CADTH

CADTH COMMON DRUG REVIEW

CADTH Canadian Drug Expert Committee Recommendation

(Final)

RISANKIZUMAB (SKYRIZI — ABBVIE)
Indication: Adult patients with moderate to severe plaque psoriasis.

RECOMMENDATION
The CADTH Canadian Drug Expert Committee (CDEC) recommends that risankizumab be reimbursed for the treatment of moderate to severe plaque psoriasis in adults only if the following conditions are met:

Conditions for Reimbursement

- In a manner similar to other biologics reimbursed for the treatment of moderate to severe plaque psoriasis.
- Treatment should be discontinued if a response to risankizumab has not been demonstrated by 16 weeks.
- The drug plan cost for risankizumab should not exceed the drug plan cost of treatment with the least costly biologic therapy reimbursed for the treatment of moderate to severe plaque psoriasis.

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CADTH

RISANKIZUMAB (SKYRIZI — ABBVIE)

Indication: Adult patients with moderate to severe plaque psoriasis.

Recommendation

The CADTH Canadian Drug Expert Committee (CDEC) recommends that risankizumab be reimbursed for the treatment of adult patients with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy if the following conditions are met:

Conditions for Reimbursement

- In a manner similar to other biologics reimbursed for the treatment of moderate to severe plaque psoriasis.
- Treatment should be discontinued if a response to risankizumab has not been demonstrated by 16 weeks.
- The drug plan cost for risankizumab should not exceed the drug plan cost of treatment with the least costly biologic therapy reimbursed for the treatment of moderate to severe plaque psoriasis.

Reasons for the Recommendation

1. In four randomized, double-blind, double-dummy, placebo- and active comparator-controlled studies, (UltIMMA-1, N = 506, UltIMMA-2, N = 491; IMMhance, N = 507; and IMMvent, N = 605), risankizumab was associated with a statistically significant and clinically meaningful improvement in skin clearance (Psoriasis Area and Severity Index [PASI] 90) and health-related quality of life (HRQoL) compared with placebo, ustekinumab, and adalimumab in the induction period (16 weeks). In UltIMMA-1 and UltIMMA-2, the benefit of risankizumab over ustekinumab for PASI 90 was maintained up to week 52. In the IMMvent trial, patients who did not exhibit an adequate response to adalimumab during the induction period had a higher rate of achieving PASI 90 response after switching to risankizumab for 28 weeks, compared with those continuing adalimumab.
2. Results of the two indirect treatment comparisons (ITCs) included in the CADTH Common Drug Review (CDR) suggest that use of risankizumab is associated with similar PASI 75 and PASI 90 responses to ixekizumab, brodalumab, and guselkumab, and was superior to placebo, apremilast, etanercept, adalimumab, ustekinumab, infliximab, and secukinumab in patients with moderate to severe chronic plaque psoriasis over short-term induction (10 to 16 weeks) treatment periods. However, there is no direct evidence comparing risankizumab with the other available interleukin (IL)-23 inhibitor, guselkumab, or any of the three available IL-17 inhibitors (brodalumab, secukinumab, ixekizumab). Furthermore, the relative efficacy and safety of risankizumab in comparison with biologics other than ustekinumab and adalimumab beyond a short-term induction period remains unknown. Finally, HRQoL was not evaluated in the ITCs.
3. At the submitted price, risankizumab is not cost-effective at a willingness-to-pay threshold of $50,000 per quality-adjusted life-year (QALY). Given the uncertainty regarding the comparative efficacy of risankizumab compared with other biologics that may be reimbursed for the treatment of moderate to severe plaque psoriasis and the limitations of the cost-utility analysis model, there is insufficient evidence to justify a cost premium over the least expensive biologic drug reimbursed for the treatment of moderate to severe plaque psoriasis.

Implementation Considerations

A response to treatment is defined as an achievement of at least a 75% reduction in the PASI score (PASI 75) by week 16.

Discussion Points

1. CDEC noted that including risankizumab, there are nine biologics approved for the treatment of moderate to severe plaque psoriasis in Canada. Risankizumab is the second anti-IL-23 inhibitor in Canada; the other is guselkumab. There is no direct evidence to suggest that risankizumab offers a superior benefit over guselkumab. Results of the two ITCs evaluated in the CDR review found no significant difference between risankizumab and guselkumab in terms of achieving PASI 75 or PASI 90 assessed during short-term induction treatment periods between 10 to 16 weeks.

2. CDEC noted that there is no comparative evidence for risankizumab versus any other biologic therapy beyond 52 weeks. Given that plaque psoriasis requires lifelong treatment, there is uncertainty regarding the long-term effectiveness and safety of risankizumab over other currently available biologics for moderate-to-severe plaque psoriasis.
3. CDEC agreed that PASI 90 is currently the standard outcome when evaluating whether skin clearance is achieved in patients with moderate to severe plaque psoriasis in Canadian clinical practice. However, comparative evidence for this outcome was not available for all biologic therapies used in Canada. For both ITCs appraised in this CDR review, PASI 75 was the only clinically relevant outcome with data available for each biologic, and was therefore the outcome upon which comparative efficacy could be assessed.
4. CDEC viewed the results of the economic analysis submitted by the manufacturer as uncertain due to structural issues with the submitted model, including the lack of long-term comparative data and uncertainty regarding longer-term discontinuation rates. CDEC also noted a lack of transparency into the true drug plan costs for biologic drugs used for moderate to severe plaque psoriasis.

Background

The Health Canada indication for risankizumab is for the treatment of adult patients with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy. Risankizumab is a humanized immunoglobulin G1 monoclonal antibody that selectively binds with high affinity to the p19 subunit of human IL-23 cytokine and inhibits IL-23 signaling in cell-based assays, including the release of the pro-inflammatory cytokine IL-17. Risankizumab is available as a solution for injection in a single-use, pre-filled syringe containing 75 mg risankizumab in 0.83 mL (90 mg/mL). The Health Canada–approved dosage is 150 mg (two 75 mg injections) administered by subcutaneous (SC) injection at week 0, week 4, and every 12 weeks thereafter.

Summary of Evidence Considered by CDEC

The committee considered the following information prepared by CDR: a systematic review of four randomized controlled trials (RCTs) of risankizumab, two ITCs, and a critique of the manufacturer's pharmacoeconomic evaluation. The committee also considered input from a clinical expert with experience in treating patients with plaque psoriasis, and patient group–submitted information about outcomes and issues important to patients.

Summary of Patient Input

Two patient input submissions were received for this CDR review: one from the Arthritis Consumer Experts (ACE) and one from the Canadian Psoriasis Network (CPN) in collaboration with the Canadian Skin Patient Alliance (CSPA) and the Canadian Association of Psoriasis Patients (CAPP). Patient perspectives were obtained from surveys and formal and informal discussions. None of the submitting organizations declared any conflicts of interest or received any assistance in preparing their submissions. CPN, CSPA, and CAPP disclosed financial support from AbbVie within the past two years. The following is a summary of key input from the perspective of the patient groups:

- In the CPN/CSPA/CAPP patient input survey, 74% of respondents described their condition as "uncontrolled." In addition to the physical symptoms of plaque psoriasis, patients reported impacts on mental and emotional health. Feelings of frustration, worry, embarrassment, anxiety, and depression were commonly mentioned.
- Some characteristics of current treatments mentioned in both of the patient group submissions include: switching therapies as one stops working or in the hope of finding something more effective, varying success from patient to patient (and a consequent desire for more and alternative treatment options), and variable experience with side effects. In the input submitted by ACE, patients were concerned about side effects associated with long-term use of currently available treatments.
- Patients expressed a desire for additional treatment options that adequately control or stop symptoms, such as itchiness, scaling, pain, bleeding, and flaking, without side effects. Treatment responses vary among patients and what works for one may not work for another, even when the symptoms are similar. Therefore, the availability of more treatment options would provide patients with choices to manage the disease. In the input submitted by ACE, patients noted that they desired an effective treatment with the lowest risk of side effects.

Clinical Trials

A total of four phase III RCTs were included in the CDR systematic review: UltIMMA-1 (N = 506), UltIMMA-2 (N = 491), IMMhance (N = 507), and IMMvent (N = 605). All four trials enrolled patients with moderate to severe plaque psoriasis (defined as body surface area involvement of ≥ 10%, PASI ≥ 12, and static Physician Global Assessment [sPGA] ≥ 3 as per the inclusion criteria of each study, which is aligned with definitions of disease severity used in clinical trials in the Canadian Guidelines for the Management of Plaque Psoriasis).[1] In each study, patients were randomized to double-blind treatment in blocks and stratified by body weight (≤ 100 kg versus > 100 kg) and prior exposure to tumour necrosis factor antagonists. All studies included patients across multiple sites in Canada.

- UltIMMA-1 and UltIMMA-2 were identically designed multi-centre, randomized, double-blind, double-dummy, placebo- and active comparator-controlled studies. Part A (weeks 0 to 16) was a 16-week double-blind treatment period in which patients were randomized in a 3:1:1 ratio to treatment with either risankizumab (150 mg SC), ustekinumab (45 mg or 90 mg SC for patients ≤ 100 kg or > 100 kg, respectively) or placebo SC at weeks 0 and 4. In part B (weeks 16 to 52), all patients randomized to placebo in part A were switched to treatment with risankizumab (150 mg every 12 weeks), while patients randomized to risankizumab or ustekinumab continued their assigned treatment (risankizumab every 12 weeks or ustekinumab at weeks 16, 28, and 40) up to week 40, and were followed up to week 52. In UltIMMA-1 and UltIMMA-2, 98% of patients completed part A and more than 95% of patients completed part B.
- IMMhance was a multi-centre, randomized, double-blind, placebo-controlled trial. In part A1 (weeks 0 to 16) patients were randomized in a 4:1 ratio to either risankizumab 150 mg or placebo SC at weeks 0 and 4 up to week 16. Patients originally randomized to risankizumab continued their treatment every 12 weeks up to week 28 (which was the beginning of part B), at which time all patients were assessed for response to risankizumab based on the sPGA. Patients who had an sPGA of clear (0) or almost clear (1) at week 28 were re-randomized in a 1:2 ratio to continue treatment with risankizumab 150 mg or placebo SC every 12 weeks up to week 88. After week 32, all re-randomized patients who experienced relapse were switched to open-label treatment with risankizumab and retreated with risankizumab. In IMMhance, 98.6% of patients completed part A1 and less than 1% of those did not continue the study. Part B of the IMMhance study is ongoing, with 4.2% of patients withdrawing from the study as of the interim analysis available for this review (cut-off date of September 1, 2017).
- IMMvent was a multi-centre, randomized, double-blind, double-dummy, active-controlled trial designed to compare risankizumab versus adalimumab (part A, weeks 0 to 16); it was followed by switching patients who had an inadequate response to adalimumab to risankizumab versus continuing treatment with adalimumab (part B, weeks 16 to 44). In part A, patients were randomized in a 1:1 ratio to either risankizumab (150 mg at weeks 0 and 4) or adalimumab SC (80 mg at randomization, and 40 mg starting at week 1 and every other week thereafter) up to week 16. Those who were responders and nonresponders to adalimumab either continued adalimumab treatment or were switched to risankizumab, respectively. In IMMvent, 96.7% of patients completed part A with all patients entering part B. Completion rates in part B were as follows: 97.2 % in patients continuing on adalimumab, 89.5% in patients switched from adalimumab to risankizumab (nonresponders), and 93.6% in re-randomized patients.

The key limitation identified was duration of the trials. Although a 16-week period is adequate to determine patient response, given that psoriasis is a chronic condition requiring lifelong treatment, the 52-week trial duration is insufficient to determine whether risankizumab will be efficacious and safe over the long term. More long-term data are required to understand the prolonged efficacy and safety of risankizumab for moderate to severe plaque psoriasis. Further, there is a lack of direct evidence comparing risankizumab with the other IL-23 inhibitor guselkumab, and the IL-17 inhibitors (brodalumab, secukinumab, ixekizumab).

Outcomes

Outcomes were defined a priori in the CDR systematic review protocol. Of these, the committee discussed the following: HRQoL, as measured by the Dermatology Life Quality Index (DLQI); and skin clearance measures, PASI 90 and sPGA. The co-primary outcomes in each of the four trials were PASI 90 and sPGA of clear or almost clear at 16 weeks. HRQoL and skin clearance were identified as being of particular importance to patients in the input received by CADTH from patient groups.

Efficacy

A statistically significantly larger proportion of patients achieved DLQI of 0 or 1 (i.e., psoriasis has no effect at on a patient's life) at week 16 in the risankizumab groups compared with the placebo and ustekinumab groups in UltIMMA-1 (65.8% versus 7.8%;

adjusted difference, 57.9; 95% confidence interval [CI], 50.4 to 65.3; and 43.0%; adjusted difference, 23.0; 95% CI, 11.9 to 34.0; *P* < 0.001 for both) and UltIMMA-2 (66.7% versus 4.1%; adjusted difference, 62.2; 95% CI, 55.5 to 68.9; and 46.5%, adjusted difference, 20.2, 95% CI, 9.1 to 31.4; *P* < 0.001 for both); and the placebo group in IMMhance (65.4% versus 3.0%; adjusted difference, 62.1; 95% CI, 56.4 to 67.9; *P* < 0.001). A DLQI score of 0 or 1 at week 16 was a ranked secondary end point in these three trials, and results were controlled for multiplicity. In IMMvent, more patients in the risankizumab group achieved a DLQI score of 0 at week 16 than in the adalimumab group (65.8% versus 48.7%; adjusted difference, 17.1; 95% CI, 9.3 to 24.8), but this outcome was not included as a ranked secondary end point and therefore was not adjusted for multiplicity. Patients in the risankizumab group appeared to continue to maintain improved HRQoL as compared with those receiving ustekinumab up to week 52 in part B of UltIMMA-1 and UltIMMA-2. Although score on the DLQI was not included in the statistical hierarchy in part B of any trials included in this review, given the magnitude of the statistical significance of these results, it is unlikely that type I error affected these results.

The magnitude of the treatment effect for PASI 90 and sPGA clear or almost clear at week 16 was approximately 20% in favour of risankizumab over ustekinumab or adalimumab in each study, which was considered likely clinically meaningful according to the clinical expert consulted for this CDR review. A statistically significantly larger proportion of patients in the intent-to-treat population achieved PASI 90 at week 16 in the risankizumab groups compared with the placebo and ustekinumab groups in UltIMMA-1 (75.3% versus 4.9%; adjusted difference, 70.3; 95% CI, 64.0 to 76.7; and 42.0% adjusted difference, 33.5; 95% CI, 22.7 to 44.3; *P* < 0.001 for both) and UltIMMA-2 (74.8% versus 2.0%; adjusted difference, 72.5; 95% CI, 66.8 to 78.2; and 47.5%; adjusted difference, 27.6; 95% CI, 16.7 to 38.5; *P* < 0.001 for both); the placebo group in IMMhance (73.2% versus 2.0%; adjusted difference, 70.8; 95% CI, 65.7 to 76.0; *P* < 0.001); and the adalimumab group in IMMvent (72.4% versus 47.4%; adjusted difference, 24.9; 95% CI, 17.5 to 32.4; *P* < 0.001).

The proportion of patients who achieved PASI 90 at week 52 was statistically significantly greater in patients who continued treatment with risankizumab versus ustekinumab in both UltIMMA-1 (81.9% versus 44.0%; adjusted difference, 38.3; 95% CI, 27.9 to 48.6; *P* < 0.001) and UltIMMA-2 (80.6% versus 50.5%; adjusted difference, 30.2; 95% CI, 19.6 to 40.9; *P* < 0.001) trials. In IMMvent, switching to risankizumab was superior to continuing adalimumab in the re-randomized patient population in terms of achieving PASI 90; 66.0% of patients re-randomized to risankizumab versus 21.4% of those who continued on adalimumab achieved PASI 90 at week 44 (adjusted difference, 45.0; 95% CI, 28.9 to 61.1; *P* < 0.001).

A larger proportion of patients achieved PASI 75 at week 16 in the risankizumab compared with the placebo and ustekinumab groups in UltIMMA-1 (89.1% versus 8.8%; adjusted difference, 80.2; 95% CI, 73.8 to 86.7; *P* < 0.001, and 76.0%; adjusted difference, 13.3; 95% CI, 4.4 to 22.3; *P* = 0.003) and UltIMMA-2 (90.8% versus 6.1%; adjusted difference, 84.7; 95% CI, 79.0 to 90.4; and 69.7%; adjusted difference, 21.2; 95% CI, 11.7 to 30.7; *P* < 0.001 for both); the placebo group in IMMhance (88.7% versus 8.0%; adjusted difference, 80.6; 95% CI, 74.5 to 86.6; *P* < 0.001); and the adalimumab group in IMMvent (90.7% versus 71.7%; adjusted difference, 18.9; 95% CI, 13.0 to 24.9; *P* < 0.001). PASI 75 at week 16 was a ranked secondary end point in IMMhance and IMMvent, but was outside the hierarchical testing procedure in UltIMMA-1 and UltIMMA-2, and statistical analyses were not controlled for multiplicity in these trials.

A statistically significantly larger proportion of patients achieved sPGA of clear or almost clear at week 16 in the risankizumab group compared with the placebo and ustekinumab groups in UltIMMA-1 (87.8% versus 7.8%; adjusted difference, 79.9; 95% CI, 73.5 to 86.3; and 63.0%; adjusted difference, 25.1; 95% CI, 15.2 to 35.0: *P* < 0.001 for both) and UltIMMA-2 (83.7% versus 5.1%; adjusted difference, 78.5; 95% CI, 72.4 to 84.5; and 61.6%; adjusted difference, 22.3; 95% CI, 12.0 to 32.5; *P* < 0.001 for both); the placebo group in IMMhance (83.5% versus 7.0%; adjusted difference, 76.5; 95% CI, 70.4 to 82.5; *P* < 0.001); and the adalimumab group in IMMvent (83.7% versus 60%; adjusted difference, 23.3; 95% CI, 16.6 to 30.1; *P* < 0.001).

Harms (Safety)

The proportion of patients experiencing an adverse event (AE) was similar or slightly lower in the risankizumab versus ustekinumab group in UltIMMA-1 and UltIMMA-2, and similar to placebo in both trials. In UltIMMA-1 and UltIMMA-2, the most frequently reported AEs were upper respiratory tract infection (12.5% and 14.0% in UltIMMA-1; 10.9% and 12.1% in UltIMMA-2) and viral respiratory tract infection (16.1% and 22.0% in UltIMMA-1; 13.9% and 20.2% in UltIMMA-2) in the risankizumab and ustekinumab group, respectively. In IMMhance, AEs occurred in a similar proportion of patients in the risankizumab and placebo groups throughout the study; the most frequently reported AEs during part B were upper respiratory tract infection (10.8% and 8.9%) and viral upper

respiratory tract infection (15.3% and 16.4%) in patients who were re-randomized to continue on risankizumab and those who switched to placebo, respectively. In IMMvent, AEs occurred in a similar proportion of patients in the risankizumab (55.8%) and adalimumab (56.9%) groups during part A, but were reported in a higher proportion of patients re-randomized to risankizumab (75.5%) than in patients re-randomized to adalimumab (66.1%) during part B. The most frequently reported AEs were upper respiratory tract infection (7.0% and 3.9%) and viral respiratory tract infection (8.6% and 7.9%) in the risankizumab and adalimumab groups, respectively.

Serious adverse events (SAEs) occurred infrequently regardless of the treatment period and treatment group in all four included trials. No SAEs were observed in more than two patients in any study. The rate of withdrawal due to AEs was low across all trials. Treatment with risankizumab did not appear to be associated with increased mortality as there were only seven deaths reported across the four included trials (i.e., two deaths each in UltIMMA-2 and IMMhance, and three deaths in IMMvent, with no deaths reported in UltIMMA-1).

Notable harms of interest to this review included infections, injection site reactions, hypersensitivity events, immunogenicity, inflammatory bowel disease, major adverse cardiovascular events, and psychiatric symptoms. Fungal infections were more common in patients treated with risankizumab, but none were considered serious. Injection site reactions and hypersensitivity reactions were infrequent in the studies and similar between active treatment groups. There were very few instances of major adverse cardiovascular events and psychiatric symptoms, and no clear differences between groups. The incidence of inflammatory bowel disease was not reported in any of the trials.

Indirect Treatment Comparisons

Two ITCs (one submitted by the manufacturer, and one conducted and published by the Institute for Clinical and Economic Review) were summarized and critically appraised in the CDR review of risankizumab. Both ITCs were conducted with adjustment for placebo response and under a random-effects model. Inclusion criteria differed between the two ITCs. The manufacturer-submitted ITC excluded studies of drugs and regimens not recommended by the National Institute for Health and Care Excellence (NICE) while allowing the inclusion of phase II trials. The Institute for Clinical and Economic Review ITC excluded phase II and pilot trials but did not use NICE recommendations as a criterion. Despite the different evidence base, the results of both ITCs were similar. One limitation common to both ITCs included the lack of an inconsistency model to assess the consistency assumption. In addition, while the use of an adjusted placebo response is practiced in reviews of this disease area, it is not without its limitations and added assumptions, which were not tested or compared with sensitivity analyses of known confounders.

Both ITCs showed similar results. Results of the adjusted network meta-analysis in both ITCs suggest that over a short-term induction treatment period (10 to 16 weeks), the proportion of patients achieving PASI 75 and PASI 90 responses is significantly greater for risankizumab than for placebo, apremilast, etanercept, adalimumab, ustekinumab, infliximab, and secukinumab in patients with moderate to severe chronic plaque psoriasis. No significant difference of risankizumab versus ixekizumab, brodalumab, or guselkumab was found for PASI 75 or PASI 90. HRQoL was not evaluated in either ITC. Safety outcomes were reported in the ITC submitted by the manufacturer, which showed that over the short-term induction treatment period (10 or 16 weeks), risankizumab had significantly smaller odds of AEs when compared with dimethyl fumarate, infliximab, secukinumab, ixekizumab, and brodalumab, and that risankizumab was associated with significantly smaller odds of discontinuation due to AEs compared with placebo, apremilast 30 mg, adalimumab 80 mg, dimethyl fumarate, infliximab 5 mg/kg, ixekizumab 160 mg, brodalumab 210 mg, and guselkumab 100 mg. No significant difference between risankizumab and other interventions in terms of SAEs was observed. There is uncertainty pertaining to the additional efficacy and safety benefit that risankizumab may have over these newer biologic treatments with long-term treatment.

Key limitations of the manufacturer-submitted ITC included cut-off date of the literature search (trials published beyond 2017 were not captured), restricting included interventions to drugs and dosages approved by NICE, lack of a sensitivity analyses to evaluate the effect of potential effect modifiers, and lack of an inconsistency model to determine if direct and indirect evidence in the network were similar. Key limitations of the Institute for Clinical and Economic Review ITC included exclusion of phase II and pilot RCTs, lack of reporting on model fitness, conducting multiple models to determine best fit, lack of inconsistency assessment, lack of conducting sensitivity analyses addressing potential studies with an outlier values of potential effect modifiers, and the potential effect of pooling different doses of the same drug.

Cost and Cost-Effectiveness

Risankizumab is available as a solution for injection in a single-use pre-filled syringe containing 75 mg risankizumab in 0.83 mL (90 mg/mL). The recommended dosage is two subcutaneous 75 mg injections to be given at week 0, week 4, and then every 12 weeks thereafter. At the manufacturer's submitted price of $2,467.50 per pre-filled syringe, the annual treatment cost per patient is $24,675 in the first year and $21,385 in all subsequent years.

The manufacturer submitted a cost-utility analysis based on a Markov state-transition model comparing risankizumab with the following biologic therapies reimbursed in Canada for moderate to severe plaque psoriasis: adalimumab, brodalumab, etanercept, guselkumab, infliximab biosimilar, ixekizumab, secukinumab, and ustekinumab. The analysis was conducted from the Canadian public health care payer perspective over a 10-year time horizon in a population with similar baseline characteristics to the clinical trials. The model had two time periods: (1) the primary response period: the time period from treatment initiation up to initial assessment of the condition (i.e., 10 to 16 weeks); and (2) the maintenance period. Treatment response was defined as achieving a PASI response score of ≥ 75. After the primary response period, patients with a PASI response score of < 75 switched to best supportive care (BSC; non-biologic supportive medications). During the maintenance period, patients with a PASI score of ≥ 75 either continued treatment in their current health state (defined by their PASI score), discontinued treatment, or died. Upon discontinuation, patients were assumed to receive BSC. In the manufacturer's base-case, etanercept had the lowest costs and fewest QALYs. Relative to etanercept, brodalumab was the next most cost-effective treatment, followed by risankizumab. The incremental cost-utility ratio (ICUR) for brodalumab compared with etanercept was $47,006 per QALY, while the ICUR for risankizumab compared with brodalumab was $203,266 per QALY.

CADTH identified the following key limitations of the manufacturer's submitted economic analysis:

- The manufacturer assumed that clinical efficacy of treatments at the end of the trial period (10 to 16 weeks) continues for up to 10 years. No consideration was given to waning of treatment effects.
- The manufacturer used treatment-specific discontinuation rates starting from week 16 until the end of the model time horizon (10 years). This was based on a manufacturer-commissioned ITC that used only short-term safety evidence reported at 10 to 16 weeks after randomization and was then inappropriately used to project long-term discontinuation rates.
- The treatment pathway in the economic model does not reflect clinical practice. In clinical practice, patients who discontinue or do not respond to initial treatment would likely receive a higher dose of the same drug or switch to another active treatment instead of switching to BSC.
- The costs attributed to BSC were estimated from the literature and consisted of a mix of phototherapy and pharmacotherapy (including biologic therapy), which is not consistent with BSC assumptions.
- Unit costs of comparator drugs were sourced from the Régie de l'assurance maladie du Québec, rather than from jurisdictions participating in CADTH CDR.
- Treatment with brodalumab was assumed to require additional nurse visits to receive counselling for suicidal ideation. The clinical expert consulted by CADTH noted that these additional counselling visits are not common in routine clinical practice.

In the CADTH reanalysis, the following assumptions were considered: same treatment discontinuation rate (20%) for all comparators, drug unit costs obtained from Ontario Drug Benefit formulary, removing the cost of additional counselling sessions for patients on brodalumab, and excluding treatment costs associated with BSC. Based on the revised assumptions, risankizumab was more effective and more costly than etanercept and brodalumab — resulting in an ICUR for risankizumab of $2,370,521 per QALY compared with brodalumab. At a willingness-to-pay threshold of $50,000 per QALY, the price of risankizumab would need to be reduced by at least 26% to be considered cost-effective. CADTH could not address limitations pertaining to the waning of treatment effect and the use of treatment sequences in clinical practice; thus, the comparative cost-effectiveness of risankizumab warrants careful interpretation.

CDEC Members

Dr. James Silvius (Chair), Dr. Ahmed Bayoumi, Dr. Bruce Carleton, Dr. Alun Edwards, Mr. Bob Gagne, Dr. Ran Goldman, Dr. Allan Grill, Dr. Peter Jamieson, Mr. Allen Lefebvre, Ms. Heather Neville, Dr. Rakesh Patel, Dr. Emily Reynen, Dr. Yvonne Shevchuk, and Dr. Adil Virani.

March 20, 2019 Meeting

Regrets

None

Conflicts of Interest

None

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