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	**upadacitinib**
Brand name	Rinvoq®
Dosage forms	15 mg, 30 mg, 45 mg extended-release tablets
Manufacturer	AbbVie Corporation
Submission type	**New Submission**
Indication reviewed	For the treatment of adult patients with moderately to severely active Crohn's disease (CD).
Canada's Drug Agency (CDA-AMC) recommendation Clinical Reimbursement Reviews (CRR)	CADTH recommended: **to Reimburse with clinical criteria and/or conditions**. Visit the CRR website for more details.
Drug Benefit Council (DBC)	The DBC met on February 5, 2024. The DBC considered various input, including the final reviews completed by the CRR, recommendations from the Canadian Drug Expert Committee (CDEC), Patient Input Questionnaire responses from two patient groups, as well as patient input provided to CDA-AMC, Clinical Practice Reviews from one specialist, and a Budget Impact Assessment.
Drug Coverage Decision	**Limited Coverage benefit**.
Date	September 17, 2024.
Reasons	Drug coverage decision is consistent with the DBC recommendation not to list upadacitinib (Rinvoq) at the submitted price for moderately to severely active CD.

	• Based on three clinical trials in patients with moderately to severely active CD who had inadequate response or were intolerant to prior conventional or biologic therapies, patients treated with Rinvoq showed an improved clinical remission and endoscopic response compared with patients who were treated with placebo. • Based on CRR's assessment of the health economic evidence, Rinvoq does not represent good value to the health care system at the public list price. • The Ministry of Health participated in the pan-Canadian Pharmaceutical Alliance (pCPA) negotiations with the manufacturer which were able to address the concerns identified by the CRR with respect to the cost-effectiveness and value for money.

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 and Health Technology Agency (CADTH)
- 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

Drug Benefit Council (DBC)
Recommendation and Reasons for Recommendation

FINAL

Upadacitinib (Rinvoq®)
AbbVie Corporation

Description:

Drug review of **upadacitinib (Rinvoq®)** for the following Health Canada approved indications:

> For the treatment of adult patients with moderately to severely active Crohn's disease (CD) who have demonstrated prior treatment failure, i.e., an inadequate response to, loss of response to, or intolerance to at least one of conventional and/or biologic therapy.

In their review, the DBC considered the following: the final reviews completed by the Canadian Agency for Drugs and Technologies in Health (CADTH) on January 9, 2024, which included clinical and pharmacoeconomic evidence review material and the CADTH recommendations. The DBC also considered Patient Input Questionnaire responses from two patient groups, as well as patient input provided to CADTH, Clinical Practice Reviews from one specialist, and a Budget Impact Assessment [and anything else].

Dosage Forms:

Rinvoq® is available as upadacitinib 15 mg, 30 mg, and 45 mg extended-release tablets.

Recommendations:

1. The Drug Benefit Council (DBC) recommends not to list upadacitinib (Rinvoq®) at the submitted price for moderately to severely active Crohn's disease (CD).

Of Note:

- If negotiations are engaged, the total drug cost of upadacitinib should not exceed the total drug cost of the lowest-cost biologic treatment reimbursed for moderately to severely active CD.
- If listed, the reimbursement conditions and criteria recommended by CADTH should be considered for adoption. Patients should have a treatment failure or intolerance to at least one other biologic before being considered for coverage.

Reasons for the Recommendation:

1. Summary

- Evidence from 3 phase III, double-blind, randomized, placebo-controlled trials showed that, compared with placebo, treatment with upadacitinib resulted in clinically meaningful improvements in clinical remission and endoscopic response after 12-week induction and 52-week maintenance in adult patients with moderately to severely active CD who have demonstrated an inadequate response to, loss of response to, or intolerance to at least 1 conventional and/or biologic therapy.
- There is insufficient evidence to suggest that upadacitinib is more effective than other biologic treatments for moderately to severely active CD, as all studies were placebo-controlled and lack active comparators.
- At the submitted price, upadacitinib is more costly than several relevant comparator treatments used in moderately to severely active CD.

2. Clinical Efficacy

- The DBC considered the CADTH review, which included three phase III, double-blind, placebo-controlled, multicentre, international randomized controlled trials (RCTs).
- Two RCTs were induction studies in adult patients with moderately to severely active CD and a history of biologic failure (U-EXCEED) or history of biologic and/or conventional therapy failure (U-EXCEL). Patients in both induction studies were randomized in a 2:1 ratio to receive upadacitinib 45 mg once daily or placebo.
- The third RCT (U-ENDURE) was a maintenance study of upadacitinib 15 mg or 30 mg once daily versus placebo in patients who had achieved adequate response in either the U-EXCEED or U-EXCEL trial, and the primary results were evaluated at 52 weeks among re-randomized patients from part 1 of the induction studies.
- The coprimary outcomes in all trials included clinical remission (based on patient-reported outcomes [PROs] or the Crohn Disease Activity Index [CDAI]), and endoscopic response (based on the Simple Endoscopic Score for Crohn Disease [SESCD]).
- Other important outcomes included endoscopic remission, proportion of patients who discontinued corticosteroid use for CD and achieved clinical remission (among patients taking corticosteroids at induction baseline), proportion of patients who achieved both clinical remission and endoscopic remission, change in health-related quality of life (HRQoL) using the Inflammatory Bowel Disease Questionnaire (IBDQ), clinical response (CR-100), resolution of extraintestinal manifestation (EIMs) in patients who had EIMs at induction baseline, the proportion who experienced CD-related hospitalizations or surgeries, and the proportion who experienced harms including serious adverse events (SAEs) or adverse events of special interest (AESIs).
- In induction trials, the difference compared to placebo in patients who achieved clinical remission based on patient-reported outcomes (PROs) was 25.9% [(18.7 to 33.1); p<0.001] in the U-EXCEED and 28.7% in U-EXCEL [(20.9 to 36.4); p<0.001]. For clinical remission based on the Crohn Disease Activity Index (CDAI), the differences compared to placebo were 17.9% [(10 to 25.8); p<0.001] in U-EXCEED and 20.8 [(12.7 to 28.8); p<0.001] in U-EXCEL.
- In patients who achieved clinical response in the induction trials and continued into the U-ENDURE maintenance trial, the between-group differences compared to placebo in clinical remission based on PROs at 52 weeks were 21.9% [(13.7 to 30); p<0.001] and 31.8% [(23.2 to 40.3); p<0.001] in the upadacitinib 15 mg group and upadacitinib 30 mg group, respectively, while the between-group

differences compared to placebo in clinical remission based on CDAI were 23.7% [(15.2 to 32.1); p<0.001] and 32.8% [(23.9 to 42.6); p<0.001], respectively.
- Induction therapy with upadacitinib also resulted in clinical benefits in endoscopic remission, improvements in HRQoL, and the proportion with CR-100. In the induction trials, the difference in endoscopic response at 12 weeks compared to placebo was 31.2% [(25.5 to 37); p<0.001] in U-EXCEED and 33.0% [(26.2 to 39.9); p<0.001] in U-EXCEL, while in U-ENDURE, the difference in endoscopic response at 52 weeks was 21% [(13.6 to 28.4); p<0.001] and 33.7% [(26 to 41.3); p<0.001] in the upadacitinib 15 mg group and upadacitinib 30 mg group, respectively.
- For detailed information on the systematic review of upadacitinib for CD please see the CDEC Final Recommendation at: https://www.cadth.ca/upadacitinib-4.

3. Safety
- Across the trials, adverse events (AEs) were common and were experienced by approximately 58% to 76% of patients. In the placebo-controlled parts of the trials, the rate of AEs and withdrawal due to AEs were generally similar between treatment arms.
- SAEs occurred to approximately 7% to 15% of patients across the different treatment arms and cohorts of the included trials and were approximately similar between upadacitinib-treated and placebo-treated patients in the comparative cohorts.
- The most commonly reported AESIs (≥ 4% in any part or cohort of any included trial) included anemia, lymphopenia, serious infections, infections and infestations, herpes zoster, hepatic disorder, and CPK elevation.
- For detailed information on the safety and tolerability of upadacitinib, please see the CDEC Final Recommendations at the links above.

4. Economic Considerations
- The CADTH reanalysis of the manufacturer's economic submission reported that, based on the sponsor's analysis and given its limitations, upadacitinib is not a cost-effective treatment option for moderately to severely active CD in patients with moderately to severely active CD with an inadequate response to, loss of response to, or intolerance to conventional care (CCF subgroup) or biologic therapy (BF subgroup). at a willingness to pay threshold of $50,000 per quality-adjusted life-year (QALY) gained.
- CADTH reported there is insufficient clinical evidence to justify a price premium for upadacitinib over currently available biologic treatments for moderately to severely active CD in either the CCF or BF subgroup.
- To ensure cost-effectiveness, upadacitinib should be priced no more than the lowest-cost biologic used to manage moderately to severely CD that is funded by participating drug plans.

5. Of Note
- Patient group input emphasized that CD is a chronic progressive form of inflammatory bowel disease (IBD) that leads to significant disability and has a negative impact on a patient's HRQoL. CD is characterized by recurrent, uncontrolled inflammation that can affect any part of the gastrointestinal (GI) tract from mouth to anus and mostly affects the ileum, colon, and rectum. Symptoms can be chronic and intermittent, and disease activity and severity can vary over time.

- The oral route of administration of upadacitinib may be more convenient or preferred for patients than other therapies for CD (i.e., biologics), which are predominantly administered through IV infusion or subcutaneous injection.