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	**ruxolitinib**
Brand Name	Jakavi®
Dosage Form(s)	5 mg and 10 mg tablets
Manufacturer	Novartis Pharmaceuticals Canada Inc.
Submission Type	**New Submission**
Use Reviewed	For the treatment of chronic graft-versus-host disease (cGvHD) in patients aged 12 years and older.
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: Ruxolitinib (Jakavi) (cadth.ca)
Drug Benefit Council (DBC)	The DBC met on November 7, 2022. The DBC considered various inputs including: final review completed by the CADTH CRR which included clinical and pharmacoeconomic evidence review material and the recommendation from the Canadian Drug Expert Committtee (CDEC). The DBC also considered Patient Input Questionnaire responses from four patients and two patient groups, as well as patient input provided to the CADTH and a Budget Impact Assessment.

Drug Coverage Decision	**Limited Coverage Benefit** **Access the ruxolitinib criteria from www.gov.bc.ca/pharmacarespecialauthority**
Date	**November 23, 2023**
Reason(s)	**Drug coverage decision is consistent with the CDEC and DBC recommendation** • One phase III, randomized, open-label trial demonstrated that compared with best available therapy (BAT) ruxolitinib was associated with statistically significant improvements in overall response rate (ORR) at Cycle 7 Day 1, failure-free survival (FFS), and the Modified Lee Symptom Scale with a higher rate of responders in the ruxolitinib group up to Cycle 7 Day 1. • Ruxolitinib met some important needs identified by patients by reducing disease symptoms of cGvHD and providing an oral drug option with tolerable side effects that can be administered as an outpatient treatment. • At the submitted price ruxolitinib was not considered cost-effective for this indication. The Ministry participated in the pan-Canadian Pharmaceutical Alliance (pCPA) negotiations with the manufacturer which were able to address the concerns identified by the CDEC with respect to the cost-effectiveness and value for money.
Other Information	In addition to the cGvHD indication, ruxolitinib was reviewed for acute graft-versus-host disease (aGvHD) and as of November 23, 2023, ruxolitinib (Jakavi®) is covered as Limited Coverage benefit for both indications.

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

CONFIDENTIAL

Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

FINAL

Ruxolitinib (Jakavi®)
Novartis Pharmaceuticals Canada Inc.

Description:

Drug review of **ruxolitinib (Jakavi®)** for the following Health Canada approved indications:

> For the treatment of chronic graft-versus-host disease (cGvHD) in patients aged 12 years and older who have inadequate response to corticosteroids or other systemic therapies.

In their review, the DBC considered the following: the final reviews completed by the Canadian Agency for Drugs and Technologies in Health (CADTH) on July 15, 2022, which included clinical and pharmacoeconomic evidence review material and the CADTH recommendations. The DBC also considered Patient Input Questionnaire responses from four patients and two patient groups, as well as patient input provided to the CADTH and a Budget Impact Assessment.

Dosage Forms:

Jakavi® is available as ruxolitinib 5 mg, 10 mg, 15 mg, and 20 mg tablets.

Recommendations:

1. The Drug Benefit Council (DBC) recommends not to list ruxolitinib (Jakavi®) at the submitted price for cGvHD.

Of Note:

- If the Ministry is able to negotiate a significant price reduction, the reimbursement criteria and conditions recommended by CADTH are an appropriate basis for coverage.

Reasons for the Recommendation:

1. **Summary**

- One phase III, randomized, open-label trial demonstrated that compared with best available therapy (BAT) ruxolitinib was associated with statistically significant improvements in overall response rate (ORR) at Cycle 7 Day 1, failure-free survival (FFS), and the Modified Lee Symptom Scale with a higher rate of responders in the ruxolitinib group up to Cycle 7 Day 1.
- cGvHD is a rare condition associated with substantial morbidity and there is an unmet need for additional treatment options in this setting. There is currently no standard of care for patients with cGvHD who have an inadequate response to corticosteroids or other systemic treatments.
- Ruxolitinib is not cost-effective at a $50,000 per quality adjusted life year (QALY) willingness to pay (WTP) threshold, and price reduction of at least 65% would be required for ruxolitinib to achieve an incremental cost-efficiency ratio (ICER) of $50,000 per QALY compared with best available treatment (BAT).

2. **Clinical Efficacy**

- The DBC considered the CADTH clinical review, which included one ongoing, international, multicentre, open-label, randomized phase III trial of ruxolitinib (10 mg, oral twice daily) compared with Investigator's choice of BAT in patients aged 12 years and older with moderate or severe SR-cGvHD (the REACH 3 trail).
- The primary outcome was ORR on Cycle 7 Day 1 and key secondary outcomes included FFS and the modified Lee Symptom Scale. Additional secondary outcomes were ORR at Cycle 4 Day 1, health-related quality of life (HRQoL), symptom severity, duration of response (DoR), best overall response (BOR), OS, non-relapse mortality (NRM), incidence of malignancy relapse or progression (MR), steroid dosing, resource utilization, and safety.
- Compared with BAT ruxolitinib was associated with statistically significant improvements in ORR at Cycle 7 Day 1, FFS, and the Modified Lee Symptom Scale with a higher rate of responders in the ruxolitinib group up to Cycle 7 Day 1.
- No definitive conclusion could be reached regarding the effects of ruxolitinib on HRQoL due to a significant decline in the number of patients available to provide assessments over time and the open-label design of the trial.
- Insufficient follow-up of survival outcomes in REACH 3 led to uncertainty regarding long-term survival benefits of ruxolitinib.
- For detailed information on the systematic review of ruxolitinib for cGvHD please see the CDEC Final Recommendation at: https://www.cadth.ca/ruxolitinib-0.

3. **Safety**

- CADTH noted there were challenges with reporting adverse events (AEs) in clinical trials given the underlying complexity of cGvHD and similarity between cGvHD symptoms and AEs resulting from study treatments in the target setting.

- Clinical experts consulted by CADTH reported that no unexpected safety concerns were observed with ruxolitinib, and that most treatment-emergent adverse events (TEAEs) associated with ruxolitinib could be managed with dose modifications and best supportive care.
- For detailed information on the safety and tolerability of ruxolitinib, please see the CDEC Final Recommendations at the links above.

4. Economic Considerations

- The CADTH reanalysis of the manufacturer's economic submission reported that a base case cost-effectiveness estimate was unable to be determined for the treatment of patients aged 12 years and older with steroid-refractory chronic graft-versus-host disease who have inadequate response to corticosteroids or other systemic therapies.
- Exploratory analyses conducted by CADTH determined that the ICER was likely closer to $1,062,977 per QALY, therefore ruxolitinib is not cost-effective at a $50,000 per QALY WTP threshold.
- CADTH reported that a price reduction of at least 65% would be required for ruxolitinib to achieve an ICER of $50,000 per QALY compared with BAT.

5. Of Note

- Patient input indicated there is a need for effective therapies with tolerable side effects that can improve health related quality of life, reduce disease symptoms, and extend survival are needed. Patients reported that other treatments for cGvHD such as prednisone had intolerable symptoms or, in the case of phototherapy, were ineffective or difficult to access.
- Three of the four patients who completed the patient input questionnaire reported trying ruxolitinib. Patients reported significant improvements to their condition with fewer side effects than with other treatments.
- Ruxolitinib met some important needs identified by patients by reducing disease symptoms of cGvHD and providing an oral drug option with tolerable side effects that can be administered as an outpatient treatment.