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	**tofacitinib**
Brand Name	Xeljanz™
Dosage Form(s)	5 mg and 10 mg tablets
Manufacturer	Pfizer Canada Inc.
Submission Type	**New Indication**
Use Reviewed	tofacitinib 5 mg and 10 mg tablets for the treatment of ulcerative colitis (UC)
Common Drug Review (CDR)	Yes, CDR recommended: **to Reimburse with clinical criteria and/or conditions**. Visit the CDR website for more details: www.cadth.ca/node/88649.
Drug Benefit Council (DBC)	DBC met on April 1, 2019. DBC considered various inputs including: the final reviews completed by the CDR on February 27, 2019, 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 patients; patient input provided to the CDR; a Clinical Practice Review from one specialist; an Other Drug Agencies Review Recommendations (ODAR-R) document prepared by the CDR; and a Budget Impact Assessment.
Drug Coverage Decision	**Limited Coverage Benefit.** Access the tofacitinib criteria from **www.gov.bc.ca/pharmacarespecialauthority**
Date	November 17, 2020
Reasons	**Drug coverage decision is consistent with the DBC recommendation.** • Tofacitinib demonstrated some advantage over placebo with respect to efficacy and safety as a treatment option for UC.

	• The Ministry participated in the pan-Canadian Pharmaceutical Alliance 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	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 Common Drug Review (CDR)
- 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.

Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

FINAL

Tofacitinib (Xeljanz®)

Pfizer Canada Inc.

Description:

Drug review of **tofacitinib (Xeljanz®)** for the following Health Canada approved indications:

> For the treatment of adult patients with moderately to severely active ulcerative colitis (UC) with an inadequate response, loss of response or intolerance to either conventional UC therapy or a TNFα inhibitor.

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on February 27, 2019, 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 patients; patient input provided to the CDR; a Clinical Practice Review from one specialist; an Other Drug Agencies Review Recommendations (ODAR-R) document prepared by the CDR; and a Budget Impact Assessment.

Dosage Forms:

Xeljanz® is available as tofacitinib 5 mg and 10 mg tablets.

Recommendations:

1. The Drug Benefit Council (DBC) recommends that **tofacitinib (Xeljanz®)** be reimbursed with the following criteria and conditions:
    a. Patient have moderately to severely active UC with an inadequate response, loss of response, or intolerance to conventional UC therapy followed by an inadequate response, loss of response, or intolerance to a TNFα inhibitor;
    b. Initial treatment of UC with tofacitinib at 10mg twice daily should be assessed after 8 weeks of therapy and discontinued if clinical response has not been achieved;
    c. Prescribing of tofacitinib for the treatment of UC should be restricted to gastroenterologists; and
    d. The cost of treatment of UC with tofacitinib 10 mg twice daily should not exceed the cost of treatment of UC with the least costly biologic TNFα inhibitor.

Reasons for the Recommendation:

1. Summary

- Three phase III randomized placebo controlled trials reported the proportion of patients with remission at week 8 was greater in the tofacitinib 10 mg arm compared with placebo, and the proportion of patients with remission at Week 52 was greater in both the tofacitinib 5 mg and the tofacitinib 10 mg arms compared with placebo.
- Indirect treatment comparisons suggest no statistically significant differences between tofacitinib and infliximab, adalimumab, golimumab or vedolizumab for the induction of clinical response, remission or mucosal healing in patients with no prior TNFα inhibitor treatment experience.
- At the manufacturer submitted price, tofacitinib is more costly than infliximab biosimilar for treatment of UC.

2. Clinical Efficacy

- The DBC considered the CDR systematic review, which included three phase III randomized placebo control trials of patients with moderately to severely active UC. OCTAVE Induction 1 and OCTAVE Induction 2 randomized patients treatment with tofacitinib 10 mg twice daily delivered orally in tablet form or treatment with placebo for eight weeks. OCTAVE Sustain randomized patients for treatment with tofacitinib 5 mg twice daily delivered orally in tablet form; tofacitinib 10 mg twice daily delivered orally in tablet form; or treatment with placebo for 52 weeks.
- In the OCTAVE Induction trials, tofacitinib was associated with statistically significant differences in the proportion of patients who achieved remission at Week 8 compared with placebo.
- In OCTAVE Sustain at Week 52, the difference in proportion of patients with remission was statistically significant for tofacitinib 5 mg and tofacitinib 10 mg versus placebo.
- The trials also showed statistically significant differences between tofacitinib and placebo in the proportion of patients with mucosal healing.
- In OCTAVE Sustain, the proportion of patients with remission at Week 52 was greater in both the tofacitinib 5 mg and the tofacitinib 10 mg arms compared with placebo. The difference in proportion from placebo was statistically significant.
- For detailed information on the systematic review of tofacitinib for treatment of UC please see the CDEC Final Recommendation at: https://www.cadth.ca/tofacitinib-5.

3. Safety

- The most common serious adverse event related to gastrointestinal disorders; specifically to UC. Adverse events were similar overall between tofacitinib and placebo.

- Infections and infestations generally occurred more often in patients in the tofacitinib arms compared with placebo, specifically in the 52-week study OCTAVE Sustain.
- An increased incidence of infection with Herpes zoster was observed in the 10 mg tofacitinib arm in OCTAVE Sustain.
- For detailed information on the safety and tolerability of [DRUG], please see the CDEC Final Recommendations at the links above.

4. Economic Considerations

- The DBC considered the CADTH re-analyses of the manufacturer-submitted economic analysis, which conducted separate re-analyses for biologic-naïve and -exposed patients.
- Tofacitinib is more costly and associated with less quality adjusted life years (QALYs) than infliximab biosimilar. For biologic-exposed patients, conventional therapy is the optimal therapy where the decision maker is willing to pay less than $143,710 per QALY and tofacitinib is the optimal therapy where the decision maker is willing to pay more than $143,710 per QALY.
- Price reductions of 44% and 74% would be required for tofacitinib to be the optimal treatment at a willingness-to-pay of $50,000 per QALY in the biologic-exposed and biologic naïve populations, respectively.
- Several important limitations in the economic analysis could not be addressed, including those related to treatment efficacy and duration of treatment effect, and the results of the CADTH economic evaluation should be viewed with caution.

5. Of Note

- Two patients who had tried tofacitinib for UC responded to Patient Input Questionnaires. Both patients had tried and failed on other treatments, including other TNFα inhibitors, and reported treatment with tofacitinib had brought bowel movements to normal. Both patients reported that, as an oral medication, tofacitinib was more convenient and less likely to lead to infections than the injections or infusions required by other treatments.