa/voretigene-neparvovec.html)
License data	US DailyMed: Voretigene neparvovec (https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=all&query=Voretigene+neparvovec)

History

It was developed by Spark Therapeutics and Children's Hospital of Philadelphia.[14][15][16]

It was granted orphan drug designation for Leber congenital amaurosis and retinitis pigmentosa.[17][18] A biologics license application was submitted to the US Food and Drug Administration (FDA) in July 2017 with Priority Review.[7] Phase III clinical trial results were published in August 2017.[19] On 12 October 2017, a key advisory panel to the FDA, composed of 16 experts, unanimously recommended approval of the treatment.[20] The FDA approved the drug in December 2017.[9][5] With the approval, Spark Therapeutics received a pediatric disease priority review voucher.[21]

The first commercial sale of voretigene neparvovec, which was also the first sale of any gene therapy product in the United States, occurred in March 2018.[22][12] The price of the treatment at the time was announced as being $425,000 per eye.[23]

References

1. "Luxturna Australian Prescription Medicine Decision Summary" (https://www.tga.gov.au/apm-summary/luxturna). *Therapeutic Goods Administration (TGA)*. 13 August 2020. Retrieved 16 August 2020.
2. "Luxturna Product information" (https://health-products.canada.ca/dpd-bdpp/info.do?lang=en&code=99512). *Health Canada*. 25 April 2012. Retrieved 21 October 2020.
3. "Summary Basis of Decision (SBD) for Luxturna" (https://hpr-rps.hres.ca/reg-content/summary-basis-decision-detailTwo.php?linkID=SBD00530&lang=en). *Health Canada*. 23 October 2014. Retrieved 29 May 2022.
4. "Luxturna- voretigene neparvovec-rzyl kit" (https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=08313a24-e7ce-457a-bb3f-161bc45517ee). *DailyMed*. 4 December 2019. Retrieved 14 August 2020.

Pregnancy category	AU: B2[1]
Routes of administration	Subretinal injection
ATC code	S01XA27 (WHO (https://www.whocc.no/atc_ddd_index/?code=S01XA27))
Legal status	
Legal status	AU: S4 (Prescription only)[1] CA: Rx-only / Schedule D[2][3] US: ℞-only[4][5] EU: Rx-only[6]
Identifiers	
CAS Number	1646819-03-5 (https://commonchemistry.cas.org/detail?cas_rn=1646819-03-5)
DrugBank	DB13932 (https://www.drugbank.ca/drugs/DB13932)
UNII	2SPI046IKD (https://precision.fda.gov/uniisearch/srs/unii/2SPI046IKD)
KEGG	D11008 (https://www.ke

5. "Luxturna" (https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/luxturna). *U.S. Food and Drug Administration (FDA)*. 19 December 2017. Retrieved 2 April 2020.
6. "Luxturna EPAR" (https://www.ema.europa.eu/en/medicines/human/EPAR/luxturna). *European Medicines Agency (EMA)*. 24 September 2018. Retrieved 21 October 2020.
7. "Press Release - Investors & Media - Spark Therapeutics" (http://ir.sparktx.com/phoenix.zhtml?c=253900&p=irol-newsArticle&ID=2286691). *Ir.sparktx.com*. Retrieved 9 October 2017.
8. McGinley L (19 December 2017). "FDA approves first gene therapy for an inherited disease" (https://www.washingtonpost.com/news/to-your-health/wp/2017/12/18/fda-approves-first-gene-therapy-for-an-inherited-disease-childhood-blindness/). *Washington Post*.
9. "FDA approves novel gene therapy to treat patients with a rare form of inherited vision loss" (https://www.fda.gov/news-events/press-announcements/fda-approves-novel-gene-therapy-treat-patients-rare-form-inherited-vision-loss). *U.S. Food and Drug Administration (FDA)*. 24 March 2020. Retrieved 28 November 2022.
10. "Luxturna" (https://www.tga.gov.au/apm-summary/luxturna). *Therapeutic Goods Administration (TGA)*. 13 August 2020. Retrieved 22 September 2020.
11. " 'I never saw stars before': Gene therapy brings back 8-year-old Canadian boy's sight" (https://www.ctvnews.ca/health/i-never-saw-stars-before-gene-therapy-brings-back-8-year-old-canadian-boy-s-sight-1.5145830). *CTVNews*. 14 October 2020. Retrieved 21 October 2020.
12. "First Gene Therapy For Inherited Disease Gets FDA Approval" (https://www.npr.org/sections/health-shots/2017/12/19/571962226/first-gene-therapy-for-inherited-disease-gets-fda-approval). *NPR*. 19 December 2017.

gg.jp/entry/D11008)

13. Russell S, Bennett J, Wellman JA, Chung DC, Yu ZF, Tillman A, et al. (August 2017). "Efficacy and safety of voretigene neparvovec (AAV2-hRPE65v2) in patients with RPE65-mediated inherited retinal dystrophy: a randomised, controlled, open-label, phase 3 trial" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5726391). *Lancet*. **390** (10097): 849–860. doi:10.1016/S0140-6736(17)31868-8 (https://doi.org/10.1016%2FS0140-6736%2817%2931868-8). PMC 5726391 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5726391). PMID 28712537 (https://pubmed.ncbi.nlm.nih.gov/28712537).
14. "Spark's gene therapy for blindness is racing to a historic date with the FDA" (https://www.statnews.com/2017/10/09/spark-gene-therapy/). *Statnews.com*. 9 October 2017. Retrieved 9 October 2017.
15. Clarke T. "Gene Therapy for Blindness Appears Initially Effective, Says U.S. FDA" (https://www.scientificamerican.com/article/gene-therapy-for-blindness-appears-initially-effective-says-u-s-fda/). *Scientific American*. Retrieved 12 October 2017.
16. "FDA approves Spark's gene therapy for rare blindness pioneered at CHOP" (http://www.philly.com/philly/business/fda-approves-sparks-gene-therapy-rare-blindness-chop-20171219.html). *Philly*. Retrieved 24 March 2018.
17. "Voretigene neparvovec - Spark Therapeutics - AdisInsight" (http://adisinsight.springer.com/drugs/800039212). *adisinsight.springer.com*.
18. Lewis R (13 October 2017). "FDA Panel Backs Gene Therapy for Inherited Blindness" (https://www.medscape.com/viewarticle/887022). *Medscape*.
19. Lee H, Lotery A (August 2017). "Gene therapy for RPE65-mediated inherited retinal dystrophy completes phase 3". *Lancet*. **390** (10097): 823–824. doi:10.1016/S0140-6736(17)31622-7 (https://doi.org/10.1016%2FS0140-6736%2817%2931622-7). PMID 28712536 (https://pubmed.ncbi.nlm.nih.gov/28712536). S2CID 26983863 (https://api.semanticscholar.org/CorpusID:26983863).
20. "Landmark Therapy to Treat Blindness Gets One Step Closer to FDA Approval" (https://www.bloomberg.com/news/articles/2017-10-12/spark-s-gene-therapy-to-treat-blindness-gets-closer-to-approval). *Bloomberg.com*. 12 October 2017. Retrieved 12 October 2017.
21. "Spark grabs FDA nod for Luxturna, a breakthrough gene therapy likely bearing a pioneering price" (https://www.fiercepharma.com/regulatory/spark-therapeutics-grabs-fda-ok-for-gene-therapy-luxturna-but-isn-t-disclosing-price). *FiercePharma*. 19 December 2017.
22. "The anxious launch of Luxturna, a gene therapy with a record sticker price" (https://www.statnews.com/2018/03/21/gene-therapy-luxturna-launch/). *STAT*. 21 March 2018. Retrieved 24 March 2018.
23. Tirrell M (3 January 2018). "A US drugmaker offers to cure rare blindness for $850,000" (https://www.cnbc.com/2018/01/03/spark-therapeutics-luxturna-gene-therapy-will-cost-about-850000.html). CNBC. Retrieved 3 January 2018.

Further reading

- Ledford H (October 2017). "FDA advisers back gene therapy for rare form of blindness" (https://doi.org/10.1038%2Fnature.2017.22819). *Nature*. **550** (7676): 314. Bibcode:2017Natur.550..314L (https://ui.adsabs.harvard.edu/abs/2017Natur.550..314L). doi:10.1038/nature.2017.22819 (https://doi.org/10.1038%2Fnature.2017.22819). PMID 29052639 (https://pubmed.ncbi.nlm.nih.gov/29052639).
- Wilson JM (March 2018). "Interview with Jean Bennett, MD, PhD". *Human Gene Therapy. Clinical Development*. **29** (1): 7–9. doi:10.1089/humc.2018.29032.int (https://doi.org/10.1089%2Fhumc.2018.29032.int). PMID 29641279 (https://pubmed.ncbi.nlm.nih.gov/29641279).
- Ameri H (March 2018). "Prospect of retinal gene therapy following commercialization of voretigene neparvovec-rzyl for retinal dystrophy mediated by RPE65 mutation" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5859497). *Journal of Current Ophthalmology*. **30** (1): 1–2. doi:10.1016/j.joco.2018.01.006 (https://doi.org/10.1016%2Fj.joco.2018.01.006). PMC 5859497 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5859497). PMID 29564403 (https://pubmed.ncbi.nlm.nih.gov/29564403).
- Russell S, Bennett J, Maguire AM, High KA (2018). "Voretigene neparvovec-rzyl for the treatment of biallelic RPE65 mutation–associated retinal dystrophy". *Expert Opinion on Orphan Drugs*. **6** (8): 457–464. doi:10.1080/21678707.2018.1508340 (https://doi.org/10.1080%2F21678707.2018.1508340). S2CID 81437112 (https://api.semanticscholar.org/CorpusID:81437112).
- Bakall B, Hariprasad SM, Klein KA (July 2018). "Emerging Gene Therapy Treatments for Inherited Retinal Diseases" (https://doi.org/10.3928%2F23258160-20180628-02). *Ophthalmic Surgery, Lasers & Imaging Retina*. **49** (7): 472–478. doi:10.3928/23258160-20180628-02 (https://doi.org/10.3928%2F23258160-20180628-02). PMID 30021033 (https://pubmed.ncbi.nlm.nih.gov/30021033).
- "Drug and Device News" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5768294). *P & T*. **43** (2): 74–104. February 2018. PMC 5768294 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5768294). PMID 29386862 (https://pubmed.ncbi.nlm.nih.gov/29386862).