CADTH

CADTH COMMON DRUG REVIEW

Pharmacoeconomic Review Report

Risankizumab (Skyrizi)

(AbbVie)

Indication: For the treatment of adult patients with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

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CADTH

About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

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Abbreviations

AE	adverse event
BSC	best supportive care
CDR	CADTH Common Drug Review
DR	discontinuation rate
ICUR	incremental cost-utility ratio
ITC	indirect treatment comparison
NICE	National Institute for Health and Clinical Excellence
PASI	Psoriasis Area Severity Index
QALY	quality-adjusted life-year

Table 1: Summary of the Manufacturer's Economic Submission

Drug Product	Risankizumab (Skyrizi) solution for injection
Study Question	Is risankizumab a cost-effective alternative to existing biologic therapies currently approved and reimbursed by Canadian public drug plans for the treatment of moderate to severe psoriasis?
Type of Economic Evaluation	Cost-utility analysis
Target Population	Adults (aged 18 years or older) with moderate to severe plaque psoriasis who are candidates for systemic therapy
Treatment	Risankizumab (150 mg at week 0 and 4, and then once every 12 weeks thereafter)
Outcome	Quality-adjusted life-years (QALYs)
Comparators	• Adalimumab • Etanercept • Infliximab biosimilar • Secukinumab • Ixekizumab • Ustekinumab • Brodalumab • Guselkumab
Perspective	Canadian public health care payer
Time Horizon	10 years
Results for Base Case	Based on a sequential probabilistic analysis: • Etanercept, brodalumab, and risankizumab were on the cost-effectiveness efficiency frontier (CEF) while other treatments were either dominated or extendedly dominated. • Etanercept had the lowest cost and fewest QALYs, followed by brodalumab, then risankizumab. • The incremental cost-utility ratio (ICUR) for brodalumab compared with etanercept was $47,006 per QALY, while the ICUR for risankizumab versus brodalumab was $203,266 per QALY.
Key Limitations	• The manufacturer assumed that the efficacy of treatment, measured in terms of a Psoriasis Area Severity Index response score of 75 (PASI 75) observed during the clinical trial (52 weeks), would continue until the end of model time horizon (10 years). No evidence has been provided to support this assumption. • The manufacturer assumed that patients who discontinue their primary treatment during the maintenance period would be switched to best supportive care (BSC). However, in clinical practice, patients who discontinue initial treatment will likely receive a higher dose of the same drug or switch to another active treatment instead of BSC. Hence, the model does not reflect clinical practice. • Treatment-specific discontinuation rates were used in the economic model from week 16 until the end of the model time horizon (10 years). However, this was inappropriately based on short-term clinical trial evidence reported at 10 to 16 weeks after randomization. Use of inappropriate discontinuation rates, along with the assumption that patients who discontinue treatment switch to BSC (instead of an active treatment), clearly favours risankizumab, which has the lowest discontinuation rate in the model.

Key Limitations	• The effectiveness of BSC in the economic model was based on the response observed from the placebo arms in the indirect treatment comparison, while the cost of BSC was based on a mix of phototherapy and pharmacotherapy. This inconsistency favoured risankizumab, which had a lower discontinuation rate. • Unit costs of drugs were based on the prescription cost in Quebec rather than in jurisdictions participating in CADTH's CDR program. For patients receiving brodalumab, the manufacturer included the cost of counselling sessions which, based on feedback from clinical experts, does not commonly occur in clinical practice in Canada.
CDR Estimate(s)	• In the CADTH base case, the same treatment discontinuation rate (20%) was used for all treatments (in line with the manufacturer's sensitivity analysis and previous psoriasis submissions). Pharmacotherapy and phototherapy costs for BSC and the counselling cost for brodalumab were excluded, and costs from the Ontario Drug Benefit Formulary were used for comparator drug costs, when available. • In the CADTH base case, etanercept, brodalumab, and risankizumab remained on the CEF; etanercept was associated with the lowest cost and fewest QALYs, followed by brodalumab, and then risankizumab. • The ICUR for brodalumab compared with etanercept was $66,344 per QALY, while the ICUR for risankizumab compared with brodalumab was $2,370,521 per QALY. • A price reduction of at least 26% would be required for risankizumab to be cost-effective at a willingness-to-pay threshold of $50,000 per QALY. • CADTH noted that uncertainty related to the lack of evidence of long-term effectiveness, and the assumption that no active treatment would follow discontinuation, could not be addressed in the reanalysis.

BSC = best supportive care; CDR = CADTH Common Drug Review; CEF = cost-effectiveness efficiency frontier; ICUR = incremental cost-utility ratio; PASI = Psoriasis Area Severity Index; QALY = quality-adjusted life-year; SEB = subsequent entry biologic.

Drug	Risankizumab (Skyrizi)
Indication	For the treatment of adult patients with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy
Reimbursement Request	• Reimburse in a manner similar to other biologics for the treatment of moderate to severe plaque psoriasis. • Treatment should be discontinued if a response (PASI 75) to treatment with risankizumab has not been demonstrated after 16 weeks.
Dosage Form	75 mg in 0.83 mL sterile solution (90 mg/mL) for subcutaneous injection
NOC Date	April 17, 2019
Manufacturer	AbbVie

Executive Summary

Background

Risankizumab is a humanized immunoglobulin G1 monoclonal antibody[1] with an indication for the treatment of adult patients with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.[2] Risankizumab is available as a solution for injection in a single-use, pre-filled syringe containing 75 mg of risankizumab in 0.83 mL (90 mg/mL) solution at a submitted price of $2,467.50 per pre-filled syringe.[2] The recommended dose is 150 mg (two 75 mg injections) to be given as subcutaneous injection at week 0, week 4, and then every 12 weeks thereafter.[1]

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.[2] The analysis was conducted from the Canadian public health care payer perspective and used four-week cycles over a 10-year time horizon. A discount rate of 1.5% was applied to costs and benefits. The model had two time periods: the primary response period (the time period from treatment initiation up to initial assessment of the condition [i.e., 10 to 16 weeks]) and the maintenance period. After the primary response period, patients who achieved a Psoriasis Area Severity Index (PASI) response score of < 75 were switched to best supportive care (BSC), which was assumed to consist of a combination of 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. Patients continuing on treatment received treatment benefit until the end of the model. Upon discontinuation, patients were assumed to receive BSC. Once patients reached the BSC state, they remained in this state until death or the end of the model.

Treatment effects were based on a manufacturer-commissioned unpublished indirect treatment comparison (ITC).[3] The annual probability of treatment discontinuation during the maintenance period was the sum of discontinuations due to adverse events (AEs) and discontinuations due to all other causes. AE-related discontinuation rates were assumed to be treatment-specific and were calculated using odds ratios obtained from the ITC.

Discontinuation due to all other causes was assumed to be [redacted] for all treatments. Health state utilities corresponding to PASI response scores were based on EuroQol 5-Dimensions questionnaire data from the UltIMMA-1 and UltIMMA-2 trials (52-week double-blind randomized studies comparing risankizumab with placebo or ustekinumab in patients with moderate to severe psoriasis). The cost of BSC was estimated from the literature[4] and consisted of health care practitioners, laboratory tests, treatment, and complementary medicines costs.[4] Unit cost of drugs were obtained from the Régie de l'assurance maladie du Québec.[5]

In the manufacturer's probabilistic base case, the cost-effectiveness efficiency frontier (i.e., drugs that were not dominated) was represented by the following three drugs: etanercept, brodalumab, and risankizumab. Etanercept had the lowest costs and lowest quality-adjusted life-years (QALYs) followed by brodalumab and risankizumab. The incremental cost-utility ratio (ICUR) for brodalumab compared with etanercept was $47,006, while the ICUR for risankizumab compared with brodalumab was $203,266 per QALY. The model results were most sensitive to treatment discontinuation rate, assuming a 20% discontinuation rate for all treatments increased the ICUR for risankizumab compared with brodalumab to $2,140,808 per QALY.

Summary of Identified Limitations and Key Results

CADTH identified several key limitations with the model submitted by the manufacturer. Firstly, the economic model assumed that patients who discontinue their primary treatment switch to BSC. In clinical practice, patients who discontinue or do not respond to initial treatment will likely receive a higher dose of the same drug or switch to another active treatment. CADTH was unable to address this limitation because of the structural limitations of the model and lack of evidence on treatment-experienced patients. Another important limitation is the assumption that clinical efficacy of treatments at the end of the observed follow-up period continues beyond the trial for up to 10 years; no consideration was given to waning of treatment effects. Unfortunately, this limitation could not be addressed through reanalysis of the model due to lack of data and the inflexibility of the model structure.

The economic model used treatment-specific discontinuation rates starting from week 16 until the end of the model time horizon (10 years). However, this was based on a manufacturer-commissioned ITC that used only short-term safety evidence reported at 10 to 16 weeks after randomization; this ITC was then inappropriately used to project long-term discontinuation rates. The use of different discontinuation rates for each treatment is inconsistent with previous submissions made to the National Institute of Health and Clinical Excellence (NICE) and the CADTH Common Drug Review (CDR) for treatment of psoriasis.[6-12] Use of inappropriate discontinuation rates, along with the assumption that patients who discontinue treatment switch to BSC (instead of an active treatment), clearly favours risankizumab, which has the lowest discontinuation rate in the model. The costs attributed to BSC are not consistent with the BSC efficacy assumptions used by the manufacturer. The effectiveness of BSC in the economic model is based on the placebo response in the manufacturer-conducted ITC, whereas the cost of BSC used in the economic model was estimated from the literature[4] and consisted of a mix of phototherapy and pharmacotherapy. Furthermore, unit costs of drugs were obtained from the Régie de l'assurance maladie du Québec[5] rather than from jurisdictions that participate in the CDR process. Finally, treatment with brodalumab was assumed to require additional nurse visits to receive counselling for suicidal ideation. However, the clinical expert consulted by CADTH noted that these additional counselling visits are not common in routine clinical practice.

CADTH addressed some of these limitations by: using the same treatment discontinuation rate (20%) for all comparators; using drug unit costs obtained from the Ontario Drug Benefit Formulary; removing the cost of additional counselling sessions for patients on brodalumab; and excluding treatment costs associated with BSC care. In the CADTH reanalysis, risankizumab was more effective and more costly when compared with etanercept and brodalumab, resulting in an incremental cost per QALY gained (ICUR) for risankizumab of $2,370,521 compared with brodalumab. At a willingness-to-pay threshold of $50,000 per QALY, risankizumab was a cost-effective strategy if the price of risankizumab was reduced by at least 26%.

Conclusions

Based on CADTH reanalyses, etanercept was the optimal therapy for moderate to severe psoriasis if the decision-maker's willingness to pay is less than $66,344 per QALY gained; brodalumab was the optimal therapy if the willingness-to-pay threshold is at least $66,344 but less than $2,370,521 per QALY gained; and risankizumab was the optimal therapy at a willingness-to-pay threshold of at least $2,370,521. A reduction of at least 26% in the submitted price would be required for risankizumab to be cost-effective at a willingness-to-pay threshold of $50,000 per QALY.

It should be noted that the economic model did not allow CADTH to assess the impact of assumptions relating to the waning of treatment effect and the use of treatment sequences in clinical practice. This implies that the results of the economic analysis warrant careful interpretation.

Information on the Pharmacoeconomic Submission

Summary of the Manufacturer's PE Submission

The manufacturer submitted a cost-utility analysis 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.[2] The perspective was that of the Canadian public health care payer, with a time horizon of 10 years. A discount rate of 1.5% was applied to costs and benefits accrued after the first year. The target population for the cost-utility analysis was adult patients, with a Psoriasis Area Severity Index (PASI) score of 10 to 12 and a Dermatology Life Quality Index score of greater than 10, who were candidates for systemic therapy and were eligible for biologic therapy. The model baseline characteristics represented a population with baseline characteristics similar to those found in the manufacturer-conducted clinical trials: UltIMMA-1, UltIMMA-2, IMMvent, and IMMhance.

The economic analysis was conducted using a Markov model, with four-week cycles. The model was developed in Microsoft Excel and had two time periods: the primary response period (the time period from treatment initiation up to initial assessment of the condition [i.e., 10 to 16 weeks]) and the maintenance period (the period following primary response). The model included the following health states defined by the PASI response categories: PASI < 50, 50 to 74, 75 to 89, 90 to 99, and 100. At the point of assessment (i.e., end of the first period), patients were in one of these preceding response categories based on response to treatment (Table 9). Patients who achieved a PASI response score of < PASI 75 (PASI 75 was the primary outcome in the clinical trials) were switched to best supportive care (BSC), which was assumed to consist of a combination of non-biologic supportive medications. From there, patients would either remain in this state or die (based on background mortality). Those with a PASI score of ≥ 75 could either continue in their existing health state, discontinue therapy, or die. Upon discontinuation, patients were assumed to receive BSC. The model assumed that patients who respond to treatment would continue to receive treatment benefit until the end of the model, i.e., 10 years.

Treatment effectiveness in the economic model was based on a manufacturer-sponsored indirect treatment comparison (ITC) that assessed the treatment response rate in terms of achieving PASI 75; the ITC included existing and upcoming treatments (including risankizumab). The ITC also estimated response rate in patients receiving placebo; this was then assumed to represent the response rate in patients on BSC in the model.

The annual probability of treatment discontinuation during the maintenance period was calculated as the sum of discontinuations related to adverse events (AEs) (assumed to be treatment-specific) plus the discontinuations due to all other causes. For the all-cause discontinuation rate (DR), data from a UK registry (the British Association of Dermatologists Biologic and Immunomodulators Register, BADBIR[13]) was used; the manufacturer assumed that all drugs have the same all-cause DR as observed for adalimumab (i.e., 14%), the most common psoriasis drug in the registry. For the AE-related DR, treatment-specific odds ratios were used from an ITC sponsored by the manufacturer and applied to the AE-related DR for adalimumab (from the registry). Based on this approach, the annual DR for risankizumab was 16.2%, while the rate for all other biologics ranged between 19.5% and 26.5%. A scenario analysis explored the impact of assuming the same DR (20%) for all biologic

therapies based on a constant DR used for all drugs in previous National Institute for Health and Clinical Excellence (NICE) technology appraisals and submissions to the CADTH Common Drug Review (CDR).[7-11,12]

Health state utilities corresponding to PASI response scores were based on EuroQol 5-Dimensions questionnaire data from the UltIMMA-1 and UltIMMA-2 trials. Mortality was based on all-cause Canadian mortality data, adjusted by age and gender. Costs included the following: drug acquisition and administration costs, patient-monitoring cost, costs of AEs, and the cost of BSC.[4] Cost of nonresponders was assumed to be the same as the BSC cost. Unit costs of drugs were obtained from the Régie de l'assurance maladie du Québec.[5]

Manufacturer's Base Case

In the base case, the manufacturer reported that brodalumab dominated infliximab, adalimumab, guselkumab, and ixekizumab (i.e., brodalumab was associated with lower total costs and higher quality-adjusted life-years [QALYs]), whereas ustekinumab and secukinumab were extendedly dominated. Thus, the cost-effectiveness efficiency frontier was represented by the following three drugs: etanercept, brodalumab, and risankizumab. Of these drugs, etanercept had the lowest costs and fewest QALYs followed by brodalumab and then risankizumab. The incremental cost-utility ratios (ICURs) were estimated in the same order: the ICUR for brodalumab compared with etanercept was $47,006, while the ICUR for risankizumab compared with brodalumab was $203,266 (Table 2).

Table 2: Summary of Results of the Manufacturer's Base Case

	Total Costs ($)	Total QALYs	ICUR (Risankizumab Versus Comparator) ($)	ICUR (Comparator Versus Lowest-Cost Option: Etanercept)[a] ($)	Sequential ICER
Non-Dominated Options					
Etanercept	76,492	0.341	101,290	–	–
Brodalumab	88,017	0.587	203,266	47,002	$47,006 vs. etanercept
Risankizumab	114,459	0.717	–	101,030	$203,266 vs. brodalumab
Dominated Options					
Ustekinumab	86,618	0.506	132,098	61,631	Subject to extended dominance through brodalumab and etanercept
Infliximab	88,023	0.485	114,119	80,468	Dominated by ustekinumab and brodalumab
Adalimumab	89,832	0.507	117,817	80,361	Dominated by brodalumab
Guselkumab	96,645	0.564	116,814	90,575	Dominated by brodalumab
Ixekizumab	96,663	0.529	95,277	107,293	Dominated by brodalumab and guselkumab
Secukinumab	99,662	0.591	118,194	92,754	Subject to extended dominance through risankizumab and etanercept

ICER = incremental cost-effectiveness ratio; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year; vs. = versus.

[a] Calculated by CADTH based on costs and QALYs reported in the manufacturer's submission.

Source: Adapted from manufacturer's pharmacoeconomic submission.[2]

Summary of Manufacturer's Sensitivity Analyses

The manufacturer conducted a number of one-way sensitivity and scenario analyses that primarily focused on the comparison of risankizumab compared with the other two treatments on the efficiency frontier (i.e., etanercept and brodalumab). The results were found to be most sensitive to the treatment DR. Using a 20% treatment DR across all treatments increased the ICUR for risankizumab compared with brodalumab from $203,266 to $2,140,808 per QALY.

Limitations of Manufacturer's Submission

- **Uncertainty in treatment effectiveness and safety**: Evidence on the long-term effectiveness of risankizumab is not available. As a result, the manufacturer assumed that the difference in PASI scores between risankizumab and placebo at the end of the observed follow-up period continues beyond the trial for up to 10 years, i.e., the model did not assess potential waning of treatment effect for risankizumab or any other biologic. However, given the structure of the model, it was not feasible to explore alternate assumptions about long-term treatment effect.

  Finally, the manufacturer used a PASI response score of 75 (PASI 75) to measure treatment response during the trial period. However, the clinical expert consulted by CADTH advised that a PASI 75 response is not consistent with how treatment success is measured in clinical practice. Therefore, CADTH conducted an exploratory analysis using PASI 90 (based on an exploratory ITC analysis reported in the manufacturer's submission) as a measure of treatment success.

- **Uncertainty in treatment DR:** The treatment DR in the economic model was the sum of discontinuations due to AEs plus discontinuations due to all other causes. The DR due to AEs was based on a manufacturer-commissioned ITC and was assumed to be specific to each treatment, while the DR due to all other causes was assumed to be constant at 14%. The overall DR was used in the economic model from week 16 until the end of the model time horizon (10 years). However, the ITC used to inform AE-related DRs only used short-term clinical trial evidence reported at 10 to 16 weeks after randomization. It is inappropriate to assume that a DR measured over such a short period can be used as an estimate of the DR of more than 10 years. This is an important assumption, because patients who discontinue treatment are assumed to receive BSC (instead of an active treatment), which is associated with a very low response rate. Since risankizumab has the lowest DR in the model, this approach clearly favours risankizumab. It is also noted that the AE-related DR for risankizumab reported in the ITC was not statistically significantly different from some of the other biologics. Additionally, the CADTH Clinical Review Report noted that the clinical trials used to inform AE-related DRs were not designed to capture differences in safety outcomes.

  CADTH also noted that previous submissions to NICE and CDR for treatments for psoriasis have used constant treatment DRs across all treatments (typically, 20%).[6-12] The DR used for risankizumab in the economic model (i.e., [redacted]) is also lower than the rates reported in the literature for other biologics (range between 19% and 31%). In line with the preceding and, based on the manufacturer's own sensitivity analysis included in its submission, CADTH used an overall DR of 20% for all treatments (including risankizumab). A lower DR of 15% was also explored in a CADTH exploratory analysis for all treatments (based on the advice of the clinical expert consulted by CADTH).

- **Treatment pathway does not reflect clinical practice:** The economic model assumed that patients who discontinue their primary treatment switch to BSC. However, according to the clinical expert consulted by CADTH, in clinical practice patients who discontinue or do not respond to initial treatment will likely receive a higher dose of the same drug or switched to another active treatment, i.e., patients typically choose to try other biologics. Therefore, the treatment pathway in the economic model does not reflect clinical practice. Moreover, the model assumes the effectiveness of BSC to be equivalent to placebo, as observed in the pivotal trial.

  The assumption that patients who discontinue treatment switch to BSC (with effectiveness of placebo) instead of an active drug, together with the assumption of a lower DR for risankizumab, strongly favours risankizumab. While the manufacturer's sensitivity analysis explored the use of active treatment sequences (instead of BSC), this analysis had limited value, as it evaluated only a limited number of treatment options and assumed that the probability of response of each successive biologic treatment is independent of its position in the treatment sequence; this assumption has been considered inappropriate in previous submissions to CDR for psoriasis,[12,14] based on the literature.[15,16] CADTH was unable to address this limitation because of the structural limitations of the model and because of a lack of evidence of effectiveness for treatment-experienced patients.
- **Cost of BSC:** The effectiveness of BSC in the economic model is based on the placebo response in the manufacturer-conducted ITC. However, the cost of BSC used in the economic model is based on the Levy et al.[4] study in which patients received a mix of phototherapy and pharmacotherapy, including 13% of patients who received a biologic therapy. Therefore, the cost estimate of BSC, based on Levy et al., is not consistent with the BSC efficacy based on placebo response. To overcome this limitation, CADTH excluded drug-related costs from the BSC arm.
- **Medication costs:** Unit costs for drugs were obtained from the Régie de l'assurance maladie du Québec[5] rather than from jurisdictions representative of participating drug programs. In CADTH reanalyses, unit costs were revised and based on the Ontario Drug Benefit Formulary.[17]
- **Inappropriate assumption of consultations to prevent suicide:** The manufacturer assumed that treatment with brodalumab would require additional nurse visits to receive counselling for suicidal ideation associated with brodalumab; however, the clinical expert consulted by CADTH noted that these additional visits are not common in routine clinical practice. Therefore, the CADTH reanalysis did not include these counselling costs.[18]

CADTH Common Drug Review Reanalyses

The CADTH reanalysis could not address the following limitations: lack of evidence on some relevant biologics approved in Canada; lack of evidence on the long-term effectiveness of risankizumab beyond the trial period; and the structural limitation of the model, which does not correctly reflect current clinical practice. The CADTH reanalyses included the following changes to the manufacturer's base case (see results in Table 3 and Table 10):

1. DR: A 20% DR was used for all biologics (as used in the manufacturer's scenario analysis)
2. BSC costs: The cost of pharmacotherapy and phototherapy were excluded, resulting in an annual cost of $421 for BSC (based on 2018 prices)
3. Unit costs: These were based on the Ontario Drug Benefit Formulary (Table 4)

4. Cost of additional counselling visits: These were excluded from the analysis to reflect current clinical practice
5. **CADTH base case (1 plus 2 plus 3 plus 4).**

The following scenario analyses were undertaken using the CADTH base case:

5a. CADTH base case plus use of PASI 90 for effectiveness evidence

5b. CADTH base case plus use of a 15% DR for all treatments (including risankizumab).

Based on CADTH's sequential reanalysis, ustekinumab, adalimumab, infliximab, secukinumab, guselkumab, and ixekizumab were either dominated or extendedly dominated; this is in line with the manufacturer's base case. The following three treatments were on the cost-effectiveness efficiency frontier: etanercept, brodalumab, and risankizumab. The CADTH reanalysis found that etanercept would be cost-effective if a decision-maker were willing to pay less than $66,344 for a QALY. Brodalumab would be cost-effective if a decision-maker were willing to pay at least $66,344 but less than $2,370,521 for a QALY. Risankizumab would be optimal if a decision-maker were willing to pay at least $2,370,521 per QALY (Table 3). At a willingness-to-pay threshold of $50,000 per QALY gained, risankizumab had a 0% probability of falling below this threshold.

Table 3: CADTH Base Case

	Total Costs ($)	Total QALYs	ICUR (Risankizumab Versus Comparator) ($)	ICUR (Comparator Versus Lowest-Cost Option: Etanercept) ($)	Sequential ICUR
Non-Dominated Treatments					
Etanercept	47,521	0.357	115,507	–	–
Brodalumab	67,116	0.652	2,370,521	66,344	$66,344 versus etanercept
Risankizumab	82,380	0.658	–	115,507	$2,370,521 versus brodalumab
Dominated Treatments					
Ustekinumab	63,203	0.534	154,081	88,433	Subject to extended dominance through etanercept and brodalumab
Adalimumab	67,114	0.531	120,369	111,982	Dominated by ustekinumab
Infliximab	70,694	0.594	180,737	97,720	Dominated by brodalumab
Secukinumab	77,590	0.609	96,735	119,191	Dominated by brodalumab
Guselkumab	78,087	0.640	230,402	107,946	Dominated by brodalumab
Ixekizumab	85,993	0.651	Dominated by risankizumab	130,686	Dominated by risankizumab

ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

An exploratory scenario analysis was conducted to investigate the use of PASI 90 (as opposed to PASI 75) as obtained from the ITC. This resulted in an ICUR of $1,580,146 for risankizumab compared with brodalumab. An additional scenario analysis using a lower DR of 15% for all treatments produced a sequential ICUR of $2,737,460 for risankizumab compared with brodalumab. Full results of the sequential analysis can be found in Table 10.

CADTH also conducted a price-reduction scenario analysis based on the CADTH base case. At a price reduction of 25%, risankizumab dominated brodalumab (i.e., lower costs and more QALYs), with an ICUR of $51,217 versus etanercept. At a price reduction of 26%, risankizumab still dominated brodalumab and had an ICUR of $48,451 compared with

etanercept (see Table 11 for detailed deterministic results and Table 12 for probabilistic results).

Patient Input

Patient input was received from two patient groups: the Canadian Psoriasis Network and Arthritis Consumer Experts. Patients reported the significant impact of "flares" on their quality of life, stating the most significant physical symptoms were itchiness, pain, skin sensitivity, redness, and skin cracking and bleeding. Due to these symptoms, patients experience frustration, worry, embarrassment, anxiety, and depression. Quality of life and patient preferences were included in the economic model by using utility values for health states defined by PASI scores, and symptoms were captured in the use of PASI scores.

Patients described having used several treatments with different levels of response. Patients mentioned that additional treatments would provide them with more options to adequately control or stop symptoms of psoriasis. However, the economic analysis did not evaluate active treatment sequences after initial treatment failure. Caregivers of patients with psoriasis often experience an increase in the amount of care required to manage the condition and to provide emotional support and manage household chores. This was reflected in the manufacturer's scenario analysis conducted from a societal perspective.

Issues for Consideration

- The manufacturer has requested reimbursement for risankizumab for patients when conventional systemic therapy or phototherapy is inadequately effective, not tolerated, or contraindicated. However, the data used to populate the base case were based on the UltIMMA-1, UltIMMA-2, IMMvent, and IMMhance trials, which included patients who were candidates for systemic therapy or phototherapy; as a result, the clinical data may not fully reflect the patient population for which the manufacturer is seeking reimbursement.
- In 2017, two biosimilars of etanercept became available in Canada,[19,20] but these are currently not approved for the treatment of psoriasis. The potential introduction of these comparators could impact the findings of the economic analysis.

Conclusions

Based on CADTH reanalyses, etanercept was the optimal therapy for moderate to severe psoriasis if the decision-maker's willingness to pay is less than $66,344 per QALY gained; brodalumab was the optimal therapy if the willingness-to-pay threshold is at least $66,344 but less than $2,370,521 per QALY gained; and risankizumab was the optimal therapy at a willingness-to-pay threshold of at least $2,370,521. If the decision-maker is willing to pay up to $50,000 per QALY, a reduction of at least 26% in the submitted price would be required for risankizumab to be cost-effective.

It should be noted that the economic model did not allow CADTH to assess the impact of assumptions relating to the waning of treatment effect and the use of treatment sequences in clinical practice. This, in addition to not evaluating the cost-effectiveness of a few other biologics available in Canada, implies that the results of economic analysis warrant careful interpretation.

Appendix 1: Cost Comparison

The comparators presented in the following table have been deemed to be appropriate by clinical experts. Comparators may be recommended (appropriate) practice, versus actual practice. Comparators are not restricted to drugs but may be devices or procedures. Costs are manufacturer list prices, unless otherwise specified. Existing Product Listing Agreements are not reflected in the table and, as such, may not represent the actual costs to public drug plans.

Table 4: Cost Comparison Table for the Treatment of Plaque Psoriasis

Drug/ Comparator	Strength	Dosage Form	Price ($)	Recommended Dose	Average Annual Drug Cost ($)
Risankizumab	75 mg/0.83 mL	Pre-filled syringe	2,467.50[a]	150 mg at week 0 and 4, followed by 150 mg every 12 weeks thereafter	First year: 24,675 Subsequent years: 21,385
Other Biologics					
Adalimumab (Humira)	40 mg/0.8 mL	Syringe or pen	769.9700	80 mg initial dose, 40 mg every other week starting 1 week after initial dose	First year: 21,559 Subsequent years: 20,019
Brodalumab (Siliq)	210 mg/1.5 mL	Pre-filled syringe	645.0000[b]	210 mg SC at weeks 0, 1, and 2, followed by every 2 weeks thereafter	First year: 17,415 Subsequent years: 16,770
Etanercept (Enbrel)	50 mg/mL 25 mg/vial	Syringe or pen vial	405.9850 202.9300	50 mg twice weekly for 12 weeks, then 50 mg weekly	First year: 25,983 Subsequent years: 21,111
Etanercept (Erelzi and/or Brenzys, SEB)	50 mg/mL 25 mg/vial	Syringe or pen vial	127.5000 255.0000		First year: 16,320 Subsequent years: 13,260
Guselkumab (Tremfya)	100 mg/mL	Pre-filled syringe	3,059.7400[c]	100 mg SC at weeks 0 and 4, followed by every 8 weeks thereafter	First year: 21,418 Subsequent years: 19,888
Infliximab (Remicade)	100 mg/vial	Vial	977.0000[d]	5 mg/kg/dose, for 3 doses (0, 2, 6 weeks) then 5 mg/kg every 8 weeks	First year: 39,080[e] Subsequent years: 31,753[e]
Infliximab (Renflexis, SEB)			493.000		First year: 19,720[e] Subsequent years: 16,023[e]
Ixekizumab (Taltz)	80 mg/1 mL	Pre-filled syringe	1,577.2600	160 mg initial dose, 80 mg at 2, 4, 6, 8, 10, and 12 weeks followed by 80 mg every 4 weeks	First year: 26,813 Subsequent years: 20,504
Secukinumab (Cosentyx)	150 mg/mL	Pre-filled syringe or pen	822.5000	300 mg SC injection at weeks 0, 1, 2, and 3, then monthly injections starting at week 4	First year: 24,675 Subsequent years: 19,740
Ustekinumab (Stelara)	45 mg/0.5 mL 90 mg/1 mL	Pre-filled syringe	4,593.1400	< 100 kg patients: 45 mg at weeks 0 and 4, followed by 45 mg every 12 weeks thereafter (> 100 kg patients: 90 mg at same frequency)	First year: 22,966 Subsequent years: 19,904

Drug/ Comparator	Strength	Dosage Form	Price ($)	Recommended Dose	Average Annual Drug Cost ($)
Conventional Systemic Treatments					
Methotrexate	2.5 mg 10 mg 20 mg/2 mL 50 mg/2 mL	Tablet Tablet Vial Vial	0.6325 2.7000[d] 12.5000 8.9200	10 mg to 25 mg by mouth or IM weekly	140 to 325 232 to 812
Cyclosporine (generics)	10 mg 25 mg 50 mg 100 mg	Capsule	0.6238 0.9952 1.9400 3.8815	2.5 mg to 5 mg/kg daily, in 2 divided doses	3,269 to 7,084[e]
Acitretin (generics)	10 mg 25 mg	Capsule	1.2965 2.2770	25 mg to 50 mg daily	831 to 1,662
Phosphodiesterase Type 4 Inhibitor					
Apremilast (Otezla)	30 mg	Tablet	19.8650[c,f]	30 mg twice daily	14,501

IM = intramuscular; SC = subcutaneous; SEB = subsequent entry biologic.

Note: Unless otherwise indicated, all prices are from the Ontario Drug Benefit Formulary[17] (accessed November 2018) and do not include dispensing fees.

[a] Manufacturer's submitted price.[2]

[b] Manufacturer's submitted price.[18]

[c] IQVIA[21] (November 2018).

[d] Saskatchewan Formulary[22] (November 2018).

[e] Assumes patient weight of 90 kg and wastage of excess medication in vials, if applicable.

[f] Quebec formulary[5] (September 2018) and IQVIA[21] (November 2018): $18.9041.

Appendix 2: Additional Information

Table 5: Submission Quality

	Yes/ Good	Somewhat/ Average	No/ Poor
Are the methods and analysis clear and transparent?		X	
Comments	The manufacturer's model did not adhere to best modelling practices regarding random number generation and number of iterations. These issues were brought to the attention of the manufacturer and a new model was submitted by the manufacturer. Changes made by the manufacturer did not fully address all issues, including long model run-time (approximately 48 hours).		
Was the material included (content) sufficient?	X		
Comments			
Was the submission well organized and was information easy to locate?	X		
Comments	None		

Table 6: Authors Information

Authors of the Pharmacoeconomic Evaluation Submitted to CDR

☐ Adaptation of global model/Canadian model done by the manufacturer
☒ Adaptation of global model/Canadian model done by a private consultant contracted by the manufacturer
☐ Adaptation of global model/Canadian model done by an academic consultant contracted by the manufacturer
☐ Other (please specify)
☐ Unclear

	Yes	No	Uncertain
Authors signed a letter indicating agreement with entire document	X		
Authors had independent control over the methods and right to publish analysis	X		

CDR = CADTH Common Drug Review.

Appendix 3: Summary of Other HTA Reviews of Drug

No reviews for risankizumab conducted by health technology assessment organizations had been completed at the time of this review.

Appendix 4: Reviewer Worksheets

Table 7: Data Sources

Data Input	Description of Data Source	Comment
Baseline cohort characteristics	Baseline reflected the average patient in the UltIMMA-1, UltIMMA-2, IMMvent, and IMMhance trials: Mean starting age of 47.5 years, 69.9% male with a mean weight of 90.6 kg.	Considered appropriate by the clinical expert consulted for this review.
Efficacy, Safety, and Withdrawals		
Efficacy (PASI response rates)	Effects of treatment on the distribution of patients across the PASI response categories were derived from the manufacturer's ITC.	The CADTH Clinical Review Report noted that the literature search was not up to date and was limited to NICE-approved drugs and dosages. This increased the uncertainty in the efficacy data (see CADTH Clinical Review Report for further details).
Adverse events	Adverse event rates were obtained from safety review studies, pivotal trials, or product monographs (non-melanoma skin cancer, malignancy other than non-melanoma skin cancer, severe infections, inflammatory bowel disease, and suicides).	Appropriate.
Discontinuation	The annual probability of treatment discontinuation during the maintenance period was calculated as the sum of adverse event–related discontinuation plus discontinuation due to all other causes. For the all-cause discontinuation rate, data from a UK registry (the British Association of Dermatologists Biologic and Immunomodulators Register [BADBIR][13]) was used; the manufacturer assumed that all drugs have the same all-cause discontinuation rate as observed for adalimumab (i.e., 14%).	Long-term AE discontinuation rates were inappropriately based on short-term clinical trial evidence reported at 10 to 16 weeks after randomization. The CADTH Clinical Review Report concluded that the AE-related discontinuation rates, based on the ITC, have limited generalizability due to the short duration of the included trials and the fact that these trails were not designed to capture differences in safety outcomes. Moreover, the discontinuation rate used for risankizumab in the economic model is lower than the discontinuation rate of 20% used in previous submissions to NICE and CDR for treatments for psoriasis; this discontinuation rate is also lower than the rates reported in the literature for other biologics. Finally, using different discontinuation rates for different biologics is inconsistent with previous submissions to NICE and CDR.[6-12]
Natural History		
Mortality	Transition to death was informed by age- and gender-specific all-cause mortality rates for the Canadian general population.	Appropriate.
Utilities		
Health state utilities	Data were derived from responses to the EQ-5D utility instrument completed as part of the UltIMMA-1 and UltIMMA-2 trials. A baseline utility was derived from responses at clinical study entry and utility scores for PASI response categories were derived from responses at the 12-, 16-, and 52-week follow-up and were derived through regression analysis.	Even though the full methodology was not reported by the manufacturer, the chosen method for the increments associated with PASI response appeared appropriate.

Data Input	Description of Data Source	Comment
Resource Use and Costs		
Costs	Cost of risankizumab provided by the manufacturer.[2] Unit costs of relevant comparators were obtained from the Régie de l'assurance maladie du Québec.[5] Dosages were assumed to be the recommended doses from product monographs. BSC costs were based upon a study by Levy et al.[4] All costs were updated to 2018 Canadian dollars.	Dosing regimens were appropriate. Since CDR-participating jurisdictions do not include Quebec, RAMQ is not an appropriate source for drug costs. A proportion of the patients in the Levy study were prescribed a biologic therapy; therefore, the total costs derived from this study are an inadequate estimate for BSC costs.

AE = adverse event; BSC = best supportive care; CDR = CADTH Common Drug Review; EQ-5D = EuroQol 5-Dimensions questionnaire; ITC = indirect treatment comparison; NICE = National Institute for Health and Clinical Excellence; PASI = Psoriasis Area Severity Index; RAMQ = Régie de l'assurance maladie du Québec.

Table 8: Manufacturer's Key Assumptions

Assumption	Comment
Baseline characteristics of cohort match clinical trial characteristics.	Appropriate, according to the clinical expert consulted by CADTH.
PASI definition of response.	Appropriate.
Data on short-term clinical effectiveness indicative of long-term benefits.	If clinical effectiveness reduces over time, then the cost-effectiveness of treatments in this clinical area will change significantly; this can potentially introduce significant bias into the analysis.
Data from indirect comparison is indicative of comparative clinical effectiveness.	CADTH Clinical Review Report.
Movement from active treatment to BSC.	Inappropriate. Firstly, it is not common for the biologic failure population to move to BSC. Secondly, the use of multiple lines of biologics is established practice, according to the clinical expert consulted by CADTH.
Brodalumab treatment associated with counselling for suicide ideology.	This assumption was not justified, according to the clinical expert consulted by CADTH. This was addressed as a limitation and an alternative assumption was used as part of CADTH's base case.

BSC = best supportive care; PASI = Psoriasis Area Severity Index.

Table 9: Distribution of Patients by Psoriasis Area Severity Index Response Score at End of the Primary Response Period (Indirect Treatment Comparison Results)

	PASI < 50	PASI 50 to 74	PASI 75 to 89	PASI 90 to 99	PASI 100
Risankizumab	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Adalimumab	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Brodalumab	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Etanercept	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Guselkumab	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Infliximab	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Ixekizumab	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Secukinumab	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Ustekinumab in-label dose	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

PASI = Psoriasis Area Severity Index.

Source: Manufacturer's pharmacoeconomic submission.

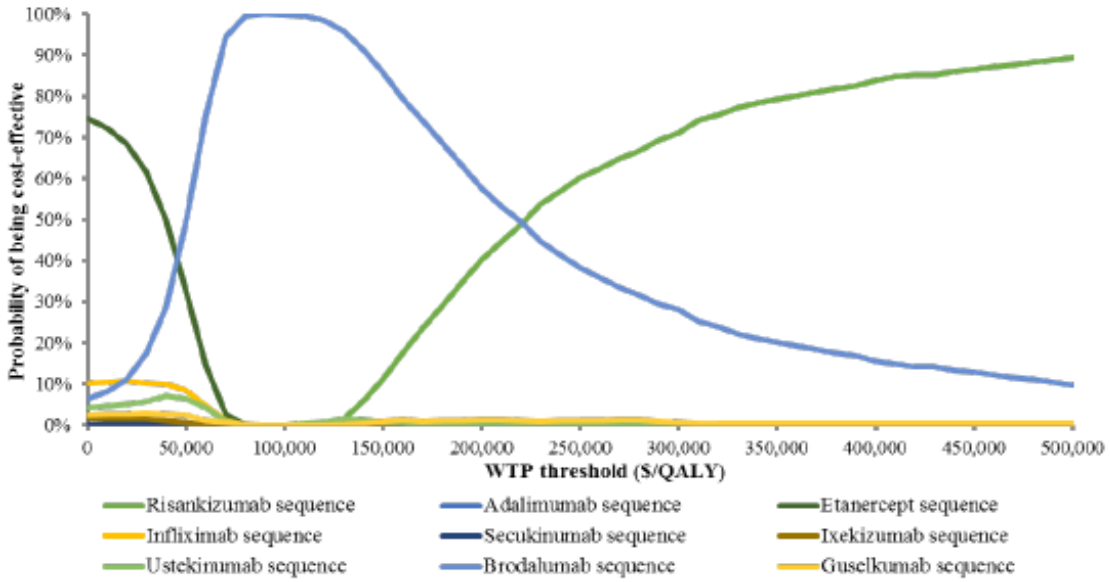
At the end of the primary response period, risankizumab had better PASI 50, 75, 90, and 100 responses than ustekinumab, secukinumab, etanercept, adalimumab, infliximab, and guselkumab (Table 9). The ITC [redacted] in the primary outcome, i.e., PASI 75 (median relative risk: [redacted]). The time to assessment was assumed to be either 10 weeks (infliximab), 12 weeks (brodalumab, etanercept, ixekizumab, and secukinumab) or 16 weeks (risankizumab, adalimumab, guselkumab, and ustekinumab), based on product monographs.

Manufacturer's Base Case

Brodalumab dominated infliximab, adalimumab, guselkumab, and ixekizumab in the base case, i.e., brodalumab was associated with lower total costs and more QALYs gained when compared with these treatments. Both ustekinumab and secukinumab were subject to extended dominance through brodalumab and etanercept, and risankizumab and etanercept, respectively i.e., combinations of brodalumab and etanercept, and risankizumab and etanercept would result in lower costs and more QALYs when compared with ustekinumab and secukinumab, respectively.

Etanercept was associated with the lowest cost ($76,492) and fewest QALYs (0.3414). When compared with etanercept, brodalumab was more costly and more effective. The incremental cost per QALY gained from brodalumab was $47,006 (compared with etanercept). When compared with brodalumab, risankizumab was more costly and more effective. The incremental cost per QALY gained from risankizumab was $203,266 compared with brodalumab (Figure 1).

Figure 1: Manufacturer's Cost-Effectiveness Acceptability Curve



QALY = quality-adjusted life-year; WTP = willingness to pay.

Source: Manufacturer's pharmacoeconomic submission.[2]

CADTH Reanalysis

Table 10: CADTH Reanalysis and Exploratory Analyses Results

Scenario		Treatments	Total Costs ($)	Total QALYs	Sequential ICUR ($ per QALY)
	Base case submitted by manufacturer	Etanercept	76,492	0.341	
		Ustekinumab	86,618	0.506	Ext. dominated
		Brodalumab	88,017	0.587	47,006
		Infliximab	88,023	0.485	Dominated
		Adalimumab	89,832	0.507	Dominated
		Guselkumab	96,645	0.564	Dominated
		Ixekizumab	96,663	0.529	Dominated
		Secukinumab	99,662	0.591	Ext. dominated
		Risankizumab	114,459	0.717	203,266
1.	**20% discontinuation rate**	Etanercept	78,069	0.358	
		Ustekinumab	89,148	0.535	Ext. dominated
		Brodalumab	93,438	0.653	52,045
		Infliximab	98,756	0.595	Dominated
		Adalimumab	92,314	0.533	Dominated
		Guselkumab	104,616	0.641	Dominated
		Ixekizumab	109,450	0.653	Dominated
		Secukinumab	101,378	0.610	Dominated
		Risankizumab	108,409	0.660	2,083,647

Scenario		Treatments	Total Costs ($)	Total QALYs	Sequential ICUR ($ per QALY)
2.	**BSC annual costs of $421**	Etanercept	40,828	0.346	
		Ustekinumab	56,458	0.510	Ext. dominated
		Brodalumab	59,757	0.590	77,416
		Infliximab	56,594	0.489	Dominated
		Adalimumab	59,546	0.510	Ext. dominated
		Guselkumab	68,946	0.575	Dominated
		Ixekizumab	65,812	0.528	Dominated
		Secukinumab	71,138	0.590	Ext. dominated
		Risankizumab	90,732	0.721	237,272
3.	**Use of costs reported in the Ontario Drug Benefit Formulary**	Etanercept	80,975	0.345	
		Ustekinumab	89,901	0.510	Dominated
		Brodalumab	87,796	0.589	27,992
		Infliximab	87,688	0.487	Ext. dominated
		Adalimumab	93,815	0.510	Dominated
		Guselkumab	97,256	0.575	Dominated
		Ixekizumab	98,404	0.528	Dominated
		Secukinumab	102,755	0.591	Ext. dominated
		Risankizumab	114,381	0.720	202,876
4.	**Remove suicide-related costs associated with brodalumab**	Etanercept	76,215	0.345	
		Ustekinumab	86,264	0.507	Ext. dominated
		Brodalumab	87,646	0.587	47,112
		Infliximab	87,410	0.484	Dominated
		Adalimumab	89,614	0.510	Dominated
		Guselkumab	96,845	0.571	Dominated
		Ixekizumab	95,650	0.524	Dominated
		Secukinumab	98,742	0.587	Ext. dominated
		Risankizumab	114,234	0.719	201,985
5.	**CADTH base-case reanalysis**	Etanercept	47,521	0.357	
		Ustekinumab	63,203	0.534	Ext. dominated
		Brodalumab	67,116	0.652	66,344
		Infliximab	70,694	0.594	Dominated
		Adalimumab	67,114	0.531	Dominated
		Guselkumab	78,087	0.640	Dominated
		Ixekizumab	85,993	0.651	Dominated
		Secukinumab	77,590	0.609	Dominated
		Risankizumab	82,380	0.658	2,370,521
5a.	**CADTH base case plus use of PASI 90 to measure response**	Etanercept	29,355	0.254	
		Ustekinumab	45,250	0.415	Ext. dominated
		Brodalumab	55,637	0.569	83,678
		Infliximab	54,267	0.487	Ext. dominated
		Adalimumab	47,129	0.413	Dominated
		Guselkumab	63,307	0.549	Dominated
		Ixekizumab	71,803	0.567	Dominated
		Secukinumab	61,025	0.507	Dominated
		Risankizumab	69,167	0.577	1,580,146

Scenario		Treatments	Total Costs ($)	Total QALYs	Sequential ICUR ($ per QALY)
5b.	**CADTH base case plus use of 15% discontinuation rate for all biologics**	Etanercept	54,461	0.400	
		Ustekinumab	73,463	0.612	Ext. dominated
		Brodalumab	79,061	0.755	Dominated
		Infliximab	82,709	0.685	Dominated
		Adalimumab	78,467	0.609	69,366
		Guselkumab	91,741	0.739	Dominated
		Ixekizumab	100,629	0.754	Dominated
		Secukinumab	90,623	0.703	Dominated
		Risankizumab	96,455	0.761	2,737,460

BSC = best supportive care; ext. = extendedly; ICUR = incremental cost-utility ratio; PASI = Psoriasis Area Severity Index; QALY = quality-adjusted life-year.

Note: As results are based on probabilistic analysis, the estimates may vary slightly between scenario analyses.

Changing the discontinuation rate had the largest impact on the results (i.e., assuming a discontinuation rate of 20% for all biologics resulted in an ICUR of $2,083,647 for risankizumab compared with brodalumab). As discussed earlier, this is because the economic model assumes that patients who discontinue will have the response level of placebo (i.e., low QALYs) while continuing to incur the cost of BSC.

Table 11: Price Reduction for Risankizumab Based on CADTH Base Case (Deterministic)

Scenario	Treatments	Total Costs ($)	Total QALYs	Sequential ICUR ($ per QALY)
CADTH base case (deterministic): submitted price for risankizumab	Etanercept	46,693	0.352	
	Ustekinumab	61,937	0.525	Ext. dominated
	Brodalumab	65,664	0.640	65,887
	Adalimumab	65,789	0.523	Dominated
	Infliximab	69,192	0.583	Dominated
	Secukinumab	75,986	0.598	Dominated
	Guselkumab	76,419	0.628	Dominated
	Risankizumab	80,718	0.647	2,178,018
	Ixekizumab	84,241	0.639	Dominated
10% reduction	Etanercept	46,693	0.352	
	Ustekinumab	61,937	0.525	Ext. dominated
	Brodalumab	65,664	0.640	65,887
	Adalimumab	65,789	0.523	Dominated
	Infliximab	69,192	0.583	Dominated
	Risankizumab	73,098	0.647	1,075,476
	Secukinumab	75,986	0.598	Dominated
	Guselkumab	76,419	0.628	Dominated
	Ixekizumab	84,241	0.639	Dominated
20% reduction	Etanercept	46,693	0.352	
	Ustekinumab	61,937	0.525	Ext. dominated
	Risankizumab	65,477	0.647	63,708
	Brodalumab	65,664	0.640	Dominated

Scenario	Treatments	Total Costs ($)	Total QALYs	Sequential ICUR ($ per QALY)
	Adalimumab	65,789	0.523	Dominated
	Infliximab	69,192	0.583	Dominated
	Secukinumab	75,986	0.598	Dominated
	Guselkumab	76,419	0.628	Dominated
	Ixekizumab	84,241	0.639	Dominated
25% reduction	Etanercept	46,693	0.352	
	Risankizumab	61,666	0.647	50,784
	Ustekinumab	61,937	0.525	Dominated
	Brodalumab	65,664	0.640	Dominated
	Adalimumab	65,789	0.523	Dominated
	Infliximab	69,192	0.583	Dominated
	Secukinumab	75,986	0.598	Dominated
	Guselkumab	76,419	0.628	Dominated
	Ixekizumab	84,241	0.639	Dominated
26% reduction	Etanercept	46,693	0.352	
	Risankizumab	60,904	0.647	48,199
	Ustekinumab	61,937	0.525	Dominated
	Brodalumab	65,664	0.640	Dominated
	Adalimumab	65,789	0.523	Dominated
	Infliximab	69,192	0.583	Dominated
	Secukinumab	75,986	0.598	Dominated
	Guselkumab	76,419	0.628	Dominated
	Ixekizumab	84,241	0.639	Dominated
30% reduction	Etanercept	46,693	0.352	
	Risankizumab	57,856	0.647	37,860
	Ustekinumab	61,937	0.525	Dominated
	Brodalumab	65,664	0.640	Dominated
	Adalimumab	65,789	0.523	Dominated
	Infliximab	69,192	0.583	Dominated
	Secukinumab	75,986	0.598	Dominated
	Guselkumab	76,419	0.628	Dominated
	Ixekizumab	84,241	0.639	Dominated

ext. = extendedly; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Note: Due to long model run-time, price-reduction scenarios were initially conducted using deterministic analysis, followed by probabilistic analysis of the most relevant price-reduction scenario (Table 12).

Table 12: Price Reduction for Risankizumab Based on CADTH Base Case (Probabilistic)

Scenario	Treatments	Total Costs ($)	Total QALYs	Sequential ICUR ($ per QALY)
CADTH base case: submitted price for risankizumab	Etanercept	47,521	0.357	
	Ustekinumab	63,203	0.534	Ext. dominated
	Adalimumab	67,114	0.531	Dominated
	Brodalumab	67,116	0.652	66,344
	Infliximab	70,694	0.594	Dominated
	Secukinumab	77,590	0.609	Dominated
	Guselkumab	78,087	0.640	Dominated
	Risankizumab	82,380	0.658	2,370,521
	Ixekizumab	85,993	0.651	Dominated
25% reduction	Etanercept	47,462	0.360	
	Risankizumab	62,827	0.660	51,217
	Ustekinumab	63,112	0.530	Dominated
	Adalimumab	67,017	0.530	Dominated
	Brodalumab	67,021	0.650	Dominated
	Infliximab	70,592	0.590	Dominated
	Secukinumab	77,481	0.610	Dominated
	Guselkumab	77,980	0.640	Dominated
	Ixekizumab	85,871	0.650	Dominated
26% reduction	Etanercept	47,539	0.357	
	Risankizumab	62,165	0.659	48,451
	Ustekinumab	63,232	0.535	Dominated
	Brodalumab	67,150	0.653	Dominated
	Adalimumab	67,151	0.532	Dominated
	Infliximab	70,731	0.595	Dominated
	Secukinumab	77,630	0.610	Dominated
	Guselkumab	78,132	0.641	Dominated
	Ixekizumab	86,034	0.652	Dominated
30% reduction	Etanercept	47,467	0.359	
	Risankizumab	58,953	0.660	38,138
	Ustekinumab	63,131	0.536	Dominated
	Adalimumab	67,029	0.533	Dominated
	Brodalumab	67,029	0.653	Dominated
	Infliximab	70,614	0.595	Dominated
	Secukinumab	77,498	0.610	Dominated
	Guselkumab	77,982	0.641	Dominated
	Ixekizumab	85,887	0.652	Dominated

ext. = extendedly; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

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