# 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** | **ustekinumab** |
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| Brand Name | **Stelara®** |
| Dosage Form(s) | Solution for intravenous infusion 130 mg/26mL and solution for subcutaneous injection 90 mg/1mL |
| Manufacturer | Janssen Inc. |
| **Submission Type** | **New Submission** |
| Use Reviewed | The treatment of moderately to severely active ulcerative colitis in adult patients. |
| Canadian Agency for Drugs and Technologies in Health (CADTH) Reimbursement Reviews (CRR) | Yes, the CRR recommended: **to Reimburse with clinical criteria and/or conditions**.<br>Visit the CRR website for more details: SR0627 Stelara - CDEC Final Recommendation July 20, 2020_for posting.pdf (cadth.ca) |
| Drug Benefit Council (DBC) | The DBC met on August 10, 2020. The DBC considered various inputs including: the final review completed by the Common Drug Review (CDR), which included clinical and pharmacoeconomic evidence review material and the recommendation from CDEC. The DBC also considered Patient Input Questionnaire responses from one patient and one patient group, patient input |

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| | provided to the CDR, a Clinical Practice Reviews from one specialist, and a Budget Impact Assessment. |
| **Drug Coverage Decision** | **Non-Benefit** |
| Date | January 17, 2023 |
| Reason(s) | **Drug coverage decision is consistent with the DBC recommendation**<br>• The drug demonstrated some advantage over placebo with respect to efficacy.<br>• Because of the uncertainty regarding the comparative clinical effectiveness of ustekinumab compared with other biologics, there is insufficient evidence to justify a cost premium over the least expensive biologic reimbursed for the treatment of moderate-to-severe UC.<br>• The pan-Canadian Pharmaceutical Alliance (pCPA) and Business Management, Supplier Relations (BMSRs) were involved in negotiations with the manufacturer for this product. The pCPA was not able to reach an agreement that provides sufficient value to result in listings in participating jurisdictions. |
| Other Information | |

**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

## Ustekinumab (Stelara/Stelara I.V.®)

## Janssen Inc.

**Description:**

Drug review of **ustekinumab (Stelara/Stelara I.V.®)** for the following Health Canada approved indications:

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

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on July 16, 2020, 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 one patient and one patient groups, patient input provided to the CDR, a Clinical Practice Reviews from one specialist, and a Budget Impact Assessment.

**Dosage Forms:**

Stelara®/Stelara I.V.® is available as ustekinumab 90 mg/1 mL pre-filled syringe for subcutaneous injection and 130 mg/26 mL (5 mg/mL) vial for intravenous infusion.

**Recommendations:**

1. The Drug Benefit Council (DBC) recommends that ustekinumab (Stelara/Stelara I.V.®) be listed as a Limited Coverage benefit for the treatment of moderately to severely active ulcerative colitis (UC) in adult patients with moderately to severely active UC.
2. As per the approved indication, coverage for ustekinumab should be as a third-line agent, for patients who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic, or have medical contraindications to such therapies.
3. Initiation of therapy of ustekinumab for the treatment of UC should be restricted to gastroenterologists, but general physicians should be able to continue maintenance therapy for patients started on ustekinumab by a gastroenterologist.
4. The cost of treatment with ustekinumab should not exceed the cost of the least costly biologic currently reimbursed for the treatment of UC.

**Reasons for the Recommendation:**

**1. Summary**

- Results of a single, two-phase, randomized controlled trial (RCT) demonstrated that treatment with ustekinumab was more effective than placebo at inducing (at eight weeks) and maintaining (for another 44 weeks) clinical remission of UC, including corticosteroid-free remission and endoscopic healing.
- The single RCT lacks head-to-head comparisons to other treatment options for UC, and so no conclusions could be drawn regarding the comparative effectiveness and safety of ustekinumab compared to these treatment options.
- Because of the uncertainty regarding the comparative clinical effectiveness of ustekinumab compared with other biologics, there is insufficient evidence to justify a cost premium over the least expensive biologic reimbursed for the treatment of moderate-to-severe UC.

**2. Clinical Efficacy**

- The DBC considered the CADTH systematic review, which included one double-blind RCT (UNIFI), composed of an eight-week induction phase and a 44-week maintenance phase.
- Outcomes were defined *a priori* in systematic review protocol and included the following: clinical remission (global and US definitions); clinical response: health-related quality of life (HRQoL) instruments such as the Inflammatory Bowel Disease Questionnaire (IBDQ), the Short Form 36 Health Survey (SF-36), and the EuroQol 5-Dimensions Visual Analogue Scale; mucosal healing; productivity; and adverse events.

- In the randomized population of the maintenance phase, the percentage of patients who had clinical remission (global and US definitions) at week 44 was statistically significantly higher among patients assigned to 90 mg of SC ustekinumab every 12 weeks (approximately 39%) or every eight weeks (approximately 43%) than among those assigned to placebo (approximately 24.0%). Sensitivity analyses supported the primary analysis, and subgroup analyses were also generally consistent with the primary analysis for the full population.
- Statistically significantly higher proportions of patients in the ustekinumab groups at week 44 maintained clinical response, corticosteroid-free remission, and endoscopic healing compared with the placebo group.
- No conclusions could be drawn regarding the comparative effectiveness of ustekinumab to other treatment options for UC because of the lack of head-to-head comparisons and the limitations associated with the sponsor-provided network meta-analysis (NMA).
- For detailed information on the systematic review of ustekinumab for UC, please see the CDEC Final Recommendation at: https://www.cadth.ca/ustekinumab-16.

**3. Safety**

- There were fewer serious adverse events in the induction and maintenance phases of UNIFI with ustekinumab (3.4% and 7.3% in the combined groups, respectively) than with placebo (6.6% and 9.7%, respectively). The higher frequency in the placebo group was seemingly driven by a larger percentage of patients reporting UC as an adverse event, likely reflecting a lack of efficacy from placebo.
- A larger percentage of patients in the placebo group (11.6%) withdrew from the maintenance phase due to an adverse event compared with those in the ustekinumab groups (5.1%); no patients withdrew from the induction phase due to an adverse event.
- Through 52 weeks of exposure, there were two deaths (one each from acute respiratory distress syndrome and hemorrhage from esophageal varices) and seven cases of cancer diagnosed among 825 patients who received ustekinumab, and no deaths and one case of cancer diagnosed among 319 patients who received placebo.
- No conclusions could be drawn regarding the comparative safety of ustekinumab to other treatment options for UC because of the lack of head-to-head comparisons and the limitations associated with the sponsor's NMA.
- For detailed information on the safety and tolerability of ustekinumab, please see the CDEC Final Recommendations at the links above.

**4. Economic Considerations**

- The DBC considered the CDR review of the manufacturer-submitted cost-utility analysis comparing ustekinumab with other biologic therapies or continuing conventional therapy (a mix of 5-aminosalicylates, corticosteroids, and immunomodulators) for Canadian adults with moderately to severely active UC who have inadequate, intolerant, or failed response to conventional therapy or biological agents.

- Several methodological concerns with the sponsor's NMA could not be addressed and as such the results of the economic evaluation should be viewed with caution.
- The cost-effectiveness of ustekinumab compared with infliximab (branded or biosimilar) and golimumab in the biologic-experienced population is also unknown.
- Given the uncertainty regarding the comparative clinical effectiveness of ustekinumab compared with other biologics and the limitations of the cost-utility analysis, there is insufficient evidence to justify a cost premium over the least expensive biologic reimbursed for the treatment of moderate-to-severe UC.

**5. Of Note**

- The DBC considered patient input from one patient, who had not tried ustekinumab, and one patient group. The patient input emphasized that UC is a chronic condition that has profound physical, emotional, and social effects on an individual's life, and that it is particularly difficult for children and young adults.
- The patient and the patient group noted that there is not one treatment that is effective in treating all patients with UC, and that a variety of different treatments for UC is needed as patients may not respond or be able to tolerate any one medication.
- Both the patient and patient group noted the convenience advantage of ustekinumab (delivered by SC injection every 8 weeks) over infliximab (delivered by IV over several hours every 8 weeks).