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	**Infliximab**
Brand Name	Remsima™ SC
Dosage Form(s)	120 mg pre-filled syringe, 120 mg pre-filled pen
Manufacturer	Celltrion Healthcare Co., Ltd.
Submission Type	**Biosimilars**
Use Reviewed	Remsima™ SC is indicated for the treatment of adult patients with rheumatoid arthritis
Common Drug Review (CDR)	Yes, the 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)	The DBC met on May 3, 2021. The DBC considered various inputs including: the final review completed by the CDR on April 22, 2021, which included clinical and pharmacoeconomic evidence review material and the recommendation from the CDEC. The DBC received no Patient Input Questionnaire responses from patients, caregivers or patient groups and instead reviewed patient input provided to the CDR. The DBC also considered a Clinical Practice Review from a specialist and a Budget Impact Assessment.
Drug Coverage Decision	**Non-Benefit**
Date	June 14, 2022

Reason(s)	**Drug coverage decision is consistent with the DBC and the CDEC recommendation.**
	• The main clinical study (CT-P13 3.5) showed that the biosimilar subcutanous (SC) infliximab (Remsima SC) was similar to intravenous (IV) infliximab in reducing disease severity and other efficacy outcomes for the treatment of rheumatoid arthritis.
	    ○ The frequency of antidrug antibodies was similar between SC and IV infliximab. It is currently unknown whether there will be less of a need to increase the dose over time when using the SC formulation.
	    ○ Due to a lack of comparative data, a conclusion regarding the benefits on health-related quality of life with infliximab SC treatment compared to infliximab IV could not be made.

	• At its submitted price, the biosimilar infliximab SC would be cost-saving compared with similar originator biologic treatments, but would result in increased costs compared with other biosimilar treatments, including infliximab IV biosimilars. • The Ministry participated in the pan-Canadian Pharmaceutical Alliance negotiations with the manufacturer, and was not able to address the concerns in 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.

Appendix

Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

FINAL

Infliximab (Remsima®)

Celltrion Healthcare Co., Ltd.

Description:

Drug review of **infliximab (Remsima®)** for the following Health Canada approved indications:

For the treatment of rheumatoid arthritis (RA).

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on April 22, 2021, which included clinical and pharmacoeconomic evidence review material and the recommendations from the Canadian Drug Expert Committee (CDEC). The DBC received no Patient Input Questionnaire responses from patients, caregivers, or patient groups, and instead reviewed patient input provided to the CDR. The DBC also considered a Clinical Practice Reviews from a specialist and a Budget Impact Assessment.

Dosage Forms:

Remsima® is available as infliximab 120 mg/mL in a 1 mL pre-filled syringe or pre-filled pen.

Recommendations:

1. The Drug Benefit Council (DBC) recommends not to list infliximab (Remsima®) at the submitted price
2. If a price reduction is achieved that is acceptable to the Ministry of Health (the Ministry), infliximab (Remsima®) could be considered for listing in a similar manner to IV formulations of infliximab.

Reasons for the Recommendation:

1. Summary

- Results from one randomized, double-dummy blinded, phase I/III study indicated that infliximab SC 120 mg was noninferior to infliximab IV 3 mg/kg.
- At the manufacturer-submitted price, infliximab SC would be a cost saving compared with branded biologic products but would result in increased costs compared with biosimilar products.

2. Clinical Efficacy

- The DBC considered the CDEC clinical review, which found one randomized, double-blind, double-dummy, noninferiority trial of patients with active RA (Study CT-P13 3.5).
- Of 357 patients enrolled in Study CT-P13 3.5, 343 received infliximab biosimilar IV 3 mg/kg at baseline and at week two as induction. Patients were then randomized 1:1 at week six to infliximab SC 120 mg biweekly until week 28 or infliximab IV 3 mg/kg every 8 weeks until week 22.
- The primary end point was change from baseline in the Disease Activity Score-28 for Rheumatoid Arthritis with CRP (DAS28-CRP) at week 22. Noninferiority between treatments could be declared if the lower bound of the two-sided 95% confidence interval (CI) for the difference between groups in DAS28-CRP at week 22 was greater than the pre-specified noninferiority margin of –0.6.
- In Study CT-P13 3.5, the least squares mean change from baseline in the DAS28-CRP improved in both the infliximab SC and infliximab IV treatment groups. The mean difference between groups was 0.27 points (95% CI, 0.02 to 0.52). The lower limit of the two-sided 95% CI of 0.02 was greater than the pre-specified noninferiority margin of –0.6, indicating noninferiority of infliximab SC 120 mg compared with infliximab IV 3 mg/kg.
- The results for other efficacy outcomes were similar between infliximab SC and infliximab IV.
- For detailed information on the systematic review of infliximab (Remsima®) please see the CDEC Final Recommendation at: https://www.cadth.ca/infliximab-21.

3. Safety

- Study CT-P13 3.5 assessed adverse events up to 64 weeks of treatment. Overall adverse events occurred in 54.8% and 66.9 of patients in the infliximab SC and infliximab IV groups, respectively. Serious adverse events occurred in 3.6% of patients in the infliximab SC group and 7.4% in the infliximab IV group. Approximately 4% of patients in the infliximab SC group and 8% in the infliximab IV group had an adverse event leading to discontinuation.
- Infusion related reaction, systemic injection reaction, and delayed hypersensitivity occurred in 3% and 5.7% of patients in the infliximab SC and infliximab IV groups, respectively. Overall injection site reactions were reported in 17.9% of those in the infliximab SC group and 12.6% in the infliximab IV group.
- For detailed information on the safety and tolerability of infliximab (Remsima®), please see the CDEC Final Recommendations at the links above.

4. Economic Considerations

- At its submitted price, infliximab SC would be cost saving compared with branded biologic products but would result in increased costs compared with biosimilar products.
- The CDEC analysis of the manufacturer-submitted cost comparison reported that the submitted price of infliximab SC would need to be reduced by 43% for its annual cost to be equivalent to that of the list price of the least expensive biosimilar comparator, infliximab IV biosimilar.

5. Of Note

- The DBC received no Patient Input Questionnaire responses from patients, caregivers, or patient groups. Patient input provided to the CDR indicated that currently available medications for RA may have serious side effects or lengthy administrations or travel times to IV clinics that disrupt daily activities. A treatment option that allowed SC administration of infliximab would be appealing to some patients.