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CADTH COMMON DRUG REVIEW

Pharmacoeconomic Review Report

Brodalumab (SILIQ)

(Valeant Canada LP)

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

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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.

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Abbreviations

AE	adverse event
BDL	brodalumab
BSC	best supportive care
CDR	CADTH Common Drug Review
EQ-5D	EuroQoL 5-Dimension questionnaire
ICER	incremental cost-effectiveness ratio
IL-17	Interleukin-17
NMA	network meta-analysis
PASI	Psoriasis Area and Severity Index
QALY	quality-adjusted life-year
SEB	subsequent entry biologic
USK	ustekinumab

Table 1: Summary of the Manufacturer's Economic Submission

Drug Product	BDL (Siliq) 100 mg/mL pre-filled syringe
Study Question	Is BDL cost-effective compared with other biologic therapies and those anticipated to be approved shortly for the treatment of adult patients with moderate-to-severe plaque psoriasis?
Type of Economic Evaluation	Cost-utility analysis
Target Population	Adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy
Treatment	BDL 210 mg SC at weeks 0, 1, and 2 followed by 210 mg every 2 weeks
Outcome	Quality-adjusted life-years
Comparator(s)	**Base-case analysis** • Best supportive care • Ixekizumab (Taltz) 160 mg SC at week 0 followed by 80 mg SC at 2 weeks, 4 weeks, 6 weeks, 8 weeks, 10 weeks, and 12 weeks, then every 4 weeks • Secukinumab (Cosentyx) 300 mg SC at weeks 0, 1, 2, 3, and 4, then monthly • Etanercept (Enbrel) 50 mg twice weekly for 3 months, then weekly • Infliximab (Remicade and SEB) 5 mg/kg infusion at 0 weeks, 2 weeks, and 6 weeks, then every 8 weeks • Adalimumab (Humira) 80 mg SC at week 0, 40 mg SC at week 1, then 40 mg every 2 weeks • USK (Stelara) 45 mg SC at weeks 0 and 4, then every 12 weeks **Scenario analysis only** • Guselkumab (Tremfya) 100mg SC at weeks 0 and 4, then every 8 weeks • Etanercept (SEB) as Enbrel • Adalimumab (SEB) as Humira
Perspective	Canadian public health care payer
Time Horizon	10 years
Results for Base Case	• Based on the manufacturer's probabilistic analysis, BDL was less costly and more effective (i.e., gained more QALYs) when compared with infliximab, infliximab SEB, secukinumab, and USK. Adalimumab and etanercept were both subject to extended dominance through BSC and brodalumab. • BDL was costlier and more effective compared with BSC, resulting in an incremental cost per QALY gained for BDL versus BSC of $118,741. • BDL was less costly but less effective compared with ixekizumab, resulting in an incremental cost per QALY gained for ixekizumab of $6.9 million (when compared with BDL). • BSC had a 100% probability of being cost-effective if a QALY was valued at $50,000.
Key Limitations	• The manufacturer assumed continued efficacy beyond the time horizon of the clinical trials (up to 48 weeks). No assumption with respect to the waning of treatment effect was included. • Uncertainty exists with the manufacturer-commissioned indirect treatment comparison estimates for treatment efficacy.

CDR Estimate(s)	• Based on the results of the manufacturer-commissioned indirect treatment comparison, BDL was not cost-effective compared with BSC. • BDL may be the optimal treatment for adult patients with plaque psoriasis when considering biologic therapies. Where a decision-maker is willing to pay $50,000 per QALY, BDL would be optimal in 70.5% of simulations, followed by adalimumab (21.5%) and etanercept (8.0%). • BDL was unlikely to be cost-effective compared with the potential therapies etanercept SEB and adalimumab SEB. • CDR was unable to conduct a reanalysis to address the issue of waning of treatment effect.

BDL = brodalumab; BSC = best supportive care; CDR = CADTH Common Drug Review; QALY = quality-adjusted life-year; SC = subcutaneous; SEB = subsequent entry biologic; USK = ustekinumab.

Drug	Brodalumab (Siliq)
Indication	For the treatment moderate-to-severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.
Reimbursement Request	As per indication
Dosage Form(s)	210 mg/1.5 mL (single-dose pre-filled syringe)
NOC Date	March 6, 2018
Manufacturer	Valeant Canada LP

Executive Summary

Background

Brodalumab (BDL) is a human anti–interleukin-17 (IL-17) receptor A monoclonal antibody that selectively targets human IL-17 receptor A and antagonizes the effects of IL-17A, IL-17F, IL-17A/F, and IL-25, all of which are pro-inflammatory cytokines implicated in the pathogenesis of psoriasis.[1,2] BDL is indicated for the treatment of adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.[3] The recommended dose of BDL is 210 mg, to be given as a subcutaneous injection at week 0, week 1, and week 2, followed by maintenance dosing every two weeks thereafter.

The manufacturer submitted a cost-utility analysis based on a Markov state-transition model comparing BDL with currently available treatments for adult patients with plaque psoriasis.[4] Comparators included ixekizumab, secukinumab, etanercept (Enbrel), infliximab (Remicade and the subsequent entry biologic [SEB]), adalimumab, ustekinumab (USK), and best supportive care (BSC). In scenario analysis, additional comparators were considered: guselkumab, etanercept (SEB), and adalimumab (SEB). At entry into the model, patients with moderate-to-severe plaque psoriasis were assigned to a health state based on the Psoriasis Area and Severity Index (PASI) response (less than 50, 50 to 74, 75 to 89, 90 to 99, or 100) based on their treatment. After the treatment induction, patients with a PASI score < 75 moved to BSC. The manufacturer then estimated the proportion of patients in

each PASI response score at the end of year 1 and all subsequent years. Patients remaining on treatment maintained the same response (i.e., did not transition between response scores), but withdrew from treatment, moved to BSC, or died, based on the background probability of death (which did not vary by health state). Thus, the manufacturer assumed full continuation of treatment effect beyond the induction period. Those moving to BSC were all assumed to obtain a PASI response of < 50. They also remained in this state each cycle or died based on the background probability of death.

Treatment effects were based on a manufacturer-commissioned unpublished network meta-analysis (NMA).[5] [redacted] Mortality was based on Canada all-cause mortality data and was adjusted by age and gender.[6] In the base-case analysis, discontinuation rates were assumed the same for all biologics based on data for BDL from the available clinical trials and clinical expert opinion.[1,2] Adverse events (AEs) were not included in the model, based on clinical advice that there were unlikely to be significant differences in AE profiles between the biologics. Utility values for baseline and PASI response score were derived from the AMAGINE-1 clinical trial. Costs included were drug costs, administration costs, physician visits, and laboratory tests.

In the base-case probabilistic analysis, the manufacturer reported that BDL was less costly and more effective (i.e., gained more quality-adjusted life-years [QALYs]) when compared with infliximab (brand and SEB), secukinumab, and USK. Etanercept and adalimumab were subject to extended dominance through BSC and BDL — that is, greater QALYs at lower costs could be achieved through use of BSC and BDL. BDL was costlier and more effective when compared with BSC, resulting in an incremental cost per QALY gained for BDL of $118,741 compared with BSC. Ixekizumab was costlier and more effective when compared with BDL, resulting in an incremental cost per QALY gained for ixekizumab of $6,948,457 (compared with BDL). BSC has a 100% probability of being optimal when a QALY is valued at $50,000.

Summary of Identified Limitations and Key Results

The key limitation identified by CADTH Common Drug Review (CDR) was the reliance on indirect estimates of the comparative clinical efficacy for BDL. Estimates were obtained from the manufacturer-commissioned NMA. Further, no studies have been conducted in populations for which there may be a need for an additional biologic treatment (e.g., patients failing on or intolerant to other biologic therapies or patients who are treatment-resistant). Results from [redacted] suggest that over the short-term induction phase, BDL may be more efficacious than a number of other biologics in attaining PASI 75, PASI 90, and PASI 100 responses, but may be similar in efficacy to ixekizumab. There is uncertainty in the results of the indirect treatment comparison for short-term efficacy, arising from between-study heterogeneity that may not have been adequately controlled. Further, longer-term comparative efficacy data from randomized controlled trials are lacking.

A further limitation is the assumption of maintained clinical efficacy for the 10-year time horizon without consideration of any waning of treatment effect. This could not be explored through reanalysis of the model, given the model structure. The analyses are based on the list price of comparators. If Product Listing Agreements are in place for any of the available biologic therapies, then the conclusions from the analysis would not hold.

CDR conducted a further analysis that involved removing BSC from the analysis. Under this analysis, BDL was costlier and more effective compared with adalimumab, resulting in an

incremental cost per QALY gained for BDL of $42,981 compared with adalimumab. There was a 70.5% probability that BDL was optimal given an incremental cost per QALY value of $50,000.

Conclusions

Based on the manufacturer's results, BDL may be cost-effective when considering all currently available biologic treatments for patients with moderate-to-severe plaque psoriasis assuming that a decision-maker's willingness to pay per QALY is between $43,071 and $6,378,680. Excluding BSC as an option, BDL had a 70.5% probability of being cost-effective at a willingness-to-pay threshold of $50,000 per QALY.

It should be noted that the economic model did not allow CDR to assess the impact of assumptions relating to the waning of treatment effect. This, combined with the lack of comparative effectiveness data versus all biologics and the inability to consider negotiated prices, suggests that the interpretation of results may warrant careful interpretation as the true cost-effectiveness of BDL is uncertain.

Compared with currently available biologics for the treatment plaque psoriasis, BDL is less costly ($18,060 in the first year, $16,770 in subsequent years) at the current list prices of comparators.

Information on the Pharmacoeconomic Submission

Summary of the Manufacturer's Pharmacoeconomic Submission

The manufacturer submitted an economic model that estimated the costs and quality-adjusted life-years (QALYs) gained using alternative treatments for plaque psoriasis.[4] The model compared the cost-effectiveness of brodalumab (BDL) and other biologic therapies reimbursed in Canada: adalimumab, etanercept, infliximab (brand and subsequent entry biologic [SEB]), ixekizumab, ustekinumab (USK), and secukinumab. In scenario analyses, additional comparators were considered: guselkumab, etanercept (SEB), and adalimumab (SEB) (Table 15). The target population was adult patients with plaque psoriasis, based on the average population in the AMAGINE-I, AMAGINE-II, and AMAGINE-III clinical trials.[1,2] The modelled patients were assumed to be 45 years old, on average, at the time of entry into the model; patients were also predominantly male (69.3%) and had a mean weight of 91 kg.

The model was run using yearly cycles over a 10-year time horizon in the base case. However, the first year allowed for initial effects up to the end of the induction period with further effects to the end of year 1. All costs and outcomes were discounted at an annual rate of 1.5%. The analysis was conducted from the perspective of the Canadian publicly funded health care system.[7]

Model Structure

The analysis was conducted using a cohort multi-state Markov model developed in Microsoft Excel. Model states related to health states combining both Psoriasis Area and Severity Index (PASI) response score (less than 50, 50 to 74, 75 to 89, 90 to 99, or 100), treatment received (either initial biologic or best supportive care [BSC]), and death. At entry into the model, patients were assigned to a health state based on their PASI score response (less than 50, 50 to 74, 75 to 89, 90 to 99, or 100) for the relevant treatment alternative. After the treatment induction, patients with a PASI response score < 75 moved to BSC. Those with a PASI response ≥ 75 could remain in their existing health state, discontinue therapy, or die. Patients remaining on treatment did not transition between response scores; as a result, the model assumed full continuation of treatment effect beyond the induction period. Those moving to BSC were all assumed to obtain a PASI response of < 50; they also remained in this state each cycle or died based on the background probability of death.

Model Inputs

At model entry, the cohort was assigned to a PASI response score based on the manufacturer's sponsored network meta-analysis (NMA).[5] The objective of the NMA was to create a network of evidence using efficacy data reported in the studies to estimate the relative effectiveness of BDL compared with other biologic drugs. The base-case analyses were performed [redacted]

[redacted](Table 11). Similar results were observed from the fixed-effects multinomial NMA.

In the base case, the manufacturer assumed equal discontinuation rates for all biologic therapies. A discontinuation rate of 3.8% was applied in the first year based on data from the BDL clinical trials.[1,2] This related to the period after the induction period (note that the actual discontinuation rates for each biologic in the first year will vary, as they will include the proportion of patients with a PASI response score < 75). A discontinuation rate of 15% for subsequent years was used for all biologics and was based on clinical expert opinion. In a scenario analysis, differential probabilities for discontinuation for adalimumab, etanercept, infliximab, and USK were obtained from an analysis of the Psoriasis Longitudinal Assessment and Registry (PSOLAR) database.[8] Data for other biologics, including BDL, were not available; the probability for USK was assumed to apply (Table 12).

The model did not account for adverse events (AEs) associated with treatments. The manufacturer argued that its clinical expert suggested that AE rates would not vary significantly between biologics and that, as a result, they would not affect the results. These arguments were accepted by the clinical expert consulted by CADTH for this review. A scenario analysis was conducted in which a rate of suicide associated with biologics was included using data from the BDL clinical trials and applying them to all biologics.

Mortality was based on Canadian all-cause mortality data, adjusted by age and gender.[6]

BSC was assumed to consist of combination therapy with biologics and traditional systemic therapies and was based on clinical expert opinion. This included topical treatments, such as calcipotriol and betamethasone, and the use of phototherapy by all patients.

Health state utilities in the model were based on PASI response score (a baseline utility at onset of treatment followed by increments for PASI response: less than 50, 50 to 74, 75 to 89, 90 to 99, or 100) and the incidence of severe infections. Data were derived from responses to the EuroQol 5-Dimensions (EQ-5D) utility instrument completed as part of the AMAGINE-1 clinical trial (Table 13).[1,9] Utility values were estimated using the Canadian EQ-5D tariff.[10] A baseline utility was derived from responses at clinical study entry; utility scores for PASI response categories were derived from responses at the 12-week follow-up and were derived through regression analysis.

Costs included were those for disease management (physician visits and laboratory fees), administration and monitoring, and drug acquisition. The schedule of treatment monitoring was developed through clinical expert opinion. The clinical expert consulted by CADTH for this review broadly supported the estimates of resource use. Dosing schedules for biologics were based on Canadian guidelines for psoriasis and product monographs. All costs were assumed to be reported in 2017 Canadian dollars. For BSC, costs were based on the distribution of patients to topical treatments, the costs of phototherapy, and clinical expert opinion. Unit costs were derived from relevant Canadian sources.[11-13]

Manufacturer's Base Case

The manufacturer reported that BDL was associated with a total cost of $90,557 and 7.134 QALYs over the 10-year analysis horizon (Table 2). BDL was costlier and more effective than BSC. The incremental cost per QALY gained for BDL versus BSC was $118,741.

BDL dominated secukinumab, USK, and infliximab (brand and SEB) in the base case; i.e., BDL was associated with lower total costs and greater QALYs gained when compared with

these treatments. Both adalimumab and etanercept were subject to extended dominance through BSC and BDL; i.e., combinations of BSC and BDL would result in lower costs and greater QALYs when compared with adalimumab and etanercept.

When compared with ixekizumab, BDL was associated with lower costs and lower QALYs. The incremental cost per QALY gained from ixekizumab was $6.9 million (compared with BDL).

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

	Total Costs ($)	Total QALYs	Incremental Cost per QALY Gained Versus BSC	Sequential ICER
Non-Dominated Options				
BSC	$16,365	6.509		
Brodalumab	$90,557	7.134	$118,741	$118,741
Ixekizumab	$112,254	7.137	$152,703	$6,948,457
Dominated Options				
Etanercept	$78,005	6.828	$193,053	Subject to extended dominance through brodalumab and BSC, through adalimumab and BSC, through infliximab SEB and BSC, through ustekinumab (45 and 90) and BSC, and through secukinumab and BSC
Adalimumab	$80,711	6.904	$162,814	Subject to extended dominance through brodalumab and BSC, through infliximab SEB and BSC, through ustekinumab 90 and BSC, and through secukinumab and BSC
Infliximab SEB	$91,698	7.093	$128,884	Dominated by brodalumab and ixekizumab
Ustekinumab 45 mg	$93,791	6.979	$164,817	Dominated by brodalumab, ixekizumab, and infliximab SEB Subject to extended dominance through ustekinumab 90 and BSC, and through secukinumab and BSC
Ustekinumab 90 mg	$98,198	7.016	$161,398	Dominated by brodalumab, ixekizumab, and infliximab SEB Subject to extended dominance through secukinumab and BSC
Secukinumab	$103,870	7.070	$156,029	Dominated by brodalumab, ixekizumab, and infliximab SEB
Infliximab	$164,619	7.093	$253,642	Dominated by brodalumab, ixekizumab, and infliximab SEB

BSC = best supportive care; ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life-year; SEB = subsequent entry biologic.
Note: All costs are presented in 2017 Canadian dollars.
Source: Total costs and QALYs are probabilistic values, as reported in the manufacturer's submission report and the original economic model submitted to CADTH.[4]

Thus, BSC was found to be the optimal therapy unless a decision-maker was willing to pay more than $118,741 per QALY gained. If a decision-maker is willing to pay this amount and less than $6.9 million, BDL would be the optimal therapy. If a decision-maker is willing to pay at least $6.9 million, ixekizumab would be the optimal therapy. The probability that BSC was optimal was 100% for all values of a QALY up to $100,000.

CADTH Common Drug Review (CDR) reran the probabilistic analysis to confirm results similar to those in the manufacturer's submission. Results were consistent, with BDL emerging as the optimal therapy assuming willingness to pay of $118,707 to $6.4 million per QALY gained. The probability that BSC was optimal was 100% for all values of a QALY up to $100,000 (Table 3).

Table 3: Summary of CADTH Common Drug Review Rerunning of the Manufacturer's Base Case (Probabilistic)

	Total Costs ($)	Total QALYs	Incremental Cost per QALY Gained Versus BSC	Sequential ICER
Non-Dominated Options				
BSC	$16,369	6.510		
Brodalumab	$90,600	7.135	$118,707	$118,707
Ixekizumab	$112,341	7.138	$152,642	$6,378,680
Dominated Options				
Etanercept	$77,992	6.829	$193,130	Subject to extended dominance through brodalumab and BSC, through adalimumab and BSC, through infliximab SEB and BSC, through ustekinumab (45 and 90) and BSC, and through secukinumab and BSC
Adalimumab	$80,669	6.904	$162,883	Subject to extended dominance through brodalumab and BSC, through infliximab SEB and BSC, through ustekinumab 90 and BSC, and through secukinumab and BSC
Infliximab SEB	$91,733	7.095	$128,837	Dominated by brodalumab and ixekizumab
Ustekinumab 45 mg	$93,898	6.980	$164,773	Dominated by brodalumab, ixekizumab, and infliximab SEB. Subject to extended dominance through ustekinumab 90 and BSC, and through secukinumab and BSC
Ustekinumab 90 mg	$98,295	7.017	$161,353	Dominated by brodalumab, ixekizumab, and infliximab SEB Subject to extended dominance through secukinumab and BSC
Secukinumab	$103,966	7.071	$155,981	Dominated by brodalumab, ixekizumab, and infliximab SEB
Infliximab	$164,684	7.095	$253,549	Dominated by brodalumab, ixekizumab, and infliximab SEB

BSC = best supportive care; ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life-year; SEB = subsequent entry biologic.
Note: All costs are presented in 2017 Canadian dollars.
Source: Total costs and QALYs are probabilistic values as reported in the manufacturer's submission report and the original economic model submitted to CADTH.[4]

Detailed information on the total cost for each comparator is provided in Appendix 4, Table 14 and Figure 2.

Summary of Manufacturer's Scenario Analyses

The manufacturer conducted a range of scenario analyses relating to both structural and methodological uncertainty. Under each scenario, results in terms of costs and QALYs were estimated using probabilistic analyses.

The following scenarios were considered:

- Inclusion of costs associated with subcutaneous or intravenous treatment administration (structural)
- Adoption of societal perspective, including productivity loss and travel costs (structural)

- Time horizon set to five years (methodological)
- Discount rates for both costs and benefits = 0%, 3%, and 5% (methodological)
- Treatment efficacy [redacted]
- Full treatment response defined as achievement of PASI 90 (methodological)
- Various alternative utility sources[1,14-17] (methodological)
- Inclusion of the risk of death due to suicide — assumed equal for all biologics (structural)
- Use of differential treatment discontinuation rates[8] (methodological)
- Include guselkumab, adalimumab SEB, and etanercept SEB as treatment comparators (structural).

The results of the manufacturer's scenario analysis lead to findings that were similar to the base-case analysis with only two exceptions.

For an analysis in which the UK EQ-5D tariff[14] was employed instead of the Canadian tariff, the incremental cost-effectiveness ratio (ICER) for BDL versus BSC was much lower than for the base case ($62,513 per QALY); the ICER for ixekizumab versus BDL was similarly lower at $3.2 million per QALY.

For the analysis including adalimumab SEB, etanercept SEB, and guselkumab, BDL was both costlier and more effective than both adalimumab SEB and etanercept SEB. The ICER for adalimumab versus BSC was $91,763. Etanercept SEB was dominated by adalimumab SEB (i.e., adalimumab was less costly and associated with greater QALYs). The ICER for BDL versus adalimumab SEB was $163,867 per QALY.

Limitations of the Manufacturer's Submission

CDR identified the following key limitations with the manufacturer's model:

- **Reliance on data from the NMA:** Direct evidence of the relative effectiveness of BDL versus other biologics is limited solely to comparison with USK and is limited to only 12 weeks follow-up. Thus, comparative efficacy inputs relating to PASI response score were sourced from a manufacturer-commissioned NMA.[5] As indicated in the CDR clinical review, based on the results of three phase III randomized controlled trials comparing BDL with placebo and USK, BDL resulted in statistically significant and clinically important improvements over the short-term induction phase in PASI and static Physician Global Assessment scores. Results from [redacted] suggest that, over the short-term induction phase, BDL may be more efficacious than a number of other biologics in attaining PASI 75, PASI 90, and PASI 100 responses, but may be similar in efficacy to ixekizumab. There is some uncertainty in the results of the indirect treatment comparison for short-term efficacy, arising from between-study heterogeneity that may not have been adequately controlled. Further, longer-term comparative efficacy data from randomized controlled trials are lacking. Further, the size and duration of the included trials were likely insufficient to assess comparative safety, particularly for rare or latent harms. However, the Health Canada–approved product monograph for BDL includes a boxed warning related to the risk of suicidality that may be expected to influence prescriber behaviour.

- **Duration of treatment efficacy:** Within the model, it is assumed that the efficacy of treatment was applied in the model at the end of the induction period and that, from that period onward, there were no further changes in PASI score. Thus, for BDL, the assumption is that comparative clinical efficacy data at 12 weeks are maintained for up to 10 years. The impact of this underlying assumption — that the treatment efficacy is maintained for the duration of the analysis — should be assessed through scenario analysis. Any assumptions relating to waning of treatment effect would likely have a significant effect on the study results.
- The recent CADTH economic guidelines recommend that the percentage of QALY gains associated with a treatment that relates to the period for which comparative clinical effectiveness data are available should be reported.[7] For the comparison of BDL and BSC, the QALY gain for the period for which clinical data were available was 0.028 (4.4% of the estimated QALY gain of 0.641 over the 10-year time horizon). For the comparison of BDL and USK 45 mg, the QALY gains with BDL were 0.005, which represented 3.3% of the estimated QALY gain of 0.158 over a 10-year time horizon. For the comparison of BDL and USK 90 mg, the QALY gains were 0.004, which represented 3.3% of the estimated QALY gain of 0.119 over a 10-year time horizon. Given limitations, this analysis was based on a deterministic analysis of outcomes.
- Thus, the assumption relating to continued relative efficacy over the 10-year time horizon may be significantly affecting the results of the analysis. However, given the design of the model, it was not possible to incorporate alternate assumptions addressing this issue.
- **Lack of data for discontinuation rates with BDL:** No data were available to inform the AE and long-term discontinuation rates for BDL. The manufacturer adopted an assumption that the rates of discontinuation were equal for all biologics. This assumption is in line with previous guidance from a CDR clinical expert.
- **Resource use within BSC:** The CADTH clinical expert suggested that resource use within BSC could differ from that suggested by the manufacturer's submission. Specifically, not all patients may receive phototherapy, and a proportion may receive cyclosporine or methotrexate instead. CDR noted that the impact of such changes on the costs of BSC would be minimal. Without substantive evidence to support other estimates, the manufacturer's baseline assumptions were adopted.

CADTH Common Drug Review Reanalyses

As noted in the limitations, CDR identified limitations relating to the lack of direct evidence of the relative effectiveness of BDL versus other biologics and the lack of evidence to support the continued relative effectiveness of BDL beyond the treatment induction period. Neither of these issues can be addressed with the submitted economic model. Thus, CDR was not able to conduct any further reanalyses to address these issues.

The results of the manufacturer's submission suggest that BDL is not cost-effective when compared with BSC. Given that biologics are reimbursed in the treatment of moderate-to-severe plaque psoriasis, the relevance of including BSC as a comparator is unclear. CDR conducted a further analysis to assess the impact of excluding BSC as a comparator. Based on a sequential probabilistic analysis, etanercept would be cost-effective if a decision-maker was willing to pay no more than $35,373 per QALY. Adalimumab would be cost-effective if a decision-maker was willing to pay at least $35,373 but no more than $43,071 per QALY. BDL would be optimal if the willingness to pay was between $43,071 and $6,378,680.

Ixekizumab would be optimal if a decision-maker was willing to pay at least $6,378,680 per QALY (Table 4). At a willingness-to-pay threshold of $50,000 per QALY gained, BDL had a 70.5% probability of being optimal: the only other biologics with a chance of being optimal were adalimumab (21.5%) and etanercept (8.0%).

Table 4: CADTH Common Drug Review Reanalysis Excluding Best Supportive Care

	Total Costs ($)	Total QALYs	Incremental Cost per QALY Gained Versus Etanercept	Sequential ICER
Non-Dominated Options				
Etanercept	$77,992	6.829		
Adalimumab	$80,669	6.904	$35,373	$35,373
Brodalumab	$90,600	7.135	$41,169	$43,071
Ixekizumab	$112,341	7.138	$110,923	$6,378,680
Dominated Options				
Infliximab SEB	$91,733	7.095	$51,682	Dominated by brodalumab and ixekizumab
Ustekinumab 45 mg	$93,898	6.980	$105,029	Dominated by brodalumab, ixekizumab, and infliximab SEB
Ustekinumab 90 mg	$98,295	7.017	$107,612	Dominated by brodalumab, ixekizumab, and infliximab SEB
Secukinumab	$103,966	7.071	$107,104	Dominated by brodalumab, ixekizumab, and infliximab SEB
Infliximab	$164,684	7.095	$326,052	Dominated by brodalumab, ixekizumab, and infliximab SEB

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life-year; SEB = subsequent entry biologic.
Note: All costs are presented in 2017 Canadian dollars.
Source: Total costs, and QALYs are probabilistic values, as reported in the manufacturer's submission report and the original economic model submitted to CADTH.[4]

The greatest uncertainty over these results relates to the comparative effectiveness of BDL and the other available biologics for plaque psoriasis and whether the relative effectiveness of treatments is maintained beyond the limited trial durations.

A further uncertainty exists in that the results will be sensitive to any negotiated price reductions for other therapies. Given the potential range of such effective prices, CDR was unable to conduct a meaningful reanalysis. For full consideration of the impact of effective prices, the negotiated prices would need to be made available to the CDR pharmacoeconomic reviewer.

Patient Input

Patient input was received from two patient groups: the Canadian Skin Patient Alliance working with Canadian Association of Psoriasis Patients as well as the Canadian Psoriasis Network and Arthritis Consumer Experts. The input indicated that patients with psoriasis experience scales and plaques that can occur anywhere on their bodies. These physical symptoms may affect patients psychologically, causing them to experience embarrassment, shame, self-confidence issues, anxiety, and depression. Other conditions that patients feel are related to their psoriasis include psoriatic arthritis, diabetes, weight gain, and heart disease. Aspects of quality of life and patient preferences were captured by the manufacturer in its model by applying utility values to health states, as defined by PASI scores.

Caregivers of patients with psoriasis often experience increases in the amount of care and household cleaning such as vacuuming, bedding changes, and laundry, along with helping patients who are in pain with simple household chores. In addition, some patients require

help to apply creams, go to phototherapy appointments, or travel to infusion clinics (i.e., if they are on infusion biologics). Information about the potential impact on caregivers was not discussed as part of the manufacturer's submission.

Issues for Consideration

- The confidential nature of the negotiated effective price for pharmaceuticals means CDR is unable to assess the impact of potentially lower prices of comparators on the results. Thus, it is unknown if the reduced effective price of comparator biologics would lead to differing conclusions than the current analysis, based on list prices.
- The clinical expert consulted by CDR for this review indicated that the black box warning regarding the potential risk of suicidality may lead physicians to monitor patients on BDL more frequently. While this would increase the costs associated with BDL, it would not significantly alter the conclusions of the analysis.

Conclusions

Based on the results of a scenario analysis presented by the manufacturer, BDL may be cost-effective when considering all currently available biologic treatments for patients with moderate-to-severe plaque psoriasis assuming that a decision-maker's willingness to pay is between $43,071 and $6,378,680 per QALY. Excluding BSC as an option, BDL had a 70.5% probability of being cost-effective at a willingness-to-pay threshold of $50,000 per QALY.

It should be noted that the economic model did not allow CDR to assess the impact of assumptions relating to the waning of treatment effect. This, combined with the lack of comparative effectiveness data versus all biologics and the inability to consider negotiated prices, suggests that the interpretation of results may warrant careful interpretation as the true cost-effectiveness of BDL is uncertain.

Compared with currently available biologics for the treatment of plaque psoriasis, BDL ($18,060 in the first year, $16,770 in subsequent years) is less costly at the current list prices of comparators.

Appendix 1: Cost Comparison

The comparators presented in Table 5 have been deemed to be appropriate by clinical experts. Comparators may be recommended (appropriate) practice rather than actual practice. Comparators are not restricted to drugs but may be devices or procedures. Costs are manufacturer's list prices, unless otherwise specified. Existing Product Listing Agreements are not reflected in the table; as a result, they may not represent the actual costs to public drug plans.

Table 5: CADTH Common Drug Review Cost Comparison Table for the Treatment of Plaque Psoriasis

Drug/ Comparator	Strength	Dosage Form	Price ($)	Recommended Dose	Average Annual Drug Cost ($)
Brodalumab (Siliq)	210 mg/mL	Pre-filled syringe	$ 645.0000[a]	210 mg SC at weeks 0, 1, and 2, followed by every 2 weeks thereafter	First year: $18, 060 Subsequent years: $16, 770
Other Biologics					
Adalimumab (Humira)	40 mg/0.8 mL	Syringe or pen	$769.9700	80 mg initial dose, then 40 mg every other week starting one week after initial dose	First year: $21,559 Subsequent years: $20,074
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: $21,169
Guselkumab (Tremfya)	100 mg/mL	Pre-filled syringe	$3,059.7400[a]	100 mg SC at weeks 0 and 4, followed by every 8 weeks thereafter	First year: $21,418 Subsequent years: $19,943
Infliximab (Remicade)	100 mg/vial	Vial	$977.0000[b]	5 mg/kg/dose for 3 doses (0 weeks, 2 weeks, 6 weeks), then 5 mg/kg every 8 weeks	First year: $39,080[c] Subsequent years: $31,840[c]
Infliximab (Inflectra, SEB)			$525.0000		First year: $21,000[c] Subsequent years: $17,063[c]
Ixekizumab (Taltz)	80 mg/ 1mL	Pre-filled syringe	$1,519.0000[d]	160 mg initial dose, 80 mg at 2, 4, 6, 8, 10, and 12 weeks; followed by 80 mg every four weeks	First year: $25,823 Subsequent years: $19,801
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 (same for > 100 kg, at 90 mg)	First year: $22,966 Subsequent years: $19,958
Conventional Systemic Treatments					
Methotrexate	2.5 mg 10 mg 20 mg/2 mL 50 mg/2 mL	Tab Tab Vial Vial	$0.6325 $2.7000[b] $12.5000 $8.9200	10 mg to 25 mg by mouth or IM weekly	$141 to $330 $233 to $325

Drug/ Comparator	Strength	Dosage Form	Price ($)	Recommended Dose	Average Annual Drug Cost ($)
Cyclosporine (generics)	10 mg 25 mg 50 mg 100 mg	Cap	$0.6238 $0.9952 $1.9400 $3.8815	2.5 mg to 5 mg/kg daily in 2 divided doses	$3,197 to $7,083[c]
Acitretin (Soriatane)	10 mg 25 mg	Cap	$2.5930 $4.5540	25 mg to 50 mg daily	$1,662 to $3,324
Phosphodiesterase Type 4 Inhibitor					
Apremilast (Otezla)	30 mg	Tab	$19.5714[e]	30 mg twice daily	$14,287

cap = capsule; IM = intramuscular; SC = subcutaneous; SEB = subsequent entry biologic; tab = tablet.
Note: All prices are from the Ontario Drug Benefit Formulary[12] (accessed September 2017), unless otherwise indicated, and do not include dispensing fees.
[a] Manufacturer's submitted price.
[b] Saskatchewan formulary[18] (September 2017).
[c] Assumes patient weight of 90 kg and wastage of excess medication in vials, if applicable.
[d] Wholesale price Newfoundland[19] and Quebec,[20] IMS Quintiles Delta PA[21] (September 2017).
[e] Wholesale price nationwide, IQVIA Delta PA[21] (September 2017).

Appendix 2: Additional Information

Table 6: Submission Quality

	Yes/ Good	Somewhat/ Average	No/ Poor
Are the methods and analysis clear and transparent?	X		
Comments Reviewer to provide comments if checking “no”			
Was the material included (content) sufficient?		X	
Comments Reviewer to provide comments if checking “poor”	Analysis is restricted by the lack of head-to-head clinical trials and the lack of long-term data relating to relative clinical effectiveness.		
Was the submission well organized and was information easy to locate?	X		
Comments Reviewer to provide comments if checking “poor”	None		

Table 7: Authors’ Information

Authors of the Pharmacoeconomic Evaluation Submitted to CADTH Common Drug Review

☐ 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

Appendix 3: Summary of Other Health Technology Assessment Reviews of Drug

The cost-effectiveness of brodalumab (BDL) was assessed by Scottish Medicines Consortium. The National Institute for Health and Care Excellence is currently reviewing BDL. The expected publication date is March 21, 2018.

Table 8: Other Health Technology Assessment Findings

	SMC (December 2017)[22]
Treatment	• BDL pre-filled syringe (210 mg).
Price	• A confidential PAS was considered by SMC, but not reported.
Similarities with CDR submission	• Efficacy inputs based on an NMA of more than 50 studies. It is unclear how similar the submitted NMAs are. • Public payer perspective. • Utility values were derived from EQ-5D questionnaire results from the AMAGINE-1 trial, although a Canadian value set was applied for the CDR-submitted model. • Treatment allocation after induction was based on PASI response, with patients with inadequate responses assigned to BSC state thereafter.
Differences with CDR submission	• Compared BDL with adalimumab, etanercept, infliximab, and USK in a CUA and with secukinumab and ixekizumab in a CMA, whereas the CDR-submitted CUA included etanercept, adalimumab, infliximab, infliximab SEB, USK, secukinumab, and ixekizumab, with guselkumab, etanercept SEB, and adalimumab SEB considered in a scenario analysis. • Markov model used rather than a combined Markov and decision tree model (submitted to CDR). • 5-year time horizon with 2-week cycles rather than 10-year time horizon with annual cycles (submitted to CDR). • 4 health states used (induction phase, maintenance phase, BSC, and death) versus 3 health states (initial treatment, BSC, and death).
Results	• Annual drug acquisition cost of BDL reported during first year of treatment was £17,280 ($28,935 CAD) and £16,640 ($27,863 CAD) in subsequent years. • ICER of £116,333 ($194,799 CAD) per QALY compared with USK. • Incremental cost of £1,315 ($2,201.97 CAD) compared with secukinumab, and £609 ($1,019 CAD) compared with ixekizumab. • Reported results do not take into account available PAS, although these were considered by SMC.
Issues noted by the review group	• Validity was questioned, as the population of interest was broader than the proposed population in the company submission. • NMA only compared induction treatment, while there was no comparison regarding safety or quality of life outcomes. • There was variability in clinical practice and the sequence of biologic treatments that may be used for the condition. • Generalizability was questioned as to whether the BSC model was relevant to Scotland. • CUA analysis did not indicate whether patients had prior treatment experience.
Results of reanalyses by the review group	None reported.

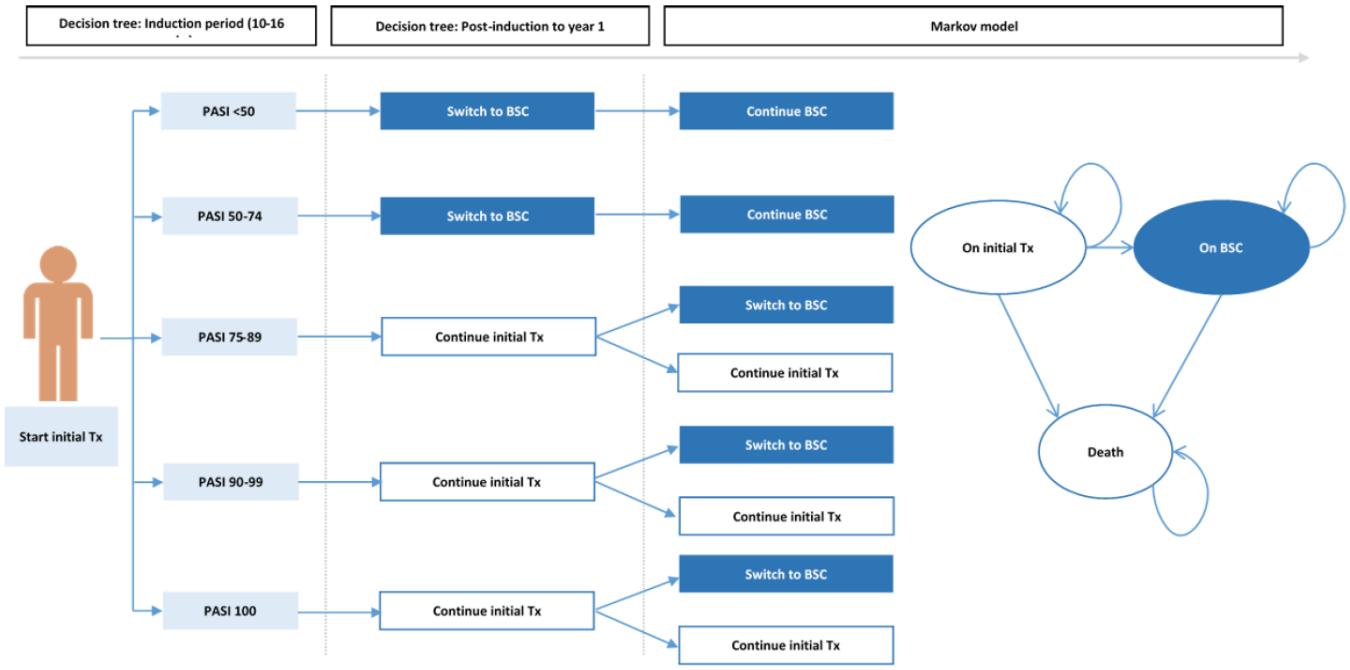
	SMC (December 2017)[22]
Recommendation	November 2017: BDL is not recommended for use in NHS Scotland. The submitting company did not present a sufficiently robust economic analysis to gain acceptance by SMC.

BDL = brodalumab; BSC = best supportive care; CDR = CADTH Common Drug Review; CEA = cost-effectiveness analysis; CMA = cost-minimization analysis; CUA = cost-utility analysis; EQ-5D = EuroQol 5-Dimensions questionnaire; ICER = incremental cost-effectiveness ratio; NMA = network meta-analysis; PAS = patient access scheme; PASI = psoriasis activity and severity index; QALY = quality-adjusted life-year; SEB = subsequent entry biologic; SMC = Scottish Medical Consortium.
Note: Currency converted based on Bank of Canada rates (https://www.bankofcanada.ca/rates/exchange/currency-converter/): $1 CAD = £0.5972.[23]

Appendix 4: Reviewer Worksheets

Manufacturer's Model Structure

Figure 1: Manufacturer's Model Structure



BSC = best supportive care; PASI = Psoriasis Area and Severity Index; Tx = treatment.
Source: Manufacturer's pharmacoeconomic submission.[4]

Table 9: Data Sources

Data Input	Description of Data Source	Comment
Efficacy, Safety, and Withdrawals		
Efficacy PASI response rates at end of induction period	The effects of treatment on the distribution of patients across the PASI response categories were derived from the manufacturer's NMA. [redacted]	CDR clinical review
Adverse Events	As per manufacturer's clinical expert's suggestion, no adverse events were included, as they were assumed equal for all biologics.	A previous CADTH clinical expert agreed that adverse events should be considered equal across all biologics. It is unclear if this holds for brodalumab. A problem with this approach is that exclusion of adverse events even when the rates are equal will likely bias results in favour of treatments, leading to longer use.
Discontinuation	The probability of discontinuation was assumed equal.	A previous CADTH clinical expert agreed with this assumption.
Natural History		
Mortality	Transition to death was informed by age- and gender-specific all-cause mortality rates for the Canadian general population.	This was appropriate.
Utilities		
Health State Utilities	A common baseline utility was applied to all treatments and was derived from the analysis of baseline utility values from the AMAGINE-1 clinical trial EQ-5D data using Canadian tariffs. The increments by PASI response score were also estimated from the same data source using data at week 12 and using the same methods.	The chosen method for the increments associated with PASI response appeared appropriate. Other estimates either gave similar results or gave results more favourable toward brodalumab.
Resource Use and Costs		
Costs	All costs appeared to be derived from appropriate sources.	Existing price reductions for comparators were unknown.

CDR = CADTH Common Drug Review; EQ-5D = EuroQol 5-Dimensions questionnaire; NMA = network meta-analysis; PASI = Psoriasis Area and Severity Index.

Table 10: Manufacturer's Key Assumptions

Assumption	Comment
Data on short-term clinical effectiveness are indicative of long-term benefits.	No justification for this assumption is provided. If clinical effectiveness wanes with time, then the cost-effectiveness of treatments in this clinical area will change dramatically. This assumption likely introduces considerable bias into the analysis.
Data from indirect treatment comparison are indicative of comparative clinical effectiveness.	It is unclear that data from the network meta-analysis are sufficiently homogenous to allow an accurate assessment of the relative comparative benefit of brodalumab over other biologics.
Same discontinuation rates.	This assumption was justified based on the comments of the previous CADTH clinical expert.
Exclusion of adverse events.	The assumption that adverse events may be equal across all biologics may be considered appropriate, but this does not warrant the exclusion of adverse events, as their impacts will differ based on different times on therapy. This assumption would likely bias the results in favour of treatments with longer time on therapy and, as a result, greater effectiveness. The effect may be minimal and is unlikely to change the interpretation of the results.

Table 11: Distribution of Patients by PASI Response Score at End of Induction Period

	PASI < 50	PASI 50 to 74	PASI 75 to 89	PASI 90 to 99	PASI 100
Best supportive care	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Brodalumab	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Adalimumab	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Etanercept	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Infliximab	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Ixekizumab	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Secukinumab	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Guselkumab	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Ustekinumab 45 mg	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Ustekinumab 90 mg	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Adalimumab SEB	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Etanercept SEB	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Infliximab SEB	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

PASI = Psoriasis Area and Severity Index; SEB = subsequent entry biologic.
Source: Manufacturer's pharmacoeconomic submission.[4]

Table 12: Base Discontinuation Rates

	Year 1	Year 2+
Best supportive care	0%	0%
All biologics	3.8%	15%

Source: Manufacturer's pharmacoeconomic submission.[4]

Table 13: Base Utility Values

Baseline Utility	Change in Utility by PASI Response Score				
	< 50	50 to 74	75 to 89	90 to 99	100
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Source: Manufacturer's pharmacoeconomic submission.[4]

Table 14: Costs for Each Comparator

	Induction Cost	Post-Induction to End Year 1 Cost	Year 1 Total Costs	Subsequent Year Costs
Brodalumab (Siliq)	$4,515.00	$12,900.00	$17,415.00	$16,770.00
Adalimumab (Humira)	$6,159.76	$15,399.40	$21,559.16	$20,019.22
Etanercept (Enbrel)	$9,743.64	$16,234.40	$25,977.04	$21,104.72
Infliximab (Remicade)	$14,813.40	$24,689.00	$39,502.40	$32,095.70
Ixekizumab (Taltz)	$12,152.00	$15,190.00	$27,342.00	$19,747.00
Secukinumab (Cosentyx)	$9,870.00	$16,450.00	$26,320.00	$19,740.00
Guselkumab (Tremfya)	$9,179.22	$12,238.96	$21,418.18	$19,888.31
Ustekinumab 45 mg (Stelara)	$9,186.28	$13,779.42	$22,965.70	$20,669.13
Ustekinumab 90 mg (Stelara)	$9,186.28	$13,779.42	$22,965.70	$20,669.13
Adalimumab SEB	$3,695.86	$9,239.64	$12,935.50	$12,011.53
Etanercept SEB	$6,456.00	$10,760.00	$17,216.00	$13,988.00
Infliximab SEB (Inflectra)	$7,875.00	$13,125.00	$21,000.00	$17,062.50

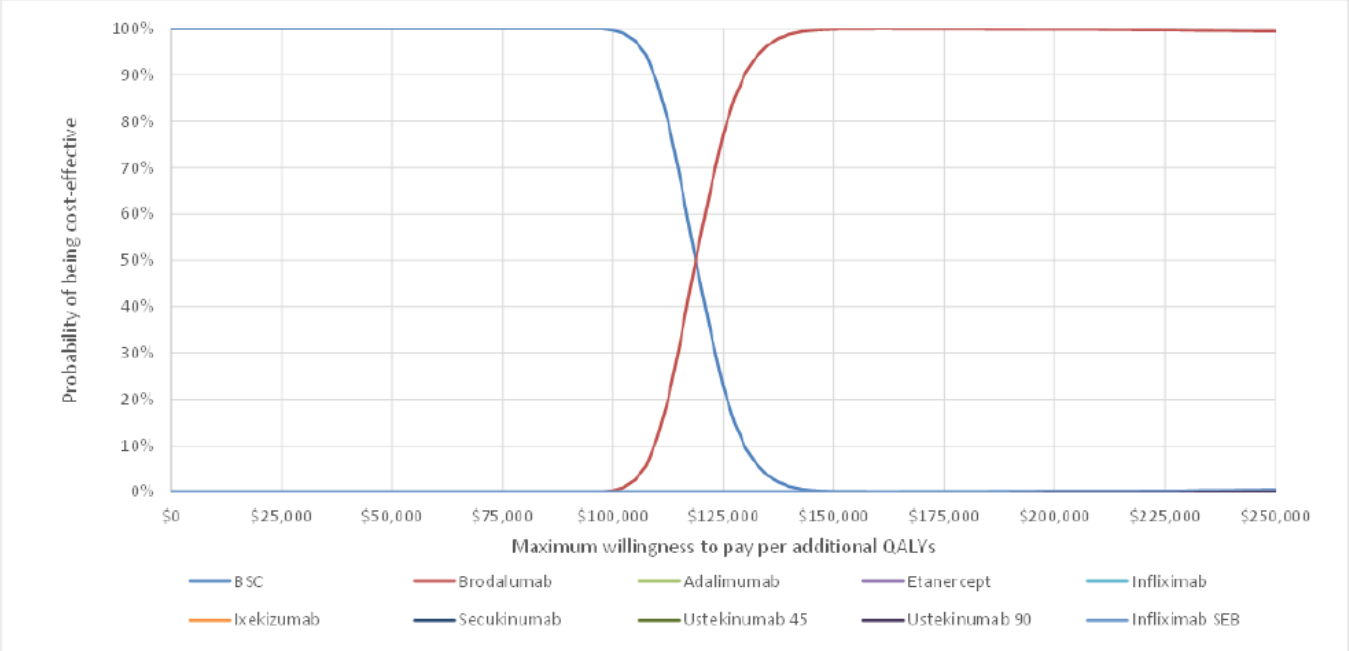
SEB = subsequent entry biologic.
Source: Manufacturer's pharmacoeconomic submission.[4]

Table 15: Biologic Dose and Induction Period

	Recommended Dose	Induction Period (Weeks)
Brodalumab	210 mg by subcutaneous injection at weeks 0, 1, and 2, followed by 210 mg every 2 weeks thereafter.	12
Adalimumab	An initial dose of 80 mg administered subcutaneously followed by 40 mg subcutaneously every other week starting one week after the initial dose. Continued therapy beyond 16 weeks should be carefully reconsidered in a patient not responding within this time period.	16
Etanercept	Starting dose for adult patients is 50 mg twice weekly (administered 3 or 4 days apart) for 3 months, followed by a reduction to a maintenance dose of 50 mg per week.	12
Infliximab	5 mg/kg given as an intravenous infusion followed by additional 5 mg/kg doses at 2 weeks and 6 weeks after the first infusion, then every 8 weeks thereafter. If a patient does not show an adequate response at week 14, after infusions at weeks 0, 2, and 6, no additional treatment should be given.	10
Ixekizumab	160 mg by subcutaneous injection (two 80 mg injections) at week 0, followed by 80 mg (one injection) at weeks 2, 4, 6, 8, 10, and 12, then 80 mg (one injection) every 4 weeks.	12
Secukinumab	300 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, and 3, followed by monthly maintenance dosing starting at week 4. Each 300 mg dose is given as two subcutaneous injections of 150 mg.	12
Guselkumab	100 mg by subcutaneous injection with initial dosing at week 0 and week 4 and every 8 weeks thereafter.	16
Ustekinumab 45	45 mg administered at weeks 0 and 4, then every 12 weeks thereafter for patients with a body weight of less than 100 kg. Consideration should be given to discontinuing treatment in patients who have shown no response after up to 12 weeks of treatment.	12
Ustekinumab 90	90 mg administered at weeks 0 and 4, then every 12 weeks thereafter for patients with a body weight greater than 100 kg. Consideration should be given to discontinuing treatment in patients who have shown no response after up to 12 weeks of treatment.	12

Source: Manufacturer's pharmacoeconomic submission.[4]

Figure 2: Manufacturer's Cost-Effectiveness Acceptability Curve



Abbreviations: SEB = subsequent entry biologic, QALYs = quality-adjusted life years

Source: Manufacturer's pharmacoeconomic submission.[4]

References

1. Papp KA, Reich K, Paul C, et al. A prospective phase III, randomized, double-blind, placebo-controlled study of brodalumab in patients with moderate-to-severe plaque psoriasis. *Br J Dermatol.* 2016;175(2):273-286.
2. Lebwohl M, Strober B, Menter A, et al. Phase 3 studies comparing brodalumab with ustekinumab in psoriasis. *N Engl J Med.* 2015;373(14):1318-1328.
3. Siliq (brodalumab): solution for injection 140 mg/mL [product monograph]. Laval (QC): Valeant Canada LP.; March 6, 2018.
4. Pharmacoeconomic evaluation. In: *CDR submission: Siliq (brodalumab), 210 mg subcutaneous injection. Company: Valeant Canada LP. [**CONFIDENTIAL** manufacturer's submission].* Laval (QC): Valeant Canada LP.; December 14, 2017.
5. Clinical evidence for brodalumab in moderate-to-severe psoriasis: network meta-analysis report. In: *CDR submission: Siliq (brodalumab), 210 mg subcutaneous injection. Company: Valeant Canada LP. [**CONFIDENTIAL** manufacturer's submission].* Laval (QC): Valeant Canada LP.; December 14, 2017.
6. Shkolnikov V, Barbieri M, Wilmoth J. *Canadian Human Mortality Database (CHMD).* Montreal: Department of Demography, Université de Montréal; 2016.
7. Guidelines for the economic evaluation of health technologies: Canada. 4th ed. Ottawa: CADTH; 2017: https://www.cadth.ca/dv/guidelines-economic-evaluation-health-technologies-canada-4th-edition. Accessed April 24, 2018.
8. Menter A, Papp KA, Gooderham M, et al. Drug survival of biologic therapy in a large, disease-based registry of patients with psoriasis: results from the Psoriasis Longitudinal Assessment and Registry (PSOLAR). *J Eur Acad Dermatol Venereol.* 2016;30(7):1148-1158.
9. EuroQol--a new facility for the measurement of health-related quality of life. *Health Policy.* 1990;16(3):199-208.
10. Bansback N, Tsuchiya A, Brazier J, Anis A. Canadian valuation of EQ-5D health states: preliminary value set and considerations for future valuation studies. *PLoS One.* 2012;7(2):e31115.
11. Ontario Ministry of Health and Long-Term Care. Schedule of benefits for physician services under the Health Insurance Act: effective December 21, 2015. Toronto: The Ministry; 2015: http://www.health.gov.on.ca/english/providers/program/ohip/sob/physserv/physserv_mn.html. Accessed September, 2017.
12. Ontario Ministry of Health and Long-Term Care. Ontario drug benefit formulary/comparative drug index. Toronto: The Ministry; 2017: https://www.healthinfo.moh.gov.on.ca/formulary/. Accessed September, 2017.
13. Ontario Ministry of Health and Long-Term Care. *Ontario schedule of benefits for laboratory services.* Toronto: The Ministry; 1999.
14. Dolan P. Modeling valuations for EuroQol health states. *Med Care.* 1997;35(11):1095-1108.
15. Knight C, Mauskopf J, Ekelund M, Singh A, Yang S, Boggs R. Cost-effectiveness of treatment with etanercept for psoriasis in Sweden. *Eur J Health Econ.* 2012;13(2):145-156.
16. Woolacott N, Bravo Vergel Y, Hawkins N, et al. Etanercept and infliximab for the treatment of psoriatic arthritis: a systematic review and economic evaluation. *Health Technol Assess.* 2006;10(31):1-239.
17. Anis AH, Bansback N, Sizto S, Gupta SR, Willian MK, Feldman SR. Economic evaluation of biologic therapies for the treatment of moderate to severe psoriasis in the United States. *J Dermatolog Treat.* 2011;22(2):65-74.
18. Drug Plan Extended Benefits Branch. Saskatchewan online formulary database. Regina: Government of Saskatchewan; 2016: http://formulary.drugplan.health.gov.sk.ca/. Accessed September, 2017.
19. The Department of Health and Community Services. Newfoundland Interchangeable Drug Products Formulary (NIDPF). St. John's (NL): The Department; 2017: http://www.health.gov.nl.ca/health/nlpdp/fmlsearch.asp. Accessed September, 2017.
20. List of medications. Quebec (QC): R'gie de l'assurance maladie du Qu'bec (RAMQ); 2015: https://www.prod.ramq.gouv.qc.ca/DPI/PO/Commun/PDF/Liste_Med/Liste_Med/liste_med_2015_03_16_en.pdf. Accessed September, 2017.
21. DeltaPA. [Ottawa]: IQVIA; 2017: https://www.iqvia.com/. Accessed September 2017.
22. Scottish Medicines Consortium. Brodalumab (Kyntheum). Glasgow: The Consortium; 2017: https://www.scottishmedicines.org.uk/medicines-advice/brodalumab-kyntheum-fullsubmission-128317/. Accessed April 24, 2018.
23. Bank of Canada currency converter. Ottawa: Bank of Canada; 2017: https://www.bankofcanada.ca/rates/exchange/currency-converter/. Accessed April 23, 2018.