Drug Coverage Decision for BC PharmaCare

About PharmaCare BC PharmaCare is a publicly funded drug plan that helps B.C. residents pay for most prescription drugs and pharmacy services, and some medical devices and supplies.

Details of Drug Reviewed

Drug	**lumasiran**
Brand name	Oxlumo®
Dosage form(s)	94.5 mg/0.5 mL solution for subcutaneous injection
Manufacturer	Alnylam Netherlands B.V.
Submission type	**New Submission**
Indication reviewed	For the treatment of primary hyperoxaluria type 1 to lower urinary oxalate levels in pediatric and adult patients
Canada's Drug Agency (CDA) recommendation	CDA recommended: **to Reimburse with clinical criteria and/or conditions**. Visit the CRR website for more details.
Drug Benefit Council (DBC)	The DBC met on May 1, 2023. The DBC considered various input, including clinical and pharmacoeconomic evidence review material and the recommendations of the Canadian Drug Expert Committee (CDEC). The DBC also considered patient input provided to CDEC and a budget impact assessment. The DBC received no Your Voice patient input questionnaire responses from patients, caregivers, or patient groups. The DBC recommended not to reimburse lumasiran for PH1.
Drug Coverage Decision	**Case-by-Case Coverage Through the Expensive Drugs for Rare Diseases (EDRD) Process**
Date	July 16, 2024
Reason(s)	**Drug coverage decision is consistent with the CDEC recommendation.** • Results from one multicentre, double-blind, phase III, randomized controlled trial demonstrated that, compared to placebo, six months of lumasiran treatment was associated with a statistically significant reduction in urinary and plasma oxalate levels.

	• There is an unmet need for effective pharmacological treatments for patients with PH1 that prevent further kidney damage, decrease oxalate accumulation throughout the body, and prevent the need for dialysis or organ transplant. • Based on economic considerations and the submitted product price, the drug was not cost effective and did not offer optimal value for money. • B.C. participated in the pan-Canadian Pharmaceutical Alliance (pCPA) negotiations with the manufacturer and the pCPA was able to address some of the concerns identified by the CDA with respect to cost-effectiveness. The negotiations concluded with an agreement on April 26, 2024.

The drug review process in B.C.

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

An independent group called the Drug Benefit Council (DBC) gives advice to the Ministry by considering:

- whether the drug is safe and effective
- advice from a national group called Canada's Drug Agency (CDA)
- what the drug costs and whether funding it provides good value to the province
- ethical considerations of covering and not covering the drug
- input from physicians, patients, caregivers, patient groups and drug submission sponsors

The Ministry makes a BC PharmaCare coverage decision by taking into account:

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

Visit BC PharmaCare and Drug reviews 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

CONFIDENTIAL

Drug Benefit Council (DBC)
Recommendation and Reasons for Recommendation

FINAL

Lumasiran (Oxlumo®)
Alnylam Pharmaceuticals Canada ULC

Description:

Drug review of **lumasiran (Oxlumo®)** for the following Health Canada approved indications:

> For the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary oxalate levels in pediatric and adult patients.

In their review, the DBC considered the following: the final reviews completed by the Canadian Agency for Drugs and Technologies in Health (CADTH) on February 8, 2023, which included clinical and pharmacoeconomic evidence review material and the CADTH recommendations. The DBC received no Patient Input Questionnaire responses from patients, caregivers, or patient groups, and instead considered patient input provided to the CDR, as well as a Budget Impact Assessment.

Dosage Forms:

Oxlumo® is available as lumasiran single use vial (94.5 mg/0.5 mL as a single use vial) for subcutaneous injection.

Recommendations:

1. The Drug Benefit Council (DBC) recommends not to list lumasiran (Oxlumo®).

Reasons for the Recommendation:

1. Summary

- Results from one multicentre, double-blind (DB), phase III, randomized controlled trial (RCT) demonstrated that, compared to placebo, 6 months of lumasiran treatment was associated with a statistically significant reduction in 24-hour urinary oxalate levels, and was associated with a statistically significant reduction in percent and absolute changes in plasma oxalate levels compared to the average in months 3 to 6.
- There is a lack of evidence to indicate lumasiran improves long-term morbidity and mortality in patients with PH1, nor is there evidence it prevents kidney stones or end-stage kidney disease (ESKD), improves health-related quality of life (HRQoL), or

delays the need for organ transplant, outcomes that were identified as important by patients and clinicians.
- At the manufacturer's submitted price, lumasiran is not considered cost-effective.

2. Clinical Efficacy
- The DBC considered the CADTH systematic review, which included three ongoing phase III trials (ILLUMINATE-A, ILLUMINATE -B, and ILLUMINATE-C) investigating the efficacy and safety of lumasiran in patients with PH1.
- ILLUMINATE-A (N = 39) is a placebo-controlled, DB, RCT that includes patients who were 6 years and older. The primary end point is percent change in 24-hour urinary oxalate excretion from baseline to month 6 corrected for body surface area (BSA). Secondary end points are absolute change in urinary oxalate at month 6, percent change in urinary oxalate:creatinine ratio at month 6, percent and absolute changes in plasma oxalate levels at month 6, proportion of patients with urinary oxalate level near normal (at or below 1.5 times the upper limit of normal [ULN]) and normal (at or below the ULN) at month 6, and change in estimated glomerular filtration rate (eGFR) at month 6.
- ILLUMINATE-B (N = 18) is a single-arm trial that includes patients who were younger than 6 years. The primary end point is percent change in urinary oxalate excretion from baseline to month 6. Secondary end points are proportion of patients with urinary oxalate near normal and normal, plasma oxalate levels, and eGFR levels.
- ILLUMINATE-C (N = 21) is a single-arm trial that includes patients who had an eGFR of 45 mL/min/1.73 m2 or lower and were either not receiving hemodialysis (cohort A) or had begun stable hemodialysis (cohort B). The primary end point is percent change in plasma oxalate levels from baseline to month 6 (predialysis for cohort B). The secondary end points are plasma oxalate level area under the curve between dialysis sessions (cohort B), urinary oxalate excretion, urinary oxalate:creatinine ratio, pediatric quality of life (PedsQL) and kidney disease quality of life questionnaire (KDQOL) scores, and eGFR.
- In ILLUMINATE-A, 6 months of lumasiran was associated with a statistically significant reduction in 24-hour urinary oxalate levels, where the between-group difference from baseline to the average of months 3 to 6 was –53.55 mmol/24 hour/1.73 m2 (95% confidence interval [CI], –62.31 to–44.78 mmol/24 hour/1.73 m2). Compared to placebo, lumasiran was also associated with a statistically significant reduction in percent and absolute changes in plasma oxalate levels compared to the average in months 3 to 6.
- In ILLUMINATE-A, 84% of patients in the lumasiran group also had a 24-hour urine oxalate measure at month 6 that was at or less than 1.5 times the ULN compared to no patients in the placebo group.
- Results from ILLUMINATE-B and ILLUMINATE-C were generally consistent with those observed in ILLUMINATE-A for the outcomes of change from baseline in the 24-hour urine oxalate and plasma oxalate measures.
- The trial outcomes are surrogate measures and there is a need for long-term efficacy and safety data to confirm the findings in the ILLUMINATE trials and to better

understand how the primary and secondary outcomes translate to improved long-term outcomes of maintained lowering of hepatic oxalate production, prevention of kidney stones, and prevention of progression to ESKD.
- The small number of patients in each treatment group (as expected given the rarity of PH1) makes it challenging to interpret the efficacy results, and the short duration of the trials for a treatment expected to be lifelong or until liver transplant occurs makes it difficult to be certain if the efficacy and safety results will persist long-term.
- For detailed information on the systematic review of lumasiran please see the CADTH Final Recommendation at: https://www.cadth.ca/lumasiran.

3. Safety
- The ILLUMINATE TRIALS reported few serious adverse events (SAEs) or withdrawals due to adverse events (WDAEs), and no deaths were reported. Of notable harms, 40% of patients reported injection site reaction and three (15%) patients experienced kidney and urinary disorders, such as nephrolithiasis, renal colic, and ureterolithiasis. Complications caused by systemic oxalosis and hypersensitivity were not reported during the study period.
- Lumasiran treatment for up to 30 months in an extension trial (ALN-GO1-002) showed a similar harms profile as the ILLUMINATE trials with no new safety signals identified. Due to the short duration of the trials thus far, further research showing adequate efficacy and safety is needed to inform broader treatment with lumasiran.
- For detailed information on the safety and tolerability of lumasiran, please see the CADTH Final Recommendations at the links above.

4. Economic Considerations
- At the manufacturer's submitted price, the incremental cost-effectiveness ratio for lumasiran was $2,165,926 per quality-adjusted life-year (QALY) gained compared with established clinical management. At this incremental cost-effectiveness ratio, lumasiran is not considered cost-effective; a price reduction would be required for lumasiran to be considered cost-effective at a $50,000 per QALY willingness-to-pay threshold for patients with PH1.

5. Of Note
- There are no approved pharmacological treatments for PH1. Other treatments for management of PH1 include dietary or over-the-counter measures that may not be covered by drug plans.
- Liver or combined liver-kidney transplant is the only cure for patients with PH1, but transplantation is associated with high morbidity and mortality and lifelong immunosuppression.
- Patient group input received by CADTH indicated that current treatments are insufficient and that therapies are required that decrease the likelihood of kidney stones, need for kidney and/or liver transplant, need for dialysis, kidney failure, oxalosis, and that reduce the requirement for other medications.