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	**selumetinib**
Brand name	Koselugo™
Dosage form(s)	10mg and 25mg oral capsules
Manufacturer	Alexion Pharma Canada Corp.
Submission type	**New Submission**
Indication reviewed	For the treatment of pediatric patients aged two years and above, with neurofibromatosis type 1 (NF1) who have symptomatic, inoperable plexiform neurofibromas (PNs).
Canada's Drug Agency (CDA-AMC) Reimbursement Reviews	CDA-AMC recommended: **to Reimburse with clinical criteria and/or conditions**. Visit the CDA-AMC website for more details.
Drug Benefit Council (DBC)	The DBC met on June 5, 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 to reimburse selumetinib for pediatric patients aged two years and above with NF1 who have symptomatic, inoperable PNs.
Drug Coverage Decision	**Limited Coverage Benefit** Access the selumetinib criteria from: https://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/programs/special-authority

Date	February 12, 2025
Reason(s)	**Drug coverage decision is consistent with the CDEC recommendation.** • Results from one phase II, single-arm study with 50 pediatric patients with NF1 with inoperable PNs reported that after a median treatment duration of 4.3 years, 68.0 percent of patients achieved a reduction from baseline in PN volumes of 20 percent or more. • Treatment with selumetinib may also improve patient-reported symptoms of pain, motor function, and health-related quality of life. • There is a significant unmet need for effective pharmacological treatments for patients with NF1-associated symptomatic, inoperable PNs, as there are no effective treatments currently available. • Based on economic considerations and the submitted product price, the cost-effectiveness of selumetinib is highly uncertain. • 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-AMC with respect to cost-effectiveness. The negotiations concluded with an agreement on November 19, 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 – L'agence des médicaments du Canada (CDA-AMC)
- 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

Selumetinib (Koselugo™)
AstraZeneca Canada Inc.

Description:

Drug review of **selumetinib (Koselugo™)** for the following Health Canada approved indications:

> For the treatment of pediatric patients aged 2 years and above with neurofibramatosis type 1 who have symptomatic, inoperable plexiform neurofibromas.

In their review, the DBC considered the following: the final reviews completed by the Canadian Agency for Drugs and Technologies in Health (CADTH) on May 10, 2023, which included clinical and pharmacoeconomic evidence review material and the CADTH recommendations. The DBC also considered Patient Input Questionnaire responses from five patients, six caregivers and one patient group, as well as patient input provided to CADTH, a Clinical Practice Review from one specialist, and a Budget Impact Assessment.

Dosage Forms:

Koselugo™ is available as selumetinib 10mg and 25mg oral capsules.

Recommendations:

1. The Drug Benefit Council (DBC) recommends listing selumetinib (Koselugo™) as a Limited Coverage benefit for patients aged 2 years and above with neurofibramatosis type 1 who have symptomatic, inoperable plexiform neurofibromas.

Of Note:

- The reimbursement criteria and conditions recommended by CADTH are an appropriate basis for coverage.
- The Ministry should seek to obtain a price reduction.

Reasons for the Recommendation:

1. **Summary**

- Evidence from a phase II, single-arm study that included 50 pediatric patients with neurofibramatosis type 1 (NF1) with inoperable plexiform neurofibromas (PNs) reported that after a median treatment duration of 4.3 years, 68.0% of patients achieved an objective response rate (ORR) that was determined by a reduction from baseline in plexiform neurofibroma (PN) volumes of 20% or more.
- Treatment with selumetinib may also improve patient-reported symptoms of pain, motor function, and health-related quality of life (HRQoL).
- The nonrandomized design of SPRINT phase II made interpreting the results and overall magnitude of treatment effect attributable to selumetinib challenging, and there is also uncertainty regarding the long-term efficacy and safety of selumetinib.
- There is significant unmet need for patients with NF1-associated symptomatic, inoperable PNs for which no other effective treatments are currently available.
- The cost-effectiveness of selumetinib is highly uncertain. CADTH reanalyses estimated that an 89% or higher reduction in price would be required for selumetinib to achieve an incremental cost-effectiveness ratio (ICER) of $50,000 per quality-adjusted life-year (QALY).

2. **Clinical Efficacy**

- The DBC considered the CADTH systematic review, which included one study (SPRINT phase II), a phase II, open-label, single-arm, multicenter study that aimed to evaluate the efficacy of 25 mg/m2 selumetinib twice daily in 50 pediatric patients with NF1 and inoperable PNs.
- The primary outcome of SPRINT phase II was ORR determined by change in PN volumes through volumetric MRI. Secondary outcomes included patient-reported outcomes and functional evaluations to determine the effect of selumetinib on pain, motor function, and HRQoL.
- After a median treatment duration of 4.3 years, 68.0% of patients achieved an objective response rate (ORR) that was determined by a reduction from baseline in PN volumes of 20% or more.
- Treatment with selumetinib resulted in an improvement in patient-reported pain (measured by the Numerical Rating Scale 11, NRS-11), Pain Interference Index (PII), motor function, upper extremity, as well as improvements in strength and range of motion. However, the magnitude of clinical benefit is uncertain due to the lack of minimal important difference (MID) or the change did not exceed the estimated clinically meaningful threshold of 2 points for the NRS-11 or 0.75 points or more for the patient-reported PII.
- The nonrandomized design of SPRINT phase II made interpreting the results and overall magnitude of treatment effect attributable to selumetinib challenging, mainly because of the open-label design and the absence of a comparator influences patient selection, patient-reported outcomes, and reporting of harms.

- For detailed information on the systematic review of selumetinib please see the CDEC Final Recommendation at: https://www.cadth.ca/selumetinib.

3. Safety

- Nearly all patients in SPRINT phase II experienced a treatment-emergent adverse event (TEAE) (98.0%). The most frequent TEAEs reported at the March 31, 2021, data cut-off (DCO) were vomiting, increased blood creatine phosphokinase, diarrhea, nausea, and dry skin. A significant number of patients discontinued treatment with selumetinib due to adverse events (AEs) in SPRINT phase II.
- There is uncertainty regarding the long-term efficacy and safety of selumetinib. In SPRINT Phase II, despite the longer follow-up at the second DCO (5.6 years), the duration of the treatment effect and safety remain unknown.
- For detailed information on the safety and tolerability of selumetinib, please see the CDEC Final Recommendations at the links above.

4. Economic Considerations

- At the manufacturer's submitted price, treatment with selumetinib is expected to cost approximately $268,678 per patient per year.
- The most likely estimated incremental cost-effectiveness ratio (ICER) is $426,286 per quality-adjusted life-year based on the CADTH reanalysis that assumed a smaller residual benefit. In all reanalyses, a price reduction would be required for selumetinib to achieve an ICER of $50,000 per quality-adjusted life-year.

5. Of Note

- NF1 is the most common form of NF. In NF1, tumours develop along nerves throughout the body, which can affect the development of non-nervous tissues such as bones and skin. NF1 can cause additional complications such as disfigurement, bone deformities, learning disabilities, and cancer. As NF1 can cause disfigurement, the social and emotional effects on patients with NF1 are significant.
- Existing treatments for PNs associated with NF1 include surgery and chemotherapy. Some patients reported enduring up to 70 weeks of chemotherapy. Most patients reported using other medications (e.g., gabapentin) to treat pain associated with NF1.
- Prior to the approval of selumetinib, there were no drug treatments available for patients with PNs that cannot be removed by surgery.
- Large or extensive PNs cannot be completely excised surgically. Surgery is associated with many complications (e.g., bleeding risk, proximity to vital structures, secondary injury), and due to the extensive and progressive nature of the disease, multiple surgeries may be required.
- None of the patients who completed the questionnaire reported trying the drug under review, and none of the caregivers reported that the person under their care had tried the drug under review.