Canada's Drug and
Health Technology Agency

CADTH Reimbursement Recommendation

Biologics for Plaque Psoriasis

Streamlined Drug Class Review

Summary of CADTH Recommendation

The CADTH Formulary Management Expert Committee (FMEC) concluded that the current evidence supports the improved efficacy of anti-interleukin (IL)-17 and anti-IL-23 drugs (new-generation biologics approved after 2015) compared to anti–tumour necrosis factor (TNF) and anti-IL-12/23 drugs (old-generation biologics, all but 1 approved before 2010) in the treatment of moderate to severe plaque psoriasis.

Based on a review of direct and indirect evidence from a recent Cochrane review, FMEC noted a consistent and meaningful benefit of anti-IL-17 and anti-IL-23 drugs compared to anti-TNF and anti-IL-12/23 drugs. The benefit was both in an improved probability of achieving clearance (e.g., Psoriasis Area and Severity Index [PASI] 90) and a lack of difference in harms.

Overall, the annual costs of branded agents appeared to be comparable, although biosimilar versions tend to be less costly. However, there was uncertainty as to actual costs due to confidential pricing, and systemic costs were not accounted for (e.g., costs of dose escalation or switching due to waning efficacy, and costs associated with worse clinical outcomes).

Based on the overall evidence on efficacy, safety, and costs, FMEC concluded that anti-TNF and anti-IL-12/23 classes of biologics were less favourable compared to anti-IL-17 and anti-IL-23 classes of biologics, although their relative costs were uncertain. Therefore, due to improved efficacy, anti-IL-17 and anti-IL-23 drugs should be prioritized in patients who are biologic-naive for the treatment of moderate to severe plaque psoriasis if the drug plan cost per patient is no more than the least expensive biologic (originator or biosimilar).

Therapeutic Landscape

What Is Moderate to Severe Plaque Psoriasis?

Plaque psoriasis is a chronic inflammatory skin disorder characterized by itchy, scaly patches of skin, and sometimes skin pain, joint pain, swelling or stiffness, and nail abnormalities. Moderate to severe psoriasis covers 10% or more of the body or is on sensitive areas like the face, hands, feet, or scalp. Approximately 30% of people with psoriasis have moderate to severe disease.

Why Did CADTH Conduct This Drug Class Review?

Publicly funded drug plans requested this streamlined drug class review, given the mounting direct evidence suggesting a benefit of anti-IL-17 and anti-IL-23 drugs despite a persistence of reimbursement requests for anti-TNF and anti-IL-12/23 drugs for patients who are biologic-naive.

Patient With Lived Experience

A patient with lived experience presented her journey with plaque psoriasis. She has been living with psoriasis for over 30 years and recalled her early struggles with finding clinicians who were comfortable treating the condition, having seen 8 dermatologists to date. She first tried conventional medications but found that methotrexate made her sick, topical tar had an unappealing smell and was difficult to use, and UV therapy didn't work. She then started treatment with etanercept but found that the efficacy waned, and she grew tired of the onerous injections with an escalated dose. Eventually, she found a dermatologist who treated her with new-generation biologics, including risankizumab and then bimekizumab. It wasn't until she started a biologic that she realized how bad her psoriasis actually was. Achieving full clearance was transformative, and getting access to the right treatment made all the difference.

Stakeholder Feedback

What Did We Hear From Patients?

Psoriasis medications should be easy to administer, provide quick and full relief of symptoms with minimal toxicity, and should be accessible and affordable. Lack of access to dermatologists and treatments are major barriers to care, and there is a negative emotional impact on patients each time a medication is changed.

What Did We Hear From Clinicians?

Special populations — including patients who are pregnant or breastfeeding, have comorbidities, or have plaques on special sites (e.g., hands, feet, or scalp) — may need special consideration for the choice of biologic. When switching treatments, patients worry about insurance coverage, out-of-pocket expenses, lack of effectiveness, and new adverse effects.

What Did We Hear From the Pharmaceutical industry?

It was suggested that there may be variability in interpretation and sensitivity of PASI scores across trials. Some manufacturers suggested supplementing the evidence with real-world data including long-term extension studies and conducting comparative cost-effectiveness analyses.

What Did We Hear From Public Drug Programs?

With the increasing prevalence of biosimilar versions of anti-TNF and anti-IL-12/23 biologics, drug plans noted that the prioritized use of anti-IL-17 and anti-IL-23 biologics would likely lead to increased costs in the future. With the prioritized use of some classes over others, drug plans noted physician autonomy as a concern in some jurisdictions.

Refer to the Stakeholder Input section of the CADTH report.

Deliberative Summary

Table 1

Why Did FMEC Make This Recommendation?

Questions or considerations	Discussion points
Is there sufficient evidence to support the added clinical benefit of anti-IL-17 and anti-IL-23 biologics compared to anti-TNF and anti-IL-12/23 biologics?	• Stakeholder input (from patient groups and clinician groups) pointed to a PASI 90 as the desired benchmark for a primary outcome measure (compared to PASI 75 in previous trials) to demonstrate the possibility of achieving complete or near-complete skin clearance. It was noted that anti-IL-17 and anti-IL-23 biologics consistently demonstrated a higher probability of a PASI 90 outcome compared to anti-TNF and anti-IL-12/23 biologics. • Direct comparative evidence against other active treatments is available for anti-IL-17 and anti-IL-23 biologics, whereas anti-TNF and anti-IL-12/23 biologics were typically compared only to placebo (during registration). • Based on direct evidence for the PASI 90 outcome, anti-IL-17 and anti-IL-23 biologics individually demonstrated greater effectiveness than anti-IL-12/23 and anti-TNF biologics except infliximab. • Based on indirect evidence from the NMA: ◦ PASI 90 for individual biologics: Infliximab, anti-IL-17 drugs (bimekizumab, ixekizumab, secukinumab, and brodalumab) and anti-IL-23 drugs (risankizumab and guselkumab) were significantly more likely to reach PASI 90 than ustekinumab, an anti-IL-12/23 drug, and 3 anti-TNF drugs (adalimumab, certolizumab, and etanercept). ◦ PASI 90 at the class level: The anti-IL-17 class was more effective than the anti-IL-23, anti-IL-12/23, and anti-TNF classes for the PASI 90 outcome. The anti-IL-23 class was more effective than the anti-IL-12/23 and anti-TNF classes for the PASI 90 outcome. ◦ Quality of life at the class level: There were no differences between the anti-IL-17, anti-IL-23, and anti-IL-12/23 classes. However, the anti-IL-23, anti-IL-17, and anti-IL-12/23 classes were more favourable than the anti-TNF class. ◦ Serious adverse events at the class level: There were no significant differences between classes of biologics.
Is there sufficient evidence to support no intraclass differences within anti-IL-17 and anti-IL-23 biologic classes and anti-TNF and anti-IL-12/23 biologic classes?	• While the anti-IL-17 and anti-IL-23 classes of biologics were deemed more effective than the anti-TNF and anti-IL-12/23 classes of biologics in general, there were some differences identified in terms of efficacy for individual agents. Overall, particularly within the anti-IL-17 and anti-IL-23 classes, there are no meaningful differences between drugs across all outcomes examined. • Infliximab (an anti-TNF biologic) showed greater probability of a PASI 90 outcome than other members of the class. There is 1 comparison of infliximab vs. etanercept demonstrating an effect size of 9.20. In the indirect comparisons at the drug level, infliximab also demonstrated a relative benefit compared to other members of the class. However, it was noted that infliximab had lower certainty of evidence for PASI 90 according to CINeMA. Moreover, it is administered intravenously (unlike the anti-IL-17 and anti-IL-23 biologics that have subcutaneous administration), which negatively impacts ease of administration. • For the anti-IL-17 and anti-IL-23 classes of biologics, there is little direct evidence comparing members within a class. Overall, there is insufficient evidence to determine differences in efficacy and safety of different drugs within a class. • Based on the NMA there were no significant differences with respect to adverse events between drugs of a class. • The clinical experts regarded all anti-IL-17 and anti-IL-23 biologics as comparable in their efficacy, including in special populations (e.g., pregnancy and breastfeeding, patients with comorbidities including psoriatic arthritis, and so on).

Questions or considerations	Discussion points
Is there a high level of confidence in the NMA to support differences between the anti-IL-17 and anti-IL-23 biologics with anti-TNF and anti-IL-12/23 biologics?	• The NMA was performed under the auspices of Cochrane and the methods were well described. Cochrane procedures were followed, heterogeneity was addressed in the selection process, risk of bias was assessed, and an assessment of the certainty of evidence was included. • CADTH assessed the quality of the Cochrane systematic review and NMA using the AMSTAR 2 and ISPOR network meta-analysis tools and found a high rating, increasing the confidence in the results.
Is there an economic benefit to prioritizing anti-IL-17 and anti-IL-23 biologics over anti-TNF and anti-IL-12/23 biologics?	• Most biologics have agreements through pCPA; thus, discounted drug costs are not publicly available. • Annual costs of branded biologics are comparable, although biosimilars tend to cost less. • Given the uncertainty of confidential prices and introduction of less costly biosimilar versions, there was limited confidence regarding the relative costs of anti-IL-17 and anti-IL-23 biologics vs. anti-TNF and anti-IL-12/23 biologics.

CINeMA = Confidence in Network Meta-Analysis; IL = interleukin; NMA = network meta-analysis; pCPA = pan-Canadian Pharmaceutical Alliance; PASI = Psoriasis Area and Severity Index; TNF = tumour necrosis factor.

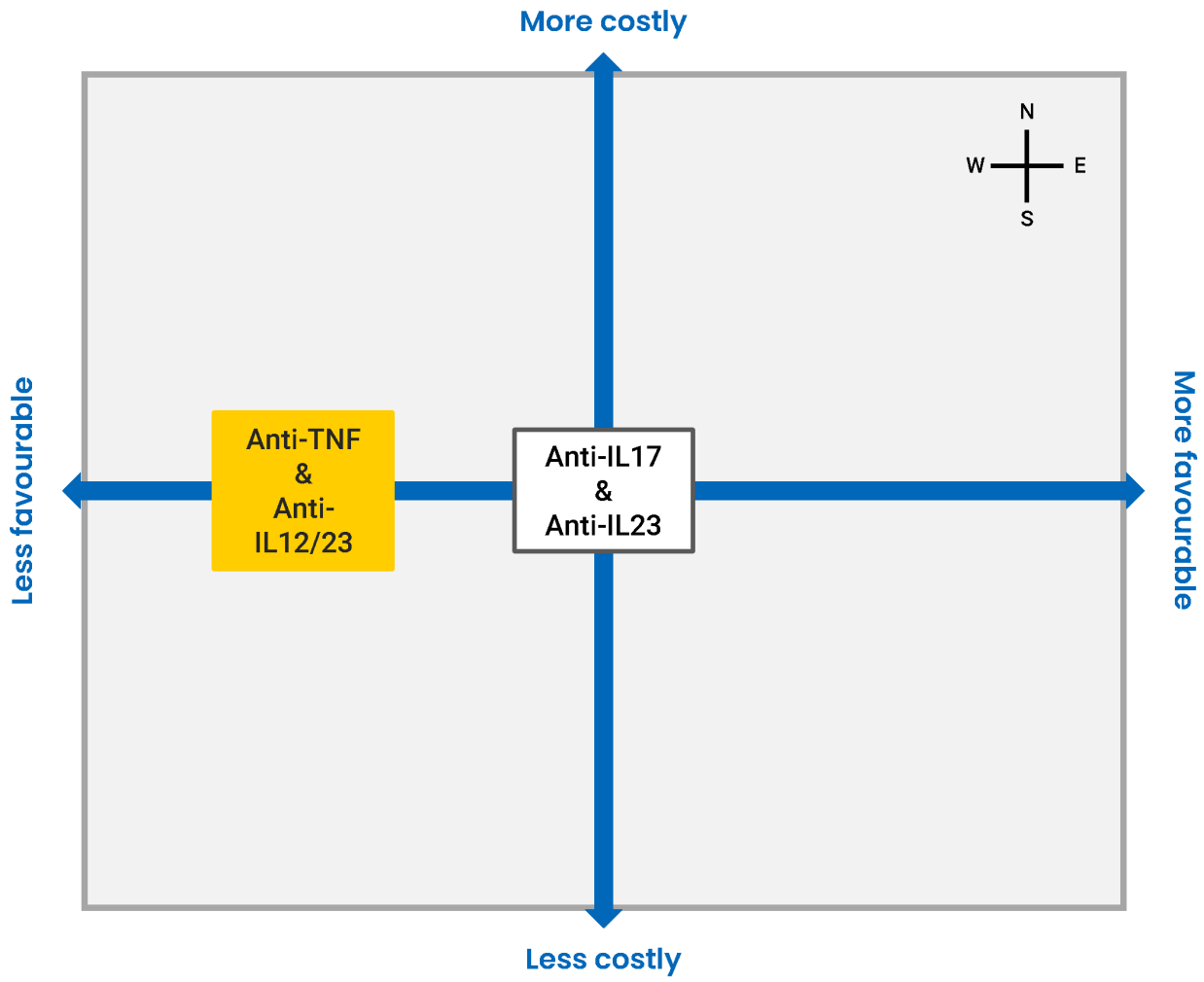
Decision Plane

A decision plane was used during the deliberation to assess the classes of biologics within 2 domains: cost and favourability (as defined by the totality of evidence on efficacy and safety). With anti-IL-17 and anti-IL-23 biologics at the origin, FMEC deliberated on the location of anti-TNF and anti-IL-12/23 biologics on the decision plane.

FMEC concluded that anti-TNF and anti-IL-12/23 biologics were less favourable compared to anti-IL-17 and anti-IL-23 biologics, but were uncertain as to their relative costs. Uncertainty in costs resulted in anti-TNF and anti-IL-12/23 biologics being placed within both the northwest and southwest quadrants.

Figure 1

Decision Plane



IL = interleukin; TNF = tumour necrosis factor.

Full Recommendation

FMEC concluded that the current evidence supports the improved efficacy of anti-IL-17 and anti-IL-23 biologics compared to anti-TNF and anti-IL-12/23 biologics in the treatment of plaque psoriasis.

Therefore, anti-IL-17 and anti-IL-23 biologics should be prioritized in patients who are biologic-naive for the treatment of moderate to severe plaque psoriasis if the drug plan cost per patient is no more than the least expensive biologic (originator or biosimilar).

Feedback on Draft Recommendation

CADTH received feedback on the draft recommendation rom 5 manufacturers and a joint submission from 3 patient groups.

Most manufacturers agreed with the proposed recommendations and the general position that anti-IL-17 and anti-IL-23 classes of biologics provide better therapeutic benefit than anti-TNF and anti-IL-12/23 classes of biologics for patients with moderate to severe psoriasis. Some manufacturers suggested incorporating intraclass differences in efficacy between the anti-IL-17 and anti-IL-23 drugs in the recommendations. However, FMEC concluded that there is insufficient evidence to determine differences in efficacy and safety of different drugs within a class. As this is a drug class review, the recommendations are based on interclass differences. As such, minor revisions were made to the final recommendation to remove references to comparisons of individual biologics. One manufacturer suggested adding clarity on patients who are biologic-experienced, although no action was taken as the recommendations are only intended for patients who are biologic-naive.

One manufacturer disagreed with the recommendations, citing a lack of an economic analysis to determine product value and the use of a single source of evidence for comparing drug classes. CADTH notes that the economic analysis was appropriate given the relative costs and efficacy of the drug classes, as demonstrated in the decision plane. The Cochrane review was chosen as the basis of the clinical review as it is the most recent, comprehensive, and well-conducted NMA on the efficacy and safety of biologics for plaque psoriasis.

Patient groups were pleased that the FMEC updates to the recommendations affirmed that all biologics for plaque psoriasis should be reimbursed, but were disappointed that prerequisite systemic therapies (e.g., methotrexate and cyclosporine) were not in the scope of the review. CADTH notes that the evidence considered in this review did not allow for a comparison of biologics to prerequisite therapies, although this could be a potential area for future review.

FMEC Information

FMEC information: Dr. Emily Reynen (Chair), Dr. Alun Edwards, Ms. Valerie McDonald, Dr. Marianne Taylor, Dr. Jim Silvius, Dr. Maureen Trudeau, Dr. Dominika Wranik, Dr. Wayne Gulliver (guest specialist), and Dr. Kevin Peter (guest specialist).

Meeting date: August 24, 2023

Conflicts of interest: None

Special thanks: CADTH extends our special thanks to the individuals who presented directly to FMEC on behalf of patients with lived experience, patient organizations representing the community of those living with plaque psoriasis, the Canadian Association of Psoriasis Patients, the Canadian Psoriasis Network, the Canadian Skin Patient Alliance, and the Canadian Dermatology Nurses Association, which include Reena Ruparelia, Helen Crawford, Antonella Scali, Rachael Manion, and Sandra Walsh.

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