CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

infliximab (Remsima SC)

(Celltrion Healthcare Co., Ltd.)

Indication: Maintenance treatment of adults with moderately to severely active Crohn's disease who have had an inadequate response or were intolerant to conventional therapy. Remsima SC should only be used as maintenance therapy after the completion of an induction period with intravenous infliximab.

April 8, 2024

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0816-000
Brand name (generic)	Remsima™ SC (infliximab)
Indication(s)	Crohn's disease
Organization	Gastrointestinal Society
Contact information[a]	Name: Jaymee Maaghop

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐

Thank you for giving a positive recommendation for the public reimbursement of Remsima™ SC (infliximab), providing a new treatment option for patients living with Crohn's disease.

Although the Health Canada approved indication requires patients to trial conventional therapy, we appreciate that CADTH recommended some flexibility in its reimbursement criteria by aligning it with those used for other reimbursed biologic therapies. However, we encourage CADTH to consider the strong evidence supporting the use of effective treatments early on in care, such as the top down approach for patients living with moderate to severe Crohn's disease. In our submission, we highlighted the intolerable side effects and prevailing unmet needs that patients face with corticosteroids and immunosuppressants. A 2024 international study, with gastroenterologists and researchers from Canada, found that a top-down treatment approach at the time of diagnosis is highly effective and safe compared to the step-up approach where patients begin with conventional therapy.[1] Recently, in March 2024, INESSS also released a recommendation for the reimbursement criteria for Crohn's disease where they removed the requirement of patients trialing conventional therapy before they can receive coverage of biologic therapies (i.e., adalimumab, infliximab, and vedolizumab).[2] These are evidence-based best practices recognized around the world, and CADTH must not leave Canadians behind!

Patients have told us how invasive and time and resource intensive colonoscopies are, and we are grateful that CADTH continues to recognize this in its recommendations for treatments for Crohn's disease. In this draft recommendation, CADTH stated that endoscopic follow-up within 12 weeks of treatment initiation is not required, and instead it is up to the treating physician to determine clinical response since other effective methods are available (e.g., fecal calprotectin).

While the CADTH review committee noted that there are some patients that fear self-injection, we know that many still choose subcutaneous injections over infusion since it gives them the ability to take it at home, or wherever is convenient for them, and that it does not require them to take more time off school/work and arrange transportation to go in to an infusion clinic.

The only concern we have with the recommendation is that most, if not all, biologic therapies that CADTH has reviewed for inflammatory bowel disease (primarily Crohn's disease and ulcerative colitis) have a reimbursement condition that the negotiated price of a new biologic or biosimilar medication must be comparable to the least costly biologic or biosimilar available. Medicines serve a purpose for patients living with a chronic disease, especially one where there is no cure, such as Crohn's disease. Having a requirement for new medicines to be valued similarly to the lowest priced biologic or biosimilar could pose a barrier for new medicines coming to Canada. We understand the

importance of savings and limitations of resources and funds in our healthcare systems, but we also emphasize the need to achieve a balance between savings and attracting innovation to Canada for new, effective treatments, providing patients with a variety of treatment options. Again, thank you for helping individuals living with Crohn's disease have access to new and advanced treatment options, such as Remsima™ SC!		
Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐
Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Jaymee Maaghop*
Position	*Health Policy and Outreach Manager*
Date	*08/04/2024*
☒	I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☒

D. New or Updated Conflict of Interest Declaration

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

[1] Noor NM *et al*. A biomarker-stratified comparison of top-down versus accelerated step-up treatment strategies for patients with newly diagnosed Crohn's disease (PROFILE): a multicenter, open-label randomised controlled trial. *Lancet Gastroenterol Hepatol*. 2024;1-13.

[2] *Institut national d'excellence en santé et en services sociaux*. Adalimumab, Infliximab et Vedolizumab: Maladie de Crohn. Available at: https://www.inesss.qc.ca/fileadmin/doc/INESSS/Inscription_medicaments/Avis_au_ministre/Avril_2024/Agents_biologiques_Crohn_2024_03.pdf. Accessed 2024-04-08.

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0816-000
Name of the drug and Indication(s)	INFLIXIMAB (REMSIMA SC) for maintenance treatment of adults with moderately to severely active Crohn's disease who have had an inadequate response or were intolerant to conventional therapy. Remsima SC should only be used as maintenance therapy after the completion of an induction period with intravenous infliximab.
Organization Providing Feedback	FWG

1. Recommendation revisions Please indicate if the stakeholder requires the expert review committee to reconsider or clarify its recommendation.		
Request for Reconsideration	**Major revisions:** A change in recommendation **category** or patient **population** is requested	☐
	Minor revisions: A change in reimbursement **conditions** is requested	☐
No Request for Reconsideration	**Editorial revisions:** Clarifications in recommendation **text** are requested	☐
	No requested revisions	X

2. Change in recommendation category or conditions Complete this section if major or minor revisions are requested
Please identify the specific text from the recommendation and provide a rationale for requesting a change in recommendation.

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
Please provide details regarding the information that requires clarification.
b) Reimbursement conditions and related reasons
Please provide details regarding the information that requires clarification.
c) Implementation guidance

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0816-000 and SR0816-001
Brand name (generic)	Remsima SC (Infliximab SC)
Indication(s)	Ulcerative Colitis / Crohn's Disease
Organization	Celltrion Healthcare Canada Ltd.
Contact information[a]	[redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☒

The sponsor agrees with the CDEC recommendation to reimburse Remsima SC (Infliximab SC) in the treatment of patients with ulcerative colitis (UC) and Crohn's disease (CD). The primary reason for the development of a subcutaneous (SC) format of infliximab was to address patient need for effective treatments that provide a more convenient route of administration, timely patient access, and improved quality of life, as stated in the reason for recommendation.

We are, however, disappointed, and respectfully disagree with the condition that *"Infliximab SC should be negotiated so that it does not exceed the drug program cost of treatment with the least costly biologic therapy reimbursed for the treatment of adult patients with moderately to severely active CD who have had an inadequate response or are intolerant to conventional therapy"*. (Draft Recommendation, Table 1)

The rationale for this recommendation was noted by CADTH as follows:

"While the LIBERTY-CD trial demonstrated infliximab SC provided benefit to patients compared to placebo, no evidence was available to estimate the comparative effectiveness of infliximab SC to other currently reimbursed treatments for moderately to severely active CD…There is insufficient evidence to justify a cost premium for infliximab SC over currently available biologic therapies reimbursed for the indicated patient population." (Draft Recommendation, Table 1)

While it is acknowledged that no data has definitively confirmed the superiority of one biologic over another, there is also no data showing equivalence of Remsima SC to the lowest cost therapy. Therefore, the pricing condition is arbitrary. The reimbursement of multiple biologics for treating the same condition indicates and affirms that each therapy is unique, has special characteristics important to patients, and are not the same nor interchangeable with one another. As noted in the draft recommendation, *"CDEC heard from the clinical expert that a subcutaneous mode of administration may reduce treatment related travel time and the need to be off work, which may*

facilitate access to treatment and allow patients a sense of independence" (Draft Recommendation, Discussion Point 2).

The introduction of biosimilars to Canada over the past decade has played an extremely important role in contributing to the sustainability of the healthcare system. It is unfortunate that reimbursement conditions such as this continue to put downward pressure on manufacturers to further reduce prices, ultimately making the Canadian biosimilar landscape increasingly unattractive for manufacturers to pursue new biosimilar product launches - thus leading to a potential decline in biosimilar investment in the Canadian market, resulting in Canada's ability to pay for new, innovative medications.

Generic products are not subject to comparative pricing analysis with different molecules, as such we would expect biosimilars to follow the same rationale. Given that, we believe that Remsima SC should be priced no lower than to Infliximab IV biosimilars for the same indication. We look forward to productive discussions with pCPA to recognize the significant value that Remsima SC and other biosimilars bring to all stakeholders, so that we can continue to bring these treatments to Canadian patients in a timely and efficient manner.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐
Not applicable		

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
Not applicable		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
Not applicable		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☒
Please see above.		

[a] CADTH may contact this person if comments require clarification.