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CADTH Reimbursement Recommendation

Infliximab (Remsima SC)

Indication: For the 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.

Sponsor: Celltrion Healthcare Co., Ltd.

Final recommendation: Reimburse with conditions

Summary

What Is the CADTH Reimbursement Recommendation for Remsima SC?

CADTH recommends that Remsima SC be reimbursed by public drug plans as maintenance treatment for adults with moderately to severely active Crohn disease (CD) whose disease has had an inadequate response, or who were intolerant to, conventional therapy if certain conditions are met.

Which Patients Are Eligible for Coverage?

Remsima SC maintenance treatment should only be covered to treat adults with moderately to severely active CD whose disease had an inadequate response, or who are intolerant, to conventional therapy. Patients are required to achieve a clinical response to induction therapy with infliximab IV at week 10 of treatment to continue with Remsima SC as maintenance therapy.

What Are the Conditions for Reimbursement?

Remsima SC should only be reimbursed if prescribed by a physician experienced in diagnosing and managing CD and should not be combined with a biologic or Janus kinase (JAK inhibitor) treatment for CD. The cost of Remsima SC should not exceed the drug program cost of treatment with the least costly biologic therapy reimbursed for the treatment of CD.

Why Did CADTH Make This Recommendation?

- One randomized controlled trial (RCT) demonstrated that patients were more likely to achieve clinical remission at week 54 when treated with Remsima SC than with placebo. Patients were also more likely to show healing of the lining of the gastrointestinal (GI) tract at week 54 with Remsima SC versus placebo.
- Remsima SC may meet some needs that are important to patients as it provides a subcutaneous (SC) drug option that can be administered in a patient's home.
- Based on CADTH's assessment of the health economic evidence, Remsima SC does not represent good value to the health care system at the publicly listed price. The committee determined that there is insufficient evidence to justify a greater cost for Remsima SC than the least costly biologic therapy for patients with moderately to severely active CD whose disease has had an inadequate response, or who were intolerant, to conventional therapy.

Summary

- Based on public list prices, Remsima SC is estimated to lead to cost savings for the public drug plans of approximately $410,674 over 3 years.

Additional Information

What Is Crohn Disease?

CD is an inflammatory bowel disease that can cause recurrent uncontrolled inflammation in any part of the GI tract, but commonly affects the small intestine, colon, and rectum. For many patients with CD, symptoms are chronic and sporadic, and disease severity can vary widely over time. Common CD symptoms include diarrhea, abdominal pain, fatigue, fever, rectal bleeding, loss of appetite, weight loss, and malnutrition. There is no cure for CD, and patients usually have symptoms on and off for life. The prevalence of CD in Canada is projected to be 493 patients per 100,000 of the population by 2030.

Unmet Needs in Crohn Disease

Treatments are needed that improve symptom resolution and quality of life, reduce the need for surgery, and avoid repetitive use of corticosteroids.

How Much Does Remsima SC Cost?

The first-year costs of Remsima SC depend on which infliximab IV product is chosen for the induction period. The expected cost in the first year, if Inflectra is chosen for induction, is $19,357 per patient, and $15,424 in each subsequent year.

Recommendation

The Canadian Drug Expert Committee (CDEC) recommends that infliximab SC be reimbursed as maintenance treatment for adults with moderately to severely active CD who have had an inadequate response or were intolerant to conventional therapy if the conditions listed in Table 1 are met.

Rationale for the Recommendation

One double-blind, placebo-controlled, phase III RCT (LIBERTY-CD) demonstrated that, compared to placebo, treatment with infliximab SC resulted in added clinical benefit in adults with moderately to severely active CD whose disease has had an inadequate response, or who were intolerant, to conventional therapy. Infliximab SC, compared with placebo, was associated with statistically significant and clinically meaningful improvements in the coprimary outcomes of clinical remission, based on the Crohn's Disease Activity Index (CDAI) at week 54 (between group difference = 32.1%; 95% confidence interval [CI], 20.9 to 42.1) and endoscopic response, based on central Simplified Endoscopic Activity Score for Crohn Disease (SES-CD) at week 54 (between groups difference of 34.7%; 95% CI, 24.2 to 43.5). The key secondary outcomes, CDAI-100 response, clinical remission based on abdominal pain and stool frequency scores, endoscopic remission based on central SES-CD, and corticosteroid-free remission, were also statistically significantly in favour of infliximab SC at week 54.

Patients identified a need for effective treatments that provide a more convenient route of administration, timely patient access, and improved quality of life. CDEC noted that infliximab SC may meet some of the needs identified by patients by providing an SC drug option that can be administered in a patient's home; however, CDEC could not reach definitive conclusions regarding the effects of infliximab SC compared to placebo on health-related quality of life (HRQoL) because of a significant decline in the number of patients available to provide assessments over time and the descriptive nature of the analyses. CDEC noted that no new safety concerns were observed with infliximab SC; however, uncertainty remained in the absence of long-term safety data.

At the sponsor-submitted price for infliximab SC of $19,357 per patient during the induction year (when inducted with Inflectra) and $15,424 per patient in the subsequent maintenance years, infliximab SC would increase costs to drug plans when compared with other infliximab IV biosimilars and adalimumab biosimilars, based on publicly available prices. There is insufficient evidence to justify a cost premium for infliximab SC over the least costly biologic therapy reimbursed for the treatment of adults with moderately to severely active CD whose disease has had an inadequate response, or who were intolerant, to conventional therapy.

Table 1: Reimbursement Conditions and Reasons

Reimbursement condition	Reason	Implementation guidance
Initiation		
1. Eligibility for reimbursement of infliximab SC should be based on the criteria used by each of the public drug plans for biologic therapies for the maintenance treatment of adults with moderately to severely active CD whose disease has had an inadequate response, or who are intolerant, to conventional therapy.	The results of 1 placebo-controlled RCT, LIBERTY-CD, demonstrated that infliximab SC is an efficacious maintenance treatment for adults with moderately to severely active CD whose disease has had an inadequate response, or who are intolerant, to conventional therapy. There is no evidence that infliximab SC should be held to a different standard than other biologic therapies currently reimbursed for the treatment of adults with moderately to severely active CD when considering initiation of therapy.	The definition of moderately to severely active CD and inadequate response, intolerance, or loss of response to other therapies should align with those used for reimbursed biologic therapies.
2. The patient must have achieved a clinical response to induction therapy with infliximab IV at week 10 of treatment to continue to maintenance therapy with infliximab SC.	In the LIBERTY-CD trial, patients had to have a clinical response at the end of the induction period with infliximab IV at week 10 to continue to the maintenance phase with infliximab SC.	The definition of clinical response should align with the definitions used for reimbursed infliximab IV (e.g., a reduction of CDAI score greater than or equal to 100 points, or an HBI score of 5 or less, or a decrease in HBI score of 4 or more). Endoscopic follow-up is not required if clinical response continues to be achieved. CDEC considered the impracticality of requiring endoscopy within 12 weeks of treatment initiation, given the invasive nature of the procedure and potential difficulties with timely access to the procedure. The clinical expert noted that surrogate markers such as fecal calprotectin and resolution of anemia can also be used. Ultimately, CDEC considered it appropriate to leave the determination of clinical response up to the treating physician's clinical judgment.
Renewal		
3. Assessment for renewal after the first assessment of treatment response should be performed every year. The patient must maintain clinical response to therapy to continue receiving infliximab SC.	Patients who lose response to infliximab SC are no longer benefiting from treatment.	—
Prescribing		
4. Infliximab SC should only be prescribed by a physician experienced in diagnosing and managing CD.	It is important to ensure that infliximab SC is only prescribed for appropriate patients.	The clinical expert indicated that prescribing infliximab SC should not be limited to IBD specialists. General gastroenterologists would have the

Reimbursement condition	Reason	Implementation guidance
		expertise required to initiate therapy, and general internists with a particular interest in IBD and/or GI may have sufficient experience and training to prescribe infliximab SC, which may be important for accessibility.
5. Infliximab SC should not be reimbursed when combined with a biologic or JAK inhibitor treatments for CD.	There is no evidence to support the use of infliximab SC in combination with a biologic or other JAK inhibitor treatment for CD.	Infliximab SC may be used in conjunction with conventional therapy.
Pricing		
6. 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 adults with moderately to severely active CD whose disease has had an inadequate response, or who are intolerant, to conventional therapy.	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 the currently available biologic therapies reimbursed for the indicated patient population.	—

CD = Crohn disease; CDAI = Crohn Disease Activity Index; CDEC = Canadian Drug Expert Committee; GI = gastrointestinal; HBI = Harvey-Bradshaw Index; IBD = inflammatory bowel disease; JAK = Janus kinase; RCT = randomized controlled trial; SC = subcutaneous.

Discussion Points

- CDEC was unable to determine the relative efficacy and safety of infliximab SC versus the currently available biologic therapies in the target patient population because of the lack of head-to-head comparisons and the limitations associated with the supportive phase I study (Study 1.6 part 2). While the results observed in Study 1.6 part 2 were suggestive of similar efficacy and safety between infliximab SC and infliximab IV, CDEC could not reach definitive conclusions regarding the comparisons to infliximab IV because Study 1.6 part 2 had a small sample size, was not designed or powered to assess comparative efficacy, and dosing of infliximab SC was inconsistent with the Health Canada–recommended dose.
- CDEC considered that maintenance infliximab IV administered every 8 weeks is currently available in the target patient population. The committee acknowledged patient and clinical expert input expressing the need for effective treatments that offer a more convenient route of administration and improve patient access and quality of life. CDEC heard from the clinical expert that an SC 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. The committee noted, however, that some patients may fear self-injection and/ or may find infliximab SC's more frequent

administration schedule (i.e., every 2 weeks versus every 8 weeks) burdensome. CDEC noted that the available evidence on HRQoL based on the LIBERTY-CD trial and Study 1.6 part 2 was insufficient to reach definitive conclusions regarding the effects of infliximab SC compared to placebo or infliximab IV. Overall, CDEC noted that uncertainty remained about the clinical value conferred by infliximab SC versus the IV mode of administration.

- CDEC heard from the clinical expert that patients who have had prior exposure to 2 or more lines of biologic drugs or JAK inhibitors and otherwise meet the trial's eligibility criteria are currently considered for treatment with infliximab IV in clinical practice. The LIBERTY-CD trial excluded patients who had previously received 2 or more biologic drugs, JAK inhibitors, or both biologic drugs and JAK inhibitors. CDEC noted that the generalizability of the LIBERTY-CD trial results to these patients is limited.
- The LIBERTY-CD trial allowed dose adjustments from infliximab SC 120 mg to infliximab SC 240 mg every 2 weeks starting from week 22 through week 54, if patients' disease initially responded but then lost response. This dose escalation explored whether infliximab SC could be used to reinitiate response; however, this is inconsistent with the Health Canada–recommended dose and approved indication, which is for infliximab SC 120 mg every 2 weeks as maintenance therapy.
- CDEC heard from the clinical expert that the dose-loading phase with infliximab IV may extend up to 16 weeks in practice to accommodate those who experience slow response, allowing patients to benefit from treatment. CDEC noted that in the LIBERTY-CD trial, only patients who experienced clinical response at week 10 after 3 full doses of infliximab IV were randomly assigned into the maintenance phase with infliximab SC. Therefore, the generalizability of the LIBERTY-CD trial results to patients with an extended induction phase with infliximab IV is uncertain. CDEC also noted that the recommended dosage in the product monograph is to start maintenance infliximab SC at week 10 following 3 infliximab IV infusion doses and that extending the induction period to 16 weeks would fall outside the recommended dosage.
- While Study 1.6 part 2 was suggestive of similar efficacy, no conclusions could be reached about the comparative clinical benefit between infliximab SC and infliximab IV. Consequently, the evidence does not support a price premium for infliximab SC when compared to infliximab IV. The comparative effectiveness and cost-effectiveness of either infliximab SC or IV compared to the other biologic treatments currently reimbursed for moderately to severely active CD is unknown. Consequently, the evidence also does not support a price premium relative to these treatments.

Background

Inflammatory bowel disease (IBD) is an umbrella term that describes chronic inflammation of the GI tract caused by 1 of 2 disorders: ulcerative colitis (UC) and CD. Canada has the highest prevalence and incidence of IBD compared to other countries in the world with estimates of about 0.8% of the population, amounting to about 322,600 people living with the disease as of 2023. The Canadian prevalence is forecasted to increase

to 493 and 436 per 100,000 by 2030, with an average annual percentage change of 2.75% and 2.87% for CD and UC, respectively.

CD is caused by inflammation of the GI tract from mouth to rectum, mainly seen around the ileum (i.e., small intestine), colon (i.e., beginning of the large intestine), and rectum. CD is most common in adolescents and adults between the ages of 20 and 30 years. The prevalence estimate of CD in Canada in 2018 was 368 per 100,000 population, translating to about 135,000 people living with CD. Common symptoms include abdominal pain, rectal bleeding, fatigue, vomiting, diarrhea, perianal disease, weight loss, and bloating. Patients may experience chronic or intermittent symptoms, and disease activity and severity can vary widely over time. While some patients experience continuous and progressive active disease, others (about 20% of patients) may experience prolonged remission after initial presentation.

CD is diagnosed based on symptoms and clinical tests such as endoscopic evaluations (e.g., endoscopy, biopsy), stool sampling, and histological, radiological, and/or biochemical investigations at initial diagnosis. The available treatment options depend on the location, extent, phenotype, and severity of the disease. Treatment options for both diseases are similar. In CD, aminosalicylates, immunosuppressants (e.g., azathioprine, cyclosporine, methotrexate, and 6-mercaptopurine), corticosteroids (e.g., prednisone), tumour necrosis factor (TNF) alpha antagonists (e.g., infliximab and adalimumab), interleukin (IL) inhibitors, and integrin inhibitors (e.g., vedolizumab) are current options. Current treatments are unable to meet all current needs of patients in terms of short-term or long-term treatment.

Infliximab SC was reviewed by Health Canada and received a Notice of Compliance (NOC) on February 15, 2024, as maintenance treatment of adults with moderately to severely active CD 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 IV infliximab.

Infliximab (Remsima SC) is an SC formulation of infliximab, available in a prefilled syringe with an automatic needle guard, and prefilled pen formats, containing 120 mg of active substance. It is recommended that infliximab SC be initiated as maintenance therapy 4 weeks after the last administration of 3 IV infusions of infliximab 5 mg/kg given at weeks 0, 2, and 6. The recommended dose for infliximab SC is 120 mg once every 2 weeks. Infliximab has also been reviewed by the FDA and received market authorization on October 20, 2023, for CD (i.e., for reducing signs and symptoms and inducing and maintaining clinical remission in adults with moderately to severely active CD whose disease has had an inadequate response to conventional therapy). It also received regulatory authorization at the European Medicines Agency on June 1, 2020, and at the Medicines and Healthcare products Regulatory Agency in July 2022.

Infliximab (Remsima SC) was approved in 2021 by Health Canada for use in patients with moderately to severely active rheumatoid arthritis. It received a positive conditional CADTH recommendation for the treatment of adults with moderately to severely active rheumatoid arthritis in 2021.

Sources of Information Used by the Committee

To make its recommendation, the committee considered the following information:

- a review of 2 trials (1 phase III, open-label induction, double-blind maintenance RCT and 1 phase I open-label RCT) in patients with moderately to severely active CD
- patients perspectives gathered by 1 patient group (GI Society)
- input from the public drug plans and cancer agencies that participate in our review process
- 1 clinical specialist with expertise diagnosing and treating patients with CD
- a review of the pharmacoeconomic model and report submitted by the sponsor.

Stakeholder Perspectives

Patient Input

One patient input was received from the GI Society and was summarized for this review. The GI Society is a national charity organization with programs and services that support research, advocate for appropriate patient access to health care, and promote GI and liver health. Information from this input was gathered via questionnaires and interviews. Information was collected from 5 surveys with a total of 1,633 respondents contributing across the surveys. Additional data from a 2020 focus group on persons living with IBD and 1-to-1 interviews with patients were also assessed for the input.

The GI Society highlighted that patients with IBD preferred sustained remission and/or treatment response over relieving 1 symptom. Respondents to the surveys expressed different concerns associated with IBD, some of which included the fear of running out of medication, how to determine when to go to the emergency department based on their symptoms, pain, fear of going out because of disease, decreased quality of life, and fear and worry of being faced with mortality at a young age. The patient group highlighted the need for effective treatments for patients that could improve quality of life and cause no symptoms, pain, frustration, or hardship. The patient advocacy group expressed that inadequate access to treatment causes patient suffering, such as continual, debilitating disease symptoms; secondary illnesses, such as depression and anxiety disorders; and loss of family and/or social interactions that could have been prevented.

According to the patient advocacy group, treatment of CD requires a multifaceted strategy that allows for the management of symptom and disease consequences with therapies that target and reduce the underlying inflammation. The treatment options outlined included 5-aminosalicylic acids, corticosteroids, immunosuppressive drugs, and biologics. The patient advocacy group highlighted that despite the treatment options available in practice, patients with CD still have trouble achieving remission and adequate symptom relief; thus, there is a need for more treatments that cater to patients' needs. There were no patients interviewed who were currently receiving the treatment under review; however, the majority of patients surveyed had received a biologic. Results from 1 survey showed that 63% of the respondents reported symptom reduction after using a biologic and 23% confirmed remission.

According to the patient advocacy group, patients would like additional effective treatment options with convenient and timely patient access and different administration methods and dosages. The GI Society highlighted that major concerns with available therapies included ensuring adequate supply and continuity of care, especially timely communication between patients and their health care providers. The patient group noted that receiving IV treatments at clinics and untimely communications between patients and health care providers could mean frequently taking time off work, which can be difficult and contribute to financial hardship for many patients. According to the patient advocacy group, patients desire options that can be administered at home, thereby reducing required time off work.

Clinician Input

Input From the Clinical Expert Consulted by CADTH

Input from 1 clinical expert with experience treating CD was summarized for this review. The clinical expert highlighted that there is no cure for CD in current practice and early treatment is crucial as the first medication prescribed has the best chance of improving patient symptoms and healing. Treatment goals highlighted for patients with CD include symptom resolution (clinical remission), improving patient quality of life (by normalizing bowel movements, resolution of pain, resolution of bowel urgency, resolution of rectal bleeding, normalization of weight and/or energy level), reducing the need for surgery, and avoiding repetitive use of corticosteroids.

According to the expert, treatment selection is complex for patients with CD and depends on disease phenotype and patient preference. Most advanced treatments (anti-TNFs, JAK inhibitors, alpha 4 beta 7 integrin inhibition, and IL-23 plus IL-12/23 inhibitors) currently available in practice target primary and secondary loss of response in both diseases. However, the expert noted that about half of patients with IBD have extraintestinal manifestations of CD, which can be disabling, and only a few treatments address this issue. There is a preference for using anti-TNFs to treat concomitant extraintestinal manifestations and patients presenting with fistulizing perianal disease. The expert did not anticipate any shift in the treatment paradigm with the use of infliximab SC aside from the option of switching from the IV route to the SC option. According to the clinical expert, patients with confirmed moderate to severe CD (based on a pathological and histological diagnosis) will be best suited for treatment with infliximab SC. The expert highlighted that misdiagnosis is rarely observed in practice, although delays in diagnosis may occur. The expert noted that not all patients respond well to anti-TNF therapy. Patients who will be less suitable for infliximab SC will be those who fear self-injection.

The clinical expert consulted noted that the frequency of assessing response to treatment in the LIBERTY-CD trial differs from real-world settings. They highlighted that colonoscopy is seldom performed every 12 weeks as was the case of the trial procedures because of logistics and patient preference. C-reactive protein and fecal calprotectin are frequently used to monitor patient response to advance treatment in practice, according to the expert, while the Harvey-Bradshaw Index tool (as opposed to the CDAI used in the trial) is used to monitor treatment response for patients with CD. According to the clinical expert consulted by CADTH, factors that will lead to treatment discontinuation will be consistent with those outlined for current advanced therapies. The expert highlighted that patients will be evaluated in practice based on clinical

symptoms presentation and assessment of objective data. The expert mentioned that some patients may present as primary nonresponders during treatment and some patients may experience loss of response during treatment (the clinical expert noted that the standard percentage of patients with CD in clinical practice who experience loss of response in the first year of treatment is approximately 10% to 20%). The clinical expert highlighted that CD diagnosis are made by gastroenterologists; however, general internists with special interest in IBD have sufficient experience to prescribe infliximab for both populations. The expert noted that treatment initiation begins in private infusion centres where costs are covered by the drug manufacturer or other patient support programs. Patients will then be transitioned to self-injection of the SC formulation.

Clinician Group Input

No clinician group input was submitted for this review.

Drug Program Input

The clinical expert consulted by CADTH provided advice on the potential implementation issues raised by the drug programs.

Table 2: Responses to Questions From the Drug Programs

Drug plan questions	Clinical expert response
Relevant comparators	
There are no direct phase III head-to-head trials with other therapies used for the treatment of CD. Is conducting a head-to-head comparative trial against 1 of the numerous comparative treatments for CD a reasonable expectation in the target population? What could be the rationale for conducting trials against placebo?	The clinical expert recommended conducting a head-to-head comparative trial against currently listed therapies and future therapies for future trials in the CD setting. However, given that the LIBERTY-CD trial assessed the efficacy of a new mode of administration (i.e., SC) for infliximab that is already approved based on IV administration for use in the indicated populations, the use of a placebo group was considered appropriate by the clinical expert. While CDEC acknowledged the clinical expert input, it noted that comparative evidence is the focus of reimbursement reviews and the lack thereof poses serious limitations.
1. For what clinical reasons would infliximab IV be selected as therapy for CD, rather than the humanized versions of anti-TNF alpha drugs, adalimumab or golimumab? 2. When conventional therapies fail, are anti-TNF alpha drugs the preferred therapy to initiate or are other biologics with different mechanisms of action being selected because of patient-specific factors? 3. Is there a significant unmet need that infliximab SC fills for the treatment of CD?	1. According to the clinical expert, infliximab SC will be selected as a treatment of choice following the same reasons as selecting any other anti-TNF alpha drugs (i.e., the choice of treatment is complex and based on the disease phenotype and patient preference); golimumab is currently not used to treat patients with CD. The clinical expert highlighted that some clinicians believe that IV infusions provide a more rapid response compared to SC options. The expert added that patients who are hospitalized with severe CD will be more likely to receive the infliximab IV formulation. 2. The clinical expert noted that treatment choice in this setting is complex and dependent on multiple factors, including patient preference. Anti-TNF alpha drugs are not the automatic preferred drug in this setting. In the LIBERTY-CD trial, 325 patients (94.8%) had taken at least 1 prior medication (225 in the infliximab SC group [94.5%] and 100 in the placebo group [95.2%]). The most common prior medications reported were drugs for constipation

Drug plan questions	Clinical expert response
	(251 [73.2%]) in total. 3. According to the clinical expert, infliximab SC provides an SC option for patients already receiving infliximab IV in practice. Sc administration of advanced therapies is often desirable for patients as it reduces the need for infusion clinic appointments (e.g., time away from work) and allows them a sense of independence. Many patients find SC administrations more convenient. CDEC acknowledged and agreed with the clinical expert's responses.
Considerations for initiation of therapy	
The LIBERTY-CD trial assessed the superiority of infliximab SC over placebo in 343 patients with moderately to severely active CD (CDAI of 220 to 450 points). Some jurisdictions use the HBI in their coverage criteria to determine disease severity. Are there any differences in how the HBI performs against the CDAI score?	CDEC acknowledged input from the clinical expert noting that although CDAI scores are recommended by regulatory guidelines for the evaluation of patients with CD, they are seldom used in clinical practice because of the complexity of deriving these scores. According to the clinical expert, the HBI is an easier tool to complete in the clinical setting for patients with CD compared to the CDAI tool used in clinical trials. Both the CDAI and HBI have limitations because of the subjective nature of the information being gathered. The HBI tool uses different parameters to derive scores than the CDAI tool. The HBI is a subset of the CDAI (e.g., the HBI uses single-day readings, only 5 of the 8 CDAI variables, and sums variables instead of applying weighted coefficients).
Infliximab SC is indicated for patients who have had inadequate response or were intolerant to conventional therapy. Also, to be started on infliximab SC, patients must first be initiated on IV infliximab. 1. How many conventional therapies are typically tried before biologics, JAK inhibitors, or S1PRMs are considered for therapy? 2. Is there a standard definition of an inadequate response to conventional (or biologic) therapy for CD? 3. In your opinion, what percentage of patients would choose to switch from IV infliximab every 8 weeks to a biweekly injection of infliximab SC?	1. The clinical expert highlighted that biologics are now considered as advanced therapies, which include S1PRMs and JAK inhibitors. According to the expert, patients with moderate to severe CD should not have to have disease that fails with conventional therapy before access to advanced therapies are considered. Corticosteroids are not indicated for maintenance of remission in CD populations. 2. According to the clinical expert, markers to determine inadequate response to conventional therapies include inability to taper patients off of corticosteroids, lack of clinical remission, lack of endoscopic mucosal healing, and worsening of objective markers (e.g., fecal calprotectin). 3. The clinical expert expressed that it will be difficult to determine the percentage of patients who will switch from IV infliximab to SC infliximab. According to the expert, many patients already on stable IV therapy may choose to remain on that treatment plan. However, the expert noted that SC injections often lead to more stable therapeutic drug levels and can be clinically advantageous for some patients. The expert felt that the choice to switch will be made based on a case-by-case approach and after thorough discussion between the clinician and the patient. CDEC acknowledged the clinical expert's responses and noted that, per the Health Canda indication, infliximab SC is recommended in patients who have had an inadequate response or were intolerant to conventional therapy; removing the criteria of being intolerant or having disease that has had an inadequate response is out of scope of this indication.

Drug plan questions	Clinical expert response
There is variation in how public drug plans reimburse infliximab across Canada. If infliximab SC is recommended for reimbursement by CDEC, is it reasonable to use the existing initiation criteria for infliximab IV in each jurisdiction?	The clinical expert expressed that it will be reasonable to use the existing initiation criteria for infliximab IV in each jurisdiction for infliximab SC, although they would prefer not to include the need for a patient to be intolerant or their disease have inadequate response to conventional therapies (immunomodulators) as criteria for initiation. CDEC acknowledged the clinical expert's responses. CDEC noted that, per the Health Canda indication, infliximab SC is recommended in patients who have had an inadequate response or were intolerant to conventional therapy; removing the criteria of being intolerant or having disease that has had an inadequate response is out of scope of this indication.
Considerations for continuation or renewal of therapy	
If infliximab SC is recommended for reimbursement by CDEC, is it reasonable to use the existing renewal criteria for infliximab IV in each jurisdiction?	The clinical expert expressed that it will be reasonable to use the existing renewal criteria for infliximab IV in each jurisdiction for infliximab SC. CDEC acknowledged and agreed with the clinical expert's responses.
Considerations for discontinuation of therapy	
LIBERTY-CD: Loss of response criteria = an increase in CDAI of ≥ 100 points from the week 10 CDAI score with a total score ≥ 220 These patients received infliximab SC 240 mg (double injection [2 shots]) every 2 weeks from week 22. 1. Is the loss of response criteria used in the studies consistent with those used in clinical practice? 2. Is a loss of response to infliximab SC 120 mg or 240 mg inevitable for most patients based on the pathophysiology of CD? 3. In clinical practice, could infliximab SC doses be escalated above 240 mg if a patient's disease initially responds to a higher dose but then experiences a loss of response? 4. Are the loss of response rates in the LIBERTY-CD trial consistent with loss of response to infliximab IV in your clinical practice?	1. The clinical expert noted that the HBI tool is commonly used for patients with CD in practice, which is a subset of the CDAI (e.g., the HBI uses single-day readings, only 5 of the 8 CDAI variables, and sums variables instead of applying weighted coefficients). 2. According to the clinical expert, loss of response for infliximab 120 and/or 240 mg SC is not inevitable for patients with CD. The expert noted that many patients will remain on their original advanced therapy for many years. The expert highlighted that they have patients currently in practice that have been on infliximab since starting the medication for their disease. The best chance of achieving remission is commonly observed with the first advanced therapy chosen. 3. The clinical expert noted that there is currently no data on the use of escalated doses of infliximab SC above 240 mg in current practice. According to the expert, as infliximab SC is an SC formulation, the likelihood of a patient benefiting from the treatment at a higher dose would be minimal except in specific cases (like for those with severe perianal disease or other penetrating disease phenotypes). The LIBERTY-CD trial allowed dose adjustments from infliximab SC 120 mg to infliximab SC 240 mg every 2 weeks starting from week 22 through week 54, if a patient's disease initially responded but then lost response; these patients were considered as nonresponders or nonremitters in primary and secondary efficacy analyses. 4. The clinical expert noted that a proportion of patients in clinical practice lose response to advanced therapies over time (10% to 20% in the first year of treatment is the standard expected loss of response in CD populations, according to the expert). In the trial, approximately 5.0% of patients with CD showed loss of response. CDEC acknowledged the responses from the clinical expert. CDEC noted that escalating the dose of infliximab SC to 240 mg is outside of the Health Canada–recommended dose for infliximab SC.

Drug plan questions	Clinical expert response
If infliximab SC is recommended for reimbursement by CDEC, is it reasonable to use the existing discontinuation criteria for infliximab IV in each jurisdiction?	The clinical expert expressed that it will be reasonable to use the existing discontinuation criteria for infliximab IV in each jurisdiction for infliximab SC. CDEC acknowledged and agreed with the clinical expert's response.
Considerations for prescribing of therapy	
If infliximab SC is recommended for reimbursement by CDEC, is it reasonable to use the existing prescribing criteria for infliximab IV in each jurisdiction?	The expert expressed that it will be reasonable to use the existing prescribing criteria for infliximab IV in each jurisdiction for infliximab SC, although they would prefer not to include the need for a patient to be intolerant or their disease to have inadequate response to conventional therapies (immunomodulators) as criteria for prescribing. CDEC acknowledged the clinical expert's response and noted that, per the Health Canda indication, infliximab SC is recommended in patients who have had an inadequate response or were intolerant to conventional therapy; removing the criteria of being intolerant or having disease that has had an inadequate response is out of scope of this indication.
Generalizability	
The LIBERTY-CD trial did not evaluate patients aged < 18 years and did not enrol many patients aged > 65 years. Is there any desire to use infliximab SC in patients who are outside the age range of 18 to 65, or are there adequate treatment options for these patients?	The expert noted that there may be a need for access to infliximab SC in pediatric populations by pediatric gastroenterologists for patients aged younger than 18 years. The expert added that anti-TNF alpha drugs are currently used in patients older than aged 65 years. CDEC acknowledged that there is currently insufficient evidence to guide a recommendation for infliximab SC for patients aged younger than 18 or older than 65 years. CDEC noted that Health Canada has not authorized an indication for pediatric use and recommends caution when treating the older population as clinical studies with infliximab SC did not include sufficient numbers of patients aged 65 and older to determine whether they respond differently than younger patients.
System and economic issues	
The costs of IV infusions are paid by public drug plans (not sponsors) as these services are intentionally negotiated as part of the total reimbursed price. Given that infliximab SC maintenance therapy does not require IV infusion services, should its reimbursed price be lower than that of infliximab IV? Would the lowest priced SC biologic be a reasonable price target?	The clinical expert highlighted that all patients in the trials received IV induction therapy, which is different from other currently approved SC advanced therapies. CDEC noted that there is insufficient evidence to support a price premium for infliximab SC over other advanced treatment options.

CD = Crohn disease; CDAI = Crohn Disease Activity Index; CDEC = Canadian Drug Expert Committee; HBI = Harvey-Bradshaw Index; JAK = Janus kinase; S1PRMs = sphingosine 1-phosphat receptor modulators; SC = subcutaneous; TNF = tumour necrosis factor.

Clinical Evidence

Systematic Review

Description of Studies

LIBERTY-CD was a randomized, double-blind, placebo-controlled, phase III trial designed to assess the superiority of infliximab SC (120 mg) administered every 2 weeks over placebo in adults (18 to 75 years) with moderately to severely active CD whose disease had an inadequate response to conventional therapy. The LIBERTY-CD trial consisted of an induction phase, where enrolled patients received 5 mg/kg doses of infliximab intravenously; a maintenance phase, which consisted of patients who had no safety concerns and were considered clinical responders before week 10, randomized in a 2:1 ratio to receive infliximab SC or placebo as maintenance treatment for up to 54 weeks; and an extension study phase, which consisted of patients who had completed treatment at week 54 in both arms who were administered open-label infliximab SC for up to week 102. The extension phase is ongoing.

The coprimary objectives of the LIBERTY-CD trial were clinical remission (based on CDAI) and endoscopic response based on central SES-CD. Key secondary end points were CDAI-100 response, clinical remission based on abdominal pain and stool frequency, endoscopic remission based on central SES-CD, and corticosteroid-free remission at week 54. HRQoL, another secondary outcome, was measured using the short inflammatory bowel disease questionnaire (SIBDQ), the patient global scale, and the visual analogue scale (VAS) for local site pain assessment. Baseline characteristics were generally well balanced between the 2 treatment groups in the trial. The majority of patients were white and male, and the mean age ranged between 32 and 36 years across the 2 groups.

Study 1.6 (n = 131) was an open-label, parallel-group, phase I, randomized trial comparing the pharmacokinetic (PK) parameters, efficacy, and safety of infliximab 5 mg/kg IV administered every 8 weeks versus infliximab SC 120 mg or 240 mg administered every 2 weeks in adults (aged 18 to 75 years) with active UC and CD. The study had 2 parts, part 1 was a PK study designed to find the optimal dose of Remsima SC and has not been include in this report. Part 2 evaluated a PK outcome as a primary end point (trough concentration [$C_{trough, week22}$]) and clinical efficacy end points as secondary outcomes (CDAI-70 and CDAI-100 response, clinical remission, endoscopic response, clinical response [based on total and partial Mayo scores], mucosal healing and SIBDQ scores). Patients in the infliximab IV arm received IV infliximab up to week 22 and switched to infliximab SC by week 30 and continued up to week 54. Baseline characteristics were generally well balanced between the 2 treatment groups in the trial; most patients were white and male, and the mean age ranged between 35 and 36 years across the 2 groups.

Efficacy Results

The LIBERTY-CD Trial

Primary Outcomes

Clinical remission: The proportion of patients who achieved clinical remission at week 54 was higher (14; 62.3%) in the infliximab SC group than in the placebo group (36; 32.1%) (estimated treatment difference of 32.1%; 95% CI, 20.9 to 42.1; P < 0.0001).

Endoscopic response: The proportion of patients who achieved endoscopic response at week 54 was higher in the infliximab SC group (118; 51.1%) than in the placebo group (20; 17.9%), with an estimated treatment difference of 34.7% (95% CI, 24.2 to 43.5; P < 0.0001). Sensitivity and other supportive analyses were consistent with the primary analyses in the LIBERTY-CD trial.

Key Secondary Outcomes

Clinical remission: The proportion of patients who achieved clinical remission at week 54 based on abdominal pain and stool frequency at week 54 was greater in the infliximab SC group (131; 56.7%) than in the placebo group (35; 31.3%). The estimated treatment difference was 27.0% (95% CI, 15.8 to 37.1; P < 0.0001).

Endoscopic remission based on central SES-CD: More patients achieved endoscopic remission based on central SES-CD score at week 54 in the infliximab SC group (80; 34.6%) than in the placebo group (12; 10.7%). The estimated treatment difference was 24.9% (95% CI, 15.4 to 32.8).

Corticosteroid-free remission: The proportion of patients who achieved corticosteroid-free remission at week 54 was higher in the infliximab SC group (39 of 98; 39.8%) than in the placebo group (10 of 44; 22.7%), with an estimated treatment difference of 17.1% (95% CI, −0.4 to 31.5; P = 0.04).

Maintenance of clinical remission: Among the patients with clinical remission at week 10, a higher proportion of those in the infliximab SC group (121 of 174; 69.5%) achieved maintenance of clinical remission than those in the placebo group (32 of 91; 35.2%), with a treatment difference of 34.5% (95% CI, 22.0 to 45.6; P < 0.0001).

HRQoL: Fewer patients completed the SIBDQ for patient-reported outcomes in the LIBERTY-CD trial at week 54 compared to baseline in both groups (infliximab SC group, n = 167 at week 54 versus 231 at baseline, respectively, and placebo group, n = 51 at week 54 versus n = 111 at baseline, respectively). The least squares (LS) mean was 54.7 (standard error = 1.4) and the LS mean change from baseline to week 54 in SIBDQ scores was 17.6 in the infliximab SC group versus 15.1 in the placebo. The estimated treatment difference was 2.6 (95% CI, −2.1 to 7.2; P = 0.28). Of note, many patients in the placebo group required dose adjustment after losing response and therefore were excluded from the descriptive summary of SIBDQ scores from week 30 onward.

Study 1.6

The mean percent coefficient of variation (CV%) observed $C_{trough, week22}$ was higher in the infliximab SC 120 mg and 240 mg group than in the infliximab IV 5 mg/kg group at week 22 (CV = 21.5 mcg/mL [46.0%] and CV

= 2.9 mcg/mL [89.0%], respectively). The ratio of the geometric LS means was 1,154.2 with a lower bound 90% CI of 786.4%, which was greater than 80%, suggesting that infliximab SC was noninferior to infliximab IV in terms of PK (noninferior margin of 80%). The geometric LS mean observed $C_{trough, week22}$ was 20.9 mcg/mL and 1.8 mcg/mL in the infliximab SC 120 mg and 240 mg group and infliximab IV 5 mg/kg treatment group, respectively.

Secondary Outcomes

CD population within Study 1.6: Clinical remission at week 30 and week 54 in the infliximab SC group was 18 (64.3%) and 16 (57.1%), respectively, versus 14 (56.0%) and 14 (56.0%) at week 30 and week 54, respectively, in the infliximab IV group.

Endoscopic remission at week 22 and week 54 in the infliximab SC group was 5 of 14 (35.7%) and 6 of 12 (50%), respectively, versus 1 of 7 (14.3%) and 5 of 10 (50.0%), respectively, in the infliximab IV group. Endoscopic response at week 22 and week 54 in the infliximab SC group was 11 of 14 (78.6) and 9 of 12 (75.0), respectively, versus 3 of 7 (42.9%) and 8 of 10 (80.0%) in the infliximab IV group.

Harms

The LIBERTY-CD Trial

Reported treatment-emergent adverse events (TEAEs) were more common in the infliximab SC group (72.3%) than the placebo group (61.9%) in the maintenance phase of the LIBERTY-CD trial. The majority of TEAEs were grade 1 or 2 in intensity. The number of patients with at least 1 serious adverse event (AE) in the maintenance phase was 16 (6.7%) and 8 (7.6%) in the infliximab SC and placebo groups, respectively. The most common serious AEs reported were GI disorders (infliximab SC group n = 5 [2.1%]; placebo group = 2 [1.9%]) and infections and infestations (infliximab SC group n = 6 [2.5%]; placebo group = 1 [1.0%]).

In the LIBERTY-CD trial, the most common grade 3 AEs reported in the infliximab SC group were decreased neutrophil count (4.6%), increased creatine phosphokinase (CPK) (2.5%), increased blood bilirubin (2.1%), and hypertriglyceridemia (2.1%); the most commonly reported grade 4 AEs were increased CPK (3.4%) and decreased neutrophil count (0.8%). In the placebo group, decreased lymphocyte count (4.8%), anemia (3.8%), and increased CPK (1.9%) were the most common grade 3 AEs and increased CPK (1.9%) was the most common grade 4 AE.

AEs of special interest (infliximab SC versus placebo) included infection (31.1% versus 18.1%), localized injection-site reaction (5.9% versus 1.0%), systemic injection reaction (1.3% versus 1.0%), and injection-related reaction (1.3% versus 1.0%).

One death was reported in the LIBERTY-CD trial during the maintenance phase.

Study 1.6

There was a higher proportion of patients in the infliximab SC group (74.2%) of Study 1.6 reporting TEAEs during the maintenance phase than in the infliximab IV group (58.5%). The most commonly reported AEs in Study 1.6 during the maintenance phase (infliximab SC versus infliximab IV) included localized injection-site reactions (22.7% versus 4.6%), colitis ulcerative (4.5% versus 12.3%), and neutropenia (7.6% versus 4.6%).

The proportion of patients who experienced at least 1 TEAE on or after week 30 (i.e., after week 30 includes the pooled safety results of the 2 treatment groups after switching to or continuing with infliximab SC at week 30) was slightly higher in the infliximab SC treatment group (31 [47.0%] and 21 [32.3%] patients for the infliximab SC and infliximab IV treatment groups, respectively).

The most common AEs of special interest reported during the maintenance phase (infliximab SC versus infliximab IV) included infections (31.8% versus 29.2%), localized injection-site reaction (22.7% versus 4.6%), systemic injection reaction (3.0% versus 0%), and malignancy (1.5% versus 0%). An AE of special interest classified as systemic injection reaction on or after week 30 was reported for 1 patient (1.5%) in the infliximab SC group only.

There were no deaths reported in Study 1.6.

Critical Appraisal

Internal Validity

The LIBERTY-CD Trial

LIBERTY-CD is a randomized, placebo-controlled, multicentre, phase III trial designed with an open-label induction phase, a double-blind treatment phase (maintenance phase), and an open-label extension phase. Appropriate methods for blinding, treatment allocation, and randomization were employed.

The coprimary and key secondary outcomes were considered appropriate and recommended by the FDA and European Medicines Agency for assessing treatment effects for patients with CD in the trial settings. The assessed outcomes (e.g., CDAI scores, patient-reported outcomes, and safety outcomes) were subjective and potentially prone to assessment bias, which could bias the results in both groups in either direction.

There were imbalances in study treatment exposures between the 2 groups in the trial as there were more dose adjustments observed in the placebo group from week 22 compared to the infliximab SC group. There is also a potential bias from treatment awareness because of the frequent dose adjustments. This may have impacted the assessment of subjective outcomes in both populations in the LIBERTY-CD trial. The direction and magnitude of this potential bias are uncertain. There was also a concern for potential bias because of missing outcomes data for HRQoL, especially in the placebo group at week 54, rendering the results inconclusive.

Concomitant drug use in the maintenance phase was similar in both groups, apart from the use of budesonide, which was numerically higher in the infliximab SC group compared to the placebo group in the LIBERTY-CD trial. This potentially biased the efficacy results in favour of infliximab SC. There was a potential for residual drug effect of continued use of corticosteroids in the maintenance phase that may have impacted disease symptoms in the placebo and infliximab SC groups.

Study 1.6

Study 1.6 study is an open-label, randomized, parallel-group, multicentre, phase I study. Appropriate methods for randomization and treatment allocation were implemented. Baseline characteristics were similar between the 2 treatment groups in the trial, suggesting successful randomization.

The key rationale of Study 1.6 was to assess the noninferiority of infliximab SC against infliximab IV based on the primary outcome PK parameter $C_{trough, week22}$. Assessing $C_{trough, week\ 22}$ was considered appropriate by the clinical expert CADTH consulted, and it aligns with regulatory guideline requirements and published literature. A noninferiority margin of 80%, 1-sided alpha level 5%, expected ratio of 1.3, and CV% of 100% were assumed for part 1 of the study, with a 20% dropout rate. The study was powered to detect a statistical difference between the 2 groups of interest for the PK outcome.

Study 1.6 was not designed or powered to formally assess comparative efficacy outcomes (i.e., CDAI response, clinical response, clinical remission, endoscopic response and remission, mucosal healing, or HRQoL) making assessments of the relative therapeutic efficacy of infliximab SC against infliximab IV challenging. The sample size of Study 1.6 (i.e., n = 135) was considered relatively small to assess efficacy outcomes in the UC and CD populations. The observed treatment effect estimates may not be replicable in a larger study sample. The protocol did not prespecify a degree of difference from which to formally conclude noninferiority between infliximab SC and infliximab IV in terms of efficacy outcomes. While the evidence from Study 1.6 suggests infliximab SC is comparable to infliximab IV in terms of PK parameters, the lack of robust evidence on efficacy outcomes (efficacy outcomes were presented descriptively without any statistical comparison) precludes firm conclusions to support switching from infliximab IV to infliximab SC. The clinical expert consulted by CADTH did not anticipate clinically meaningful differences in efficacy between infliximab SC and infliximab IV due the products' same active ingredient (i.e., infliximab). They also did not anticipate any clinical concerns switching from the IV route to an SC option of infliximab as long as the choice to switch was made based on a case-by-case approach and after thorough discussion between the clinician and the patient.

There were concerns related to missing data between the 2 groups for HRQoL data assessed using the SIBDQ and VAS (for local site pain assessment) as fewer patients completed questionnaires at week 30 and week 54 compared to baseline for the CD and UC populations, which may have impacted the findings. It is therefore uncertain whether switching patients from infliximab IV to infliximab SC at week 30 in Study 1.6 resulted in comparable HRQoL outcomes in the UC and CD populations, respectively.

External Validity

The LIBERTY-CD Trial and Study 1.6 Part 2

LIBERTY-CD and Study 1.6 part 2 were multicentre, international trials that recruited adults aged 18 to 75 years. The inclusion and exclusion criteria of the trials were generally aligned with the selection criteria used in current practice to identify suitable patients for infliximab, according to the clinical expert consulted by CADTH. However, the exclusion of patients with prior experience with 2 or more lines of biologic therapy and/or JAK inhibitors was inconsistent with clinical practice as patients with prior exposure to other biologic drugs, including JAK inhibitors, are currently considered for treatment with infliximab IV in clinical practice, according to the clinical expert consulted by CADTH. Baseline disease characteristics of the patients in the LIBERTY-CD trial, such as CDAI scores (for patients with CD), the proportion of patients with moderate to severe disease, type of prior surgeries conducted, and other important objective outcomes, such as C-reactive protein and fecal calprotectin, that are important for monitoring patients in practice were

presented. There were no major differences between baseline characteristics in the infliximab SC group compared to the placebo group in the LIBERTY-CD trial.

The primary and key secondary outcomes were considered relevant to decision-making and adequately reflected efficacy and harms measures, according to the clinical expert consulted by CADTH. Concomitant medications used in the trial were reflective of clinical practice (except for mesazaline, which is seldom used in current practice). Corticosteroid tapering was consistent with regulatory guidelines, though the rates differed slightly from clinical practice.

Although the study design (induction and maintenance phases) in both trials is consistent with regulatory guidelines and reflects clinical practice, it generates an enriched population in the trial setting consisting of responders who can better tolerate infliximab and have disease that responds to infliximab. The induction period was also considered short (4 weeks for Study 1.6 and 10 weeks for the LIBERTY-CD trial) and failed to accommodate those whose disease was slow to respond, which is inconsistent with current practice, according to the clinical expert consulted by CADTH (dose-loading periods may extend up to 16 weeks). The duration of the maintenance phase was considered adequate to assess treatment effect by the clinical expert consulted by CADTH. The trial frequency of assessments (endoscopic assessments) was considered standard for clinical trials but differed from current practice because of the logistic constraints associated with conducting the assessments (i.e., practical limitations and the invasiveness of the procedure) and patient preferences.

The clinical expert consulted by CADTH noted that clinicians may consider higher doses of infliximab IV for patients with more severe disease in the induction and/or dose-loading phase, which could then be further adjusted based on patient response, patient preference, and safety profile. The dose of infliximab SC in Study 1.6 differed to the dose that is recommended by Health Canada for infliximab SC, in that weight-based dosing was performed (i.e., 120 mg or 240 mg of infliximab SC based on body weight [< 80 kg and ≥ 80 kg, respectively]), dose escalation to infliximab SC 240 mg every 2 weeks was allowed from week 30, and patients received only 2 doses during the induction phase rather than 3 doses, per the Health Canada recommendations. There is some uncertainty if the results of Study 1.6 are generalizable to the use of infliximab SC per the Health Canda–recommended dosage.

Indirect Comparisons

No indirect treatment comparison was submitted for this review.

Economic Evidence

Cost and Cost-Effectiveness

At the submitted price, the first-year costs of infliximab SC depend on which infliximab IV product is chosen for the induction period. Costs per patient when Inflectra is chosen for induction are $19,357 per patient for the first year and $15,424 in each subsequent year.

The sponsor submitted a cost comparison assessing infliximab SC compared with other infliximab IV biosimilars (Inflectra, Renflexis, and Avsola), adalimumab biosimilars, adalimumab (Humira), golimumab SC (Simponi), vedolizumab (Entyvio) IV and SC, and ustekinumab (Stelara).

CADTH identified the following limitations with the sponsor's submitted cost comparison:

- The comparative efficacy of infliximab SC with respect to non-infliximab comparators is uncertain.
- The sponsor-submitted pricing for infliximab SC at parity on a per mg basis does not align with annual costs.

The annual costs associated with infliximab SC are less than those associated with the branded IV product (Remicade) and with other branded biologic comparators such as adalimumab (Humira), golimumab SC (Simponi), vedolizumab (Entyvio) IV and SC, and ustekinumab (Stelara). Alternatively, infliximab SC is associated with increased annual costs when compared to other infliximab IV biosimilars (Inflectra, Renflexis, and Avsola) and adalimumab biosimilars, even though it is priced at parity with the least costly biosimilar per mg. These incremental costs or savings are based on publicly available list prices and may not reflect the actual prices paid by Canadian drug plans.

Based on publicly available list prices, the price of infliximab SC would have to be reduced by 16% for the annual cost of treatment acquisition to be equivalent to that of the least costly infliximab IV drugs (i.e., Renflexis and Avsola). Similarly, the submitted price of infliximab SC would have to be reduced by 40% to be equivalent to the treatment acquisition costs of other biologic disease-modifying antirheumatic drugs.

Budget Impact

CADTH identified the following key limitations with the sponsor's analysis: use of a claims-based approach to estimate the market size introduces uncertainty with the anticipated budget impact of infliximab, the average patient population weight did not align with clinical expectations, and the actual prices paid for the biologic comparators by Canadian jurisdictions is unknown.

CADTH did not conduct a base-case analysis, as the sponsor's submission provided adequate presentation of the budget impact for infliximab SC. The sponsor's base case suggested 3-year budgetary cost savings of $410,674 over 3 years.

CADTH presented a series of scenario analyses to test the impact of alternative assumptions on the estimated budget impact. The budget impact was sensitive to assumptions about the average patient weight and the price of infliximab SC.

CDEC Information

Members of the Committee

Dr. James Silvius (Chair), Dr. Sally Bean, Mr. Dan Dunsky, Dr. Edward Xie, Mr. Bob Gagne, Dr. Ran Goldman, Dr. Peter Jamieson, Mr. Morris Joseph, Dr. Christine Leong, Dr. Kerry Mansell, Dr. Alicia McCallum, Dr. Srinivas Murthy, Dr. Trudy Huyghebaert, Dr. Danyaal Raza, and Dr. Peter Zed

Meeting date: February 28, 2024

Regrets: Two expert committee members did not attend.

Conflicts of interest: None

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