Drug Coverage Decision for B.C. PharmaCare

About PharmaCare B.C. PharmaCare is a government-funded drug plan. It helps British Columbians with the cost of eligible prescription drugs and specific medical supplies.

Details of Drug Reviewed

Drug	**voretigene neparvovec**
Brand Name	Luxturna®
Dosage Form(s)	5 x 10^{12} vector genomes/mL concentrate for solution for subretinal injection
Manufacturer	Novartis Pharmaceuticals Canada Inc.
Submission Type	**New Submission**
Use Reviewed	For the treatment of adult and pediatric patients with vision loss due to inherited retinal dystrophy (IRD) caused by confirmed biallelic RPE65 mutations and who have sufficient viable retinal cells.
Canadian Agency for Drugs and Technologies in Health (CADTH) Reimbursement Reviews (CRR)	Yes, the CRR recommended: **to Reimburse with clinical criteria and/or conditions**. Visit the CRR website for more details: SG0643 Luxturna - CDEC Final Recommendation November 16, 2020_for posting.pdf (cadth.ca)
Drug Benefit Council (DBC)	The DBC met on January 4, 2021. In their review, the DBC considered the following: the final reviews completed by the CRR on November 12, 2020, which included clinical and pharmacoeconomic evidence review material and the recommendations from the Canadian Drug Expert Committee (CDEC). The DBC also considered Patient Input Questionnaire responses from 37 patients, 13 caregivers, and one patient group, as well as patient input provided to the CRR. The DBC also considered Clinical Practice Reviews from two specialists and a Budget Impact Assessment. The DBC recommended that voretigene neparvovec not be listed.
Drug Coverage Decision	**Non-Benefit; Exceptional Case-by-Case Coverage Through the Expensive Drugs for Rare Diseases (EDRD) Process**

Date	February 28, 2023
Reason(s)	**Drug coverage decision is consistent with the CRR recommendation and not consistent with the DBC recommendation.** • In one randomized open-label trial, voretigene neparvovec demonstrated a statistically significant improvement in functional vision under low light conditions as measured by multi-luminance mobility testing at one year post-treatment compared with best supportive care and a statistically significant improvement in full-field sensitivity threshold one year post-treatment. • There is an unmet need for a pharmaceutical and/or surgical treatments for vision loss due to IRD caused by confirmed biallelic RPE65 mutations. Voretigene neparvovec is the first treatment approved in Canada that targets the underlying mechanism of IRD. • The Ministry of Health participated in the pan-Canadian Pharmaceutical Alliance negotiations with the manufacturer and were able to address some concerns identified by the DBC with respect to the cost-effectiveness and value for money.
Other Information	See the DBC Recommendation & Reasons

The Drug Review Process in B.C.

A manufacturer submits a request to the Ministry of Health (Ministry).

An independent group called the Drug Benefit Council (DBC) gives advice to the Ministry. The DBC looks at:

- whether the drug is safe and effective
- advice from a national group called the Canadian Agency for Drugs and Technologies in Health (CADTH) Reimbursement Reviews(CRR)
- what the drug costs and whether it is a good value for the people of B.C.
- ethical considerations involved with covering or not covering the drug
- input from physicians, patients, caregivers, patient groups and drug submission sponsors

The Ministry makes PharmaCare coverage decisions by taking into account:

- the existing PharmaCare policies, programs and resources
- the evidence-informed advice of the DBC
- the drugs already covered by PharmaCare that are used to treat similar medical conditions
- the overall cost of covering the drug

Visit The Drug Review Process in B.C. - Overview and Ministry of Health - PharmaCare for more information.

This document is intended for information only.
It does not take the place of advice from a physician or other qualified health care provider.

Appendix
Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

FINAL

Voretigene neparvovec (Luxturna®)
Novartis Pharmaceuticals Canada Inc.

Description:

Drug review of **voretigene neparvovec (Luxturna®)** for the following Health Canada approved indications:

> For the treatment of adult and pediatric patients with vision loss due to inherited retinal dystrophy (IRD) caused by confirmed biallelic retinal pigment epithelium 65 kDA protein (RPE65) mutations and who have sufficient viable retinal cells.

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on November 12, 2020, which included clinical and pharmacoeconomic evidence review material and the recommendations from the Canadian Drug Expert Committee (CDEC). The DBC also considered Patient Input Questionnaire responses from 37 Patients, 13 Caregivers, and one Patient Group as well as patient input provided to the CDR. The DBC also considered Clinical Practice Reviews from two specialists and a Budget Impact Assessment.

Dosage Forms:

Luxturna®) is available as voretigene neparvovec 5 x 1012 vector genomes/mL concentrate for solution for subretinal injection.

Recommendations:

1. The Drug Benefit Council (DBC) recommends not to list voretigene neparvovec (Luxturna®).

Of Note:
- The Ministry is willing to support the possibility of case-by-case access to the drug through a company-funded post marketing trial.
- Funding should be considered on an exceptional, case-by-case basis only. Each case should be followed closely and should generate evidence to address the uncertainty in clinical benefit and improvement in quality of life. During this period, the cost of the drug and the required genetic testing should be borne by the sponsor.

Reasons for the Recommendation:

1. Summary

- In one randomized open-label trial, voretigene neparvovec demonstrated a statistically significant improvement in functional vision under low light conditions as measured by multi-luminance mobility testing (MLMT) at one year post-treatment compared with best supportive care (BSC) and a statistically significant improvement in full-field sensitivity threshold (FST) one year post-treatment.
- There is uncertainty regarding whether the observed magnitude of difference in MLMT score between voretigene neparvovec and the control group can be considered clinically meaningful, and there is significant uncertainty associated with the duration of the treatment effect.
- Some patients may experience serious adverse events (SAEs) associated with the administration procedure of voretigene neparvovec.
- There is substantial uncertainty regarding the cost-effectiveness of voretigene neparvovec, due largely to the uncertainty associated with its long-term efficacy.

2. Clinical Efficacy

- The DBC considered the CDR systematic review which included one randomized, open-label, phase III trial (Study 301) in 31 patients that evaluated the efficacy and safety of sequential subretinal injections of voretigene neparvovec to each eye in patients diagnosed with leber congenital amaurosis (LCA) due to RPE65 mutations.
- Voretigene neparvovec demonstrated a statistically significant improvement in functional vision under low light conditions as measured by MLMT at one year post-treatment compared with best supportive care. This improvement in functional vision would likely be considered meaningful to patients.
- Treatment also resulted in a statistically significant improvement in full-field sensitivity threshold (FST) one year post-treatment.
- There is uncertainty regarding whether the observed magnitude of difference in MLMT score between voretigene neparvovec and the control group in Study 301 can be considered clinically meaningful.
- There is uncertainty associated with the duration of the treatment effect. Improvements observed after one year appeared to be maintained up to four years; however, these data were limited by the open-label trial design, the lack of a comparator and statistical analysis one year after randomization.
- For detailed information on the systematic review of voretigene neparvovec please see the CDEC Final Recommendation at: https://www.cadth.ca/voretigene-neparvovec.

3. Safety

All patients in Study 301 experienced at least one treatment-emergent adverse event (TEAE). Most adverse events were mild in severity and no patient had adverse events that led to study discontinuation or death. Overall, 13 (65%) patients in the voretigene

- neparvovec group had at least one TEAE considered to be related to the study drug administration procedure.
- During the control period, two (10%) patients in the voretigene neparvovec group experienced three SAEs at time points distant from vector administration. Additionally, one ocular SAE occurred in Study 301, where a patient who received voretigene neparvovec experienced retinal disorder which was foveal thinning and loss of central vision and was related to the subretinal injection in this patient with pre-existing atrophy of the retina.
- For detailed information on the safety and tolerability of voretigene neparvovec, please see the CDEC Final Recommendations at the links above.

1. Economic Considerations

- The DBC considered the CADTH reanalysis of the manufacturer-submitted economic model, which reported that treatment with voretigene neparvovec is associated with an incremental cost-effectiveness ratio (ICER) of $200,477 per quality-adjusted life-year (QALY) gained compared with best supportive care (BSC).
- However, this estimate is associated with significant uncertainty as the majority of the modelled benefits were accrued in time periods beyond when clinical data are available.
- Based on the CADTH reanalysis, a price reduction of more than 74% would be required to achieve ICERs below $50,000 per QALY.

2. Of Note

- The DBC considered Patient Input Questionnaire responses from 37 Patients, 13 Caregivers, and one Patient Group, as well as patient input provided to the CDR.
- IRD caused by biallelic RPE65 mutations eventually leads to complete blindness. Patients with IRD experience progressive, profound reduction of visual acuity, concentric reduction of visual fields, night blindness and nystagmus.
- IRD typically manifests in children and young people, with more than half of the patients having severe visual impairment before adulthood. IRD has a profound impact on the health related quality of life of patients and their families as well as on the patients' ability to perform activities of daily living.
- There is an unmet need for a pharmaceutical and/or surgical treatment of vision loss due to IRD caused by confirmed biallelic RPE65 mutations. Voretigene neparvovec is the first treatment approved in Canada that targets the underlying mechanism of IRD.
- According to patients, a meaningful treatment for IRD would enable them to recover some overall sight, cure their condition, or improve night vision and mobility at night.
- Genetic testing required to confirm the presence of biallelic RPE65 mutations may not be available in all jurisdictions.