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	**upadacitinib**
Brand Name	Rinvoq®
Dosage Form(s)	15 mg and 30 mg extended-release tablets
Manufacturer	Abbvie Corporation
Submission Type	**New Submission**
Use Reviewed	Moderate to severe atopic dermatitis
Canadian Agency for Drugs and Technologies in Health (CADTH) Reimbursement Reviews (CRR)	Yes, CRR recommended: **to Reimburse with clinical criteria and/or conditions**. Visit the CRR website for more details: https://www.cadth.ca/sites/default/files/DRR/2022/SR0685REC-Rinvoq%20AD-KH_BF-KH-meta.pdf
Drug Benefit Council (DBC)	The DBC met on September 12, 2022. The DBC considered various inputs including: the final reviews completed by the CRR on June 8, 2022, 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 two patient groups, as well as patient input provided to the CRR and a Budget Impact Assessment.
Drug Coverage Decision	**Limited Coverage Benefit. Access the upadacitinib criteria from www.gov.bc.ca/pharmacarespecialauthority**
Date	**November 23rd, 2023**

Reasons	**Drug coverage decision is consistent with the CDEC and DBC recommendation.** • Results from three randomized controlled trials (RCTs) indicated that treatment with upadacitinib reduced atopic dermatitis severity and symptoms compared to placebo. • In terms of safety profile, treatment was well tolerated in the RCTs when compared with placebo. • At the submitted price, upadacitinib is 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 with respect to the cost-effectiveness and value for money.
Other Information	None

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

Upadacitinib (Rinvoq™)
AbbVie Corporation

Description:

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

> For the treatment of adults and adolescents 12 years of age and older with refractory moderate to severe atopic dermatitis (AD) who are not adequately controlled with a systemic treatment (e.g., steroid or biologic) or when use of those therapies is inadvisable.

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on June 8, 2022, 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 two patient groups, as well as patient input provided to the CDR and a Budget Impact Assessment.

Dosage Forms:

Upadacitinib (Rinvoq™) is available as 15 mg and 30 mg extended-release tablets.

Recommendations:

1. The Drug Benefit Council (DBC) recommends that upadacitinib (Rinvoq™) not be listed for AD at the submitted price.

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

- Results from three studies indicated that treatment with upadacitinib reduced AD severity and symptoms compared to placebo.

- Results from one study comparing treatment with upadacitinib 30 mg with dupilumab 300 mg found upadacitinib had superior efficacy in reducing disease severity and symptoms in two primary outcomes at week 16; however, after 24 weeks this difference was no longer observed.
- The CADTH reanalysis of the manufacturer submission determined that the cost-effectiveness of upadacitinib at the Health Canada–recommended dosing strategy could not be estimated owing to a lack of clinical data and limitations with the sponsor's model.

2. Clinical Efficacy

- The DBC considered the CADTH systematic review, which included four studies: Measure Up 1 and Measure Up 2, the AD Up study, and the Heads Up study.
- Measure Up 1 and Measure Up 2 (n=847 and 836, respectively) both had a double-blind, placebo-controlled parallel design. Eligible patients were adults and adolescents (≥ 40 kg) with chronic AD and a documented history of inadequate response to topical AD treatments or use of systemic treatment. Both studies randomized patients to upadacitinib 15 mg, 30 mg, or placebo. The studies evaluated co-primary outcomes, the proportion of responders based on Eczema Area and Severity Index (EASI) 75 score (i.e., a 75% or greater improvement from baseline in the EASI score) and a validated Investigator Global Assessment for Atopic Dermatitis (vIGA-AD) score of 0 or 1 at week 16.
- AD Up had a similar design to the Measure Up 1 and Measure Up 2 studies, with the same inclusion criteria and population (n=901) but using topical corticosteroids in combination therapy with upadacitinib 15 mg, 30 mg, or placebo, and also using the same co-primary end points at 16 weeks.
- Heads Up was a double-blind, double-dummy, active controlled randomized study (n=692) comparing upadacitinib 30 mg to dupilumab 300 mg subcutaneous in adults (18 to 75 years old) with chronic AD and documented history of inadequate response to topical treatments or documented treatment with systemic therapies. The primary end point includes the proportion of patients achieving an EASI 75 at week 16.
- Measure Up 1, Measure Up 2, and AD Up demonstrated that upadacitinib 15 mg and 30 mg improved disease severity based on the EASI) 75 score and the vIGA-AD scores index when compared to placebo. Disease severity was improved whether upadacitinib was used as monotherapy (Measure Up 1 and 2) or in addition to topical corticosteroids (AD Up study).
- The evidence from these studies also indicates that upadacitinib (15 mg and 30 mg) is likely to reduce AD symptoms and improve health-related quality of life.
- Heads Up demonstrated superior efficacy of upadacitinib 30 mg in reducing disease severity and symptoms (based on the EASI 75 and pruritus NRS) when compared to dupilumab 300 mg at week 16; however, after 24 weeks this difference was no longer observed.
- The subgroup analysis of patients who previously used systemic therapies was not defined a priori and may be underpowered; as a result, there was uncertainty about the generalizability of the results from the included studies to the approved indication.
- For detailed information on the systematic review of upadacitinib for AD please see the CDEC Final Recommendation at: https://www.cadth.ca/upadacitinib-1.

3. Safety

- Upadacitinib 15 mg and 30 mg doses in all studies were well tolerated as compared to placebo at week 16, and without significant increases in adverse events (AEs) or serious adverse events (SAEs) up to the latest follow-up of 52 weeks in the blinded extension studies. The most frequently reported AEs were acne, upper

respiratory tract infection, nasopharyngitis, headache, elevation in creatine phosphokinase levels, and AD. No deaths were reported.
- In the Heads Up study, the safety profile of upadacitinib was similar to the Measure Up and AD Up studies. One death was reported in a patient treated with upadacitinib due to influenza-associated bronchopneumonia.
- 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 submission determined that the cost-effectiveness of the Health Canada-recommended dosing strategy could not be estimated owing to a lack of clinical data and limitations with the sponsor's model. As such, the cost-effectiveness of upadacitinib is unknown.
- CADTH was unable to address the lack of comparative clinical data for omitted relevant treatment comparators, the cost-effectiveness of upadacitinib among adolescents or by disease severity, the impact of adverse events on the incremental cost-effectiveness ratio (ICER), or the lack of long-term comparative effectiveness data.

5. Of Note
- Patient Input Questionnaire responses from two patient groups indicated that many patients with AD were dissatisfied with currently available treatments, including oral corticosteroids and phototherapy. Other treatments may be ineffective or, in the case of oral corticosteroids, have significant side effects.
- Patients expressed a need for treatments that would improve managing the itchiness, reduce flares and rashes, improve quality of life, and improve sleep. Patients also want to improve the appearance of their hands and eyes, have less apparent eczema, and obtain pain relief.