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	**ozanimod**
Brand Name	Zeposia®
Dosage Forms	0.23 mg, 0.46 mg, and 0.92 mg capsules
Manufacturer	Bristol-Myers Squibb Canada
Submission Type	**New Submission**
Use Reviewed	For the treatment of adults with moderately to severely active ulcerative colitis who have had an inadequate response, loss of response, or were intolerant to either conventional therapy or a biologic agent
Canada's Drug and Health Technology Agency (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/SR0714%20Zeposia%20-%20Final%20CADTH%20Recommendation%20SC%20-%20KH-meta.pdf
Drug Benefit Council (DBC)	The DBC met on December 5, 2022. The DBC considered various inputs including: the final reviews completed by the CADTH on November 17, 2022, which included clinical and pharmacoeconomic evidence review material and the recommendations from the CADTH. The DBC also considered Patient Input Questionnaire responses from 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 ozanimod for ulcerative colitis criteria from www.gov.bc.ca/pharmacarespecialauthority**

Date	**January 16, 2024**
Reasons	**Drug coverage decision is consistent with the DBC and CDEC recommendations.** • The drug demonstrated some advantage over placebo with respect to efficacy in achieving clinical remission in adult patients with moderately to severely active ulcerative colitis. • Based on economic considerations and the submitted product price, the drug was not cost effective at the submitted price. • 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 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

Ozanimod (Zeposia®)
Celgene Inc., Bristol Myers Squibb

Description:

Drug review of **ozanimod (Zeposia®)** for the following Health Canada approved indications:

For the treatment of adult patients with moderately to severely active ulcerative colitis (UC).

In their review, the DBC considered the following: the final reviews completed by the Canadian Agency for Drugs and Technologies in Health (CADTH) on December 5, 2022, which included clinical and pharmacoeconomic evidence review material and the recommendations from CADTH. The DBC also considered Patient Input Questionnaire responses from two patient groups, as well as patient input provided to CADTH and a Budget Impact Assessment.

Dosage Forms:

Zeposia® is available as ozanimod 0.23 mg, 0.46 mg and 0.92 mg oral capsules.

Recommendations:

1. The Drug Benefit Council (DBC) recommends not to list ozanimod (Zeposia®) at the submitted price.

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

Reasons for the Recommendation:

1. Summary
- Results from one clinical trial demonstrated that patients with UC were more likely to have disease remission after 10 weeks and after 52 weeks of treatment with ozanimod than with placebo. Patients were also more likely to have healing of the lining of the large intestine with ozanimod versus placebo.
- Ozanimod was compared only to placebo in the clinical trial, and limitations in a manufacturer-submitted network meta-analysis (NMA) meant it was not possible to conclude ozanimod was superior or inferior in efficacy or safety to other treatments for UC such as biologics or tofacitinib.

- At the submitted price, ozanimod was more costly than several relevant comparator treatments used in moderately to severely active UC.

2. Clinical Efficacy

- The DBC considered the CADTH systematic review, which included a phase III, multicenter, randomized, double-blind, placebo-controlled trial of oral ozanimod as induction and maintenance therapy for adult patients with moderate to severe UC.
- The primary outcome of the TRUE NORTH study was clinical remission as measured by the 3-component Mayo score, which includes rectal bleeding, stool frequency, and endoscopy findings components, each of which is rated from 0 to 3, yielding a total score of 0 to 9.
- The primary end point and the following key secondary end points of TRUE NORTH were assessed in both the induction and maintenance periods: clinical response, endoscopic improvement, and mucosal healing. Key secondary end points assessed only in the maintenance period were clinical remission in patients who were in remission at week 10, corticosteroid-free remission, and durable clinical remission.
- In TRUE NORTH, greater percentages of patients in the ozanimod group compared with the placebo group had clinical remission during the induction period at week 10 and maintenance period at week 52.
- Statistically significant between-group differences favoured the ozanimod group for clinical response, endoscopic improvement, and mucosal healing at weeks 10 and 52. During the maintenance period, statistically significant between-group differences favoured the ozanimod group for corticosteroid-free remission, durable clinical remission, and maintenance of clinical remission.
- The CADTH review of the manufacturer's submitted NMA concluded that, because of limitations in study design and analyses it was not possible to conclude ozanimod was superior or inferior in efficacy or safety to biologics or tofacitinib for UC.
- For detailed information on the systematic review of ozanimod (Zeposia®) please see the CDEC Final Recommendation at: https://www.cadth.ca/ozanimod-0.

3. Safety

- During the induction period, at least 1 treatment emergent adverse event (TEAE) was reported by 40.1% and 38.0% of patients in the cohort 1 ozanimod and cohort 1 placebo group, respectively. Among patients who were rerandomized to placebo and those who continued on ozanimod during the maintenance period, 36.6% and 49.1% reported at least 1 TEAE, respectively.
- During the induction period, serious TEAEs were reported by 4.0% and 3.2% of patients in the cohort 1 ozanimod group and cohort 1 placebo group, respectively. The most common serious TEAE reported in the induction period was colitis ulcerative in both treatment groups (approximately 1.4%). Additional serious TEAEs reported in the cohort 1 ozanimod group were anemia (0.9%) and appendicitis (0.2%). During the maintenance period, 7.9% of patients who were rerandomized to placebo and 5.2% of patients who continued ozanimod reported at least 1 serious TEAE. Serious TEAEs reported in at least 2 patients in the rerandomized placebo group included colitis ulcerative (4% in the rerandomized placebo group and 0.4% in the ozanimod group) and complicated appendicitis (0.9% in the rerandomized placebo group and none in the ozanimod group).
- Withdrawal from the study due to TEAEs during the induction period was similar across the treatment groups at approximately 3%. The most common reason for withdrawal due to TEAEs was colitis ulcerative (cohort 1 ozanimod = 0.7% and cohort 1 placebo = 1.9%). Two (0.5%) patients in the cohort 2 ozanimod group discontinued due to bradycardia.

- The percentage of patients who withdrew from the study during the maintenance period was 2.6% among those who were rerandomized to placebo and 1.3% in patients who remained on ozanimod. Four (1.8%) patients in the group of those who were rerandomized to placebo withdrew from the study due to colitis ulcerative.
- For detailed information on the safety and tolerability of ozanimod (Zeposia®) please see the CDEC Final Recommendations at the links above.

4. Economic Considerations

- Based on the submitted price for ozanimod and the publicly accessible list prices of all biologic drugs and tofacitinib, ozanimod was more costly than several relevant comparator treatments used in moderately to severely active UC.
- Given the lack of direct comparative evidence with other treatments, the uncertainty associated with the reviewed indirect treatment comparisons (ITCs), and the limitations with the submitted cost-utility analysis, the total drug cost of ozanimod should not exceed the total drug cost of the least expensive biologic or targeted synthetic drug reimbursed for the treatment of moderately to severely active UC.

5. Of Note

- Patients indicated a need for new and effective treatment options to achieve sustained remission or response and symptom relief as patients may not have a response or may lose response to currently available treatment options. Ozanimod is effective in inducing and maintaining clinical remission and has a different mechanism of action from currently available therapies for UC.
- The oral route of administration of ozanimod may be more convenient for patients than other therapies for UC (i.e., biologics), which are predominantly administered through IV infusion or subcutaneous injection.