Drug Coverage Decision for B.C. PharmaCare

About PharmaCare B.C. PharmaCare is a government-funded drug plan. It helps British Columbians with the cost of eligible prescription drugs and specific medical supplies.

Details of Drug Reviewed

Drug	**guselkumab**
Brand Name	Tremfya® and Tremfya® One-Press™
Dosage Forms	100 mg/1 mL solution for injection in a pre-filled syringe 100 mg/1 mL solution for injection in a patient-controlled injector
Manufacturer	Janssen Inc.
Submission Type	**New Submission**
Use Reviewed	For the treatment of moderate to severe plaque psoriasis in adults.
Common Drug Review (CDR)	Yes, CDR recommended: **to Reimburse with clinical criteria and/or conditions**. Visit the CDR website for more details: www.cadth.ca/sites/default/files/cdr/complete/SR0530_Tremfya_complete_Feb-23-18.pdf
Provincial Review	The Drug Benefit Council (DBC) now screens drug submissions under review by the Common Drug Review (CDR) to determine whether or not a full DBC review is necessary, based on past DBC reviews, recommendations, and existing PharmaCare coverage. If a full DBC review is determined to not be required, the Ministry of Health's (the Ministry) drug coverage decision will be based on the Canadian Drug Expert Committee's (CDEC) recommendation and an internal review only. The DBC screened guselkumab on November 6, 2017. The DBC advised that, because guselkumab is similar to some of the other drugs used for the treatment of plaque psoriasis in adults, the Ministry may accept the CDEC's recommendation for guselkumab.
Drug Coverage Decision	**Non-Benefit**
Date	May 5, 2020
Reason	Drug coverage decision is consistent with the CDEC recommendation. • At the submitted price, guselkumab was not considered cost-effective for the treatment of moderate to severe plaque psoriasis in adults. The British Columbia Ministry of Health participated in the pan-Canadian Pharmaceutical Alliance (pCPA) negotiations with Janssen Inc., which were not able to address the concerns identified by the CDEC with respect to the cost-effectiveness and value for money. As such, the pCPA has advised Janssen Inc. that the participating jurisdictions will not be listing guselkumab for plaque psoriasis at this time.
Other Information	None

The Drug Review Process in B.C.

A manufacturer submits a request to the Ministry of Health (Ministry).

An independent group called the Drug Benefit Council (DBC) gives advice to the Ministry. The DBC looks at:

- whether the drug is safe and effective
- advice from a national group called the Common Drug Review (CDR)
- what the drug costs and whether it is a good value for the people of B.C.
- ethical considerations involved with covering or not covering the drug
- input from physicians, patients, caregivers, patient groups and drug submission sponsors

The Ministry makes PharmaCare coverage decisions by taking into account:

- the existing PharmaCare policies, programs and resources
- the evidence-informed advice of the DBC
- the drugs already covered by PharmaCare that are used to treat similar medical conditions
- the overall cost of covering the drug

Visit The Drug Review Process in B.C. - Overview and Ministry of Health - PharmaCare for more information.

This document is intended for information only.
It does not take the place of advice from a physician or other qualified health care provider.

CADTH

CADTH COMMON DRUG REVIEW

CADTH Canadian Drug Expert Committee Recommendation

(Final)

Guselkumab (Tremfya — Janssen Inc.)
Indication: For the treatment of adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

RECOMMENDATION:
The CADTH Canadian Drug Expert Committee (CDEC) recommends that guselkumab be reimbursed for adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy, with the following criteria and condition:

Clinical Criteria:
- Reimburse in a manner similar to other biologics for the treatment of moderate-to-severe plaque psoriasis.
- Treatment should be discontinued if a response to treatment with guselkumab has not been demonstrated after 16 weeks.

Conditions:
- Drug plan cost for guselkumab should not exceed the drug plan cost of treatment with the least costly biologic reimbursed for moderate-to-severe plaque psoriasis.

Service Line:	CADTH Drug Reimbursement Recommendation
Version:	1.0
Publication Date:	TBC
Report Length:	9 Pages

CADTH

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Guselkumab (Tremfya — Janssen Inc.)

Indication: Moderate-to-severe plaque psoriasis.

Recommendation:

The CADTH Canadian Drug Expert Committee (CDEC) recommends that guselkumab be reimbursed for adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy, with the following criteria and condition:

Criteria:

- Reimburse in a manner similar to other biologics for the treatment of moderate-to-severe plaque psoriasis.
- Treatment should be discontinued if a response to treatment with guselkumab has not been demonstrated after 16 weeks.

Condition:

- Drug plan cost for guselkumab should not exceed the drug plan cost of treatment with the least costly biologic reimbursed for moderate-to-severe plaque psoriasis.

Reasons for the Recommendation:

1. Results of two double-blind, randomized controlled trials (RCTs) (VOYAGE-1 [N = 837] and VOYAGE-2 [N = 992]) demonstrated that those allocated to treatment with guselkumab experienced statistically and clinically significant improvements in health-related quality of life (HRQoL) as measured by the Dermatology Life Quality Index (DLQI) compared with placebo after 16 weeks of treatment. Guselkumab was also shown to be superior to placebo and to adalimumab in achieving a higher proportion of patients with an Investigator Global Assessment (IGA) score of 0 or 1 (i.e., cleared or minimal disease) and a Psoriasis Area and Severity Index (PASI) 90 response at week 16. In a third double-blind RCT (NAVIGATE [N = 268]), patients with an inadequate response to ustekinumab, who were switched to guselkumab, had a statistically significantly higher number of health care provider visits in which they achieved an IGA score of 0 or 1 and at least a two-grade improvement compared with patients who continued ustekinumab. The safety profile of guselkumab was similar to that of adalimumab.
2. The results of a manufacturer-submitted indirect comparison (IDC) based on a network meta-analysis (NMA) suggested that guselkumab was more efficacious than adalimumab and etanercept in terms of PASI 75, PASI 90, PASI 100, and DLQI responses. The analysis also suggested that guselkumab may be less efficacious than ixekizumab, but may be as efficacious in treating moderate-to-severe plaque psoriasis as other interleukin (IL) inhibitors (i.e., secukinumab and ustekinumab) and the tumour necrosis factor antagonist, infliximab. There were no consistent differences between the safety profile of guselkumab and the other biologics or apremilast. However, the comparative benefit and safety of guselkumab versus other biologics for the treatment of moderate-to-severe plaque psoriasis remains unclear because of variation in results of the IDC depending on the specific outcome and/or model analyzed and important limitations of the analysis.
3. Based on the CADTH Common Drug Review reanalyses to account for limitations in the manufacturer's economic model, guselkumab — at the submitted price of $3,059.74 for the 100 mg/1.0 mL solution for subcutaneous injection — was not considered to be a cost-effective treatment option for moderate-to-severe plaque psoriasis. Guselkumab was dominated by ixekizumab, and the incremental cost per quality-adjusted life-year (QALY) gained for guselkumab versus infliximab was $1.6 million. The probability that guselkumab was cost-effective at a willingness-to-pay threshold of $50,000 per QALY was 11.9%.

Of Note:

A response to treatment is defined as an achievement of at least a 90% reduction in the PASI score (PASI 90) and/or achievement of a score of 0 or 1 on the IGA by week 16.

Discussion Points:

- There was no study in which guselkumab was compared directly with other IL inhibitors approved to treat plaque psoriasis, namely secukinumab, ixekizumab, and ustekinumab, although the manufacturer provided an IDC in which a NMA was employed to compare guselkumab with other biologic drugs used to treat plaque psoriasis.

Background:

Guselkumab is a humanized monoclonal antibody that binds to the p19 subunit of IL-23 and blocks the IL-23 cytokine pathway. Guselkumab has a Health Canada-approved indication for the treatment of adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy. The recommended dose of guselkumab is 100 mg to be given at week 0 and week 4, followed by maintenance dosing every eight weeks thereafter. Guselkumab is available as a solution for subcutaneous injection in a pre-filled syringe.

Summary of CDEC Considerations:

CDEC considered the following information prepared by the CADTH Common Drug Review: a systematic review of three double-blind RCTs of guselkumab, a manufacturer-provided IDC, and a critique of the manufacturer's pharmacoeconomic evaluation, as well as information submitted by patient groups about outcomes and issues important to patients.

Patient Input Information

Patient input was contributed by the Canadian Skin Patient Alliance (CSPA), which authored a joint submission that included input from the Canadian Association of Psoriasis Patients (CAPP) the Canadian Psoriasis Network (CPN), and the Arthritis Consumer Experts (ACE). The information for the submissions was gathered through interviews with patients and caregivers affected by plaque psoriasis as well as interviews with health care professionals; surveys, social media, and informal discussions that included patients diagnosed with plaque psoriasis were also gathered. The following is a summary of key input from the perspective of the patient groups:

- The most significant physical symptoms of psoriasis that patients report include scales and flaking that can occur anywhere on their bodies, itching, and pain. Joint pain, lesion pain, and pain from itching lesions can limit activities such as employment, socialization, everyday household chores, and sports.
- Psoriasis also psychologically affects patients, with most experiencing embarrassment, diminished self-confidence, and depression. Caregivers often find themselves psychologically negatively affected and dysfunctional as the whole family tends to absorb the shame, depression, and isolation associated with the disease.
- According to a patient survey, responses to the treatment options available can vary significantly, with a large proportion of patients failing to achieve adequate relief from symptoms. Patients with psoriasis would welcome any treatment allowing them to live a normal life, without interruption by frequent and time-consuming visits for phototherapy or long travel times/distances to access infusion clinics.

Clinical Trials

The CDR systematic review included three manufacturer-sponsored, published, phase III, multicentre, double-blind, parallel-group, RCTs in adult patients with moderate-to-severe plaque psoriasis.

VOYAGE-1 (N = 837) and VOYAGE-2 (N = 992) were placebo and active (adalimumab) controlled trials with randomization stratified by investigational site. The first 24 weeks of treatment were identical in the two trials, which comprised a 16-week induction period in which guselkumab 100 mg at weeks 0, 4, and 12, and every eight weeks thereafter was compared with placebo, after which placebo-treated patients were switched to guselkumab 100 mg at weeks 16, 20, and every eight weeks thereafter. In VOYAGE-1, treatment with guselkumab 100 mg every eight weeks or adalimumab 80 mg at week 0, and 40 mg at week 1 and every two weeks thereafter was continued for 48 weeks after which patients entered open-label guselkumab treatment to week 160. In VOYAGE-2, a subset of guselkumab-treated patients who were PASI 90 responders at week 28 were re-randomized to continued guselkumab 100 mg every eight weeks (maintenance) or placebo (withdrawal/re-treatment) through to week 76 after which they entered open-label guselkumab

treatment to week 160. Discontinuation rates during the initial 16-week period of the VOYAGE trials were low (≤ 6.0%); however, during the maintenance period in VOYAGE-1, almost twice as many adalimumab-treated patients (15.6%) discontinued compared with guselkumab-treated patients (8.5%) by week 48.

NAVIGATE (N = 268 randomized patients) was an active (ustekinumab) controlled trial that employed an enrichment design. All patients underwent an open-label run-in treatment period with ustekinumab 45 mg or 90 mg (based on baseline [week 0] body weight) at weeks 0 and 4. At week 16 patients were assessed according to IGA. Patients with inadequate response (i.e., IGA score ≥ 2 [moderate-to-severe disease]) were randomized to either guselkumab 100 mg at weeks 16 and 20 and every eight weeks thereafter or to continued ustekinumab every 12 weeks through week 40, after which patients entered follow-up to week 60. Randomization was stratified by baseline body weight (≤ 100 kg, > 100 kg) and investigational site). Discontinuation rates were 15.0% in patients who continued ustekinumab compared with 6.7% in patients switched to guselkumab.

Key limitations of the included trials are the head-to-head comparison of guselkumab with only one active comparator (adalimumab) and not directly with another Health Canada-approved IL inhibitor (i.e., secukinumab, ixekizumab, or ustekinumab), the size and short duration of the trials which precludes assessment of long-term efficacy and safety or rare or latent adverse events (AEs), differential withdrawal between treatment groups, compromised randomization due to diminished sample sizes following re-randomization of PASI 90 responders in VOYAGE-2 or in subgroup analyses, and lack of adjustment for multiplicity for secondary outcomes that were not considered to be major. The NAVIGATE trial should not be considered to be a head-to-head comparison of guselkumab and ustekinumab, but more appropriately as a switch study. Furthermore, the NAVIGATE trial is limited by bias in favour of guselkumab due to comparison with ustekinumab in patients who were previously identified as inadequate responders to ustekinumab.

Outcomes

Outcomes were defined a priori in the CDR systematic review protocol. Of these, CDEC discussed the following:

- HRQoL as assessed by the DLQI
- PASI response
- IGA (overall and regional disease)
- Nail Psoriasis Severity Index (NAPSI) response
- AEs, serious AEs (SAEs), withdrawal due to AEs (WDAEs), and notable harms (infections, injection-site reactions, serious hypersensitivity reactions, major cardiovascular events, and malignancy).

Of these, HRQoL and PASI response were outcomes identified as important to patients based on the patient input received.

In the VOYAGE-1 and VOYAGE-2 trials, the co-primary outcomes were the proportion of patients achieving an IGA score of 0 (cleared) or 1 (minimal) disease and the proportion of patients achieving PASI 90 response. Non-inferiority and superiority of guselkumab to adalimumab based on these outcomes was also evaluated as a major secondary outcome at week 16 in both trials. In the NAVIGATE trial, the primary outcome was the number of visits during which patients achieved an IGA score of 0 or 1 and ≥ 2 grade improvement from week 16 during weeks 28 to week 40.

Efficacy

In VOYAGE-1 and VOYAGE-2, patients treated with guselkumab experienced a statistically significant greater reduction in DLQI score from baseline to week 16 compared with placebo. The mean (standard deviation [SD]) magnitude of the reduction was –11.2 (7.2) and –11.3 (6.8) with guselkumab compared with –0.6 (6.4) and –2.6 (6.9) with placebo in the two trials, respectively (P <0 .001; adjusted for multiplicity). The reduction in DLQI score from baseline to week 16 with adalimumab (–9.3 [7.8] and –9.7 [6.8]) was also larger than the change from baseline with placebo; however, the testing was not adjusted for multiplicity. The changes in DLQI scores with guselkumab are considered to be clinically relevant as the minimal clinically important difference in patients with psoriasis is reported to range from 2.2 to 6.9. In the NAVIGATE trial, the mean (SD) change in overall DLQI score from baseline to week 28 was reported, but not compared statistically, between guselkumab (–11.6 [6.9]) and ustekinumab (–7.3 [6.9]).

The proportion of patients achieving a PASI 90 score was statistically significantly higher with guselkumab compared to placebo in both the VOYAGE-1 and VOYAGE-2 trials at week 16 (i.e., 73.3% and 70.0% with guselkumab compared with 2.9% and 2.4% with placebo, respectively); $P < 0.001$ for both. The proportion of patients achieving a PASI 90 response with adalimumab was 49.7% and 46.8% in the two trials, respectively, which was also statistically significantly different from placebo; $P < 0.001$. The proportion of patients achieving a PASI 90 response at week 24 was statistically significantly larger with guselkumab (80.2% and 75.2%) compared with adalimumab (53.0% and 54.8%) in VOYAGE-1 and VOYAGE-2, respectively ($P < 0.001$ for both; adjusted for multiplicity). In VOYAGE-1, statistically significantly more patients treated with guselkumab (76.3%) achieved a PASI 90 response compared with adalimumab (47.9%) at week 48 ($P < 0.001$; adjusted for multiplicity).

The proportion of patients who achieved an IGA score of 0 (cleared) or 1 (minimal) disease at week 16 was statistically significantly higher with guselkumab (85.1% and 84.1%) and adalimumab (65.9% and 67.7%) when compared with placebo (6.9% and 8.5%), in VOYAGE-1 and VOYAGE-2 respectively ($P < 0.001$ for both). A statistically significantly higher proportion of patients treated with guselkumab compared to adalimumab in VOYAGE-1 achieved an IGA score of 0 or 1 at week 24 or week 48 ($P < 0.001$; adjusted for multiplicity). The clinical expert consulted on this review concurred that an IGA score of 0 or 1 is a clinically meaningful improvement from baseline given that patients were required to have an IGA score ≥ 3 (moderate disease) at study entry.

In VOYAGE-1 and VOYAGE-2, non-inferiority and superiority testing of the proportion of patients with PASI 90 or PASI 75 response or IGA score of 0 or 1 at week 16 between guselkumab and adalimumab was conducted and tested according to the fixed sequence statistical testing. For all three outcomes, the non-inferiority margin was –10% (i.e., if the lower bound of the 95% confidence interval [CI] for the difference between treatments was greater than or equal to –10% for guselkumab versus adalimumab), then non-inferiority was concluded. In both trials, non-inferiority of guselkumab with adalimumab was demonstrated and subsequently, guselkumab was also found to be statistically significantly superior to adalimumab for all three outcomes.

In VOYAGE-2, a secondary end point included in the fixed sequence testing was the loss of PASI 90 response between the guselkumab maintenance group and the withdrawal/re-treatment group. PASI 90 responses appeared to be maintained for a longer duration of time in patients who were maintained on guselkumab compared with patients who were withdrawn/re-treated. Median time to loss of response in the withdrawal/re-treatment group was 15.2 weeks. At week 32, 90.6% (95% CI, 85.3 to 94.1) of patients in the withdrawal/re-treatment group maintained PASI 90 response and at week 48, 35.4% maintained a PASI 90 response. In the guselkumab maintenance group, 88.6% of patients maintained a PASI 90 response through week 48. The median time to loss of PASI 90 response in patients initially randomized to adalimumab and withdrawn at week 28 was 8.6 weeks.

In the NAVIGATE trial, a major secondary end point was the number of visits where patients achieved a PASI 90 response from week 28 to week 40 in randomized patients with an inadequate response to ustekinumab (IGA score ≥ 2 at week 16). The mean (SD) number of visits was 2.2 (1.7) in patients randomized to guselkumab and 1.1 (1.5) in patients continued on ustekinumab, which was statistically significant ($P < 0.001$; adjusted for multiplicity). The number of visits in which patients achieved an IGA score of 0 or 1 and at least a two-grade improvement (from week 16) during week 28 through week 40 was higher in the guselkumab-treated group compared with those who continued ustekinumab. The mean (SD) number of visits was1.5 (1.6) with guselkumab compared with 0.7 (1.3) with ustekinumab; ($P < 0.001$).

Various regional psoriasis end points were included in VOYAGE-1 and VOYAGE-2, of which one was the NAPSI score; however, the testing of this outcome was not included in the fixed sequence statistical testing. In general, the results of the regional psoriasis end points corroborated those of the overall disease and primary end points of the VOYAGE trials and appeared to favour guselkumab over placebo; however, these comparisons were all made without adjustment for multiplicity.

Harms (Safety and Tolerability)

In the VOYAGE-1 and VOYAGE-2 trials, during the 16-week induction period, AEs ranged between 47.5% to 51.5% with guselkumab, 48.4% to 51.1% with adalimumab, and 44.8% to 49.4% with placebo. During the active-controlled periods of the respective VOYAGE trials, the frequency of AEs was similar between guselkumab (73.9% and 58.3%) and adalimumab (74.5% and 62.9%) up to week 48 in VOYAGE-1 or week 28 in VOYAGE-2. The most frequently reported AEs across all trials and treatment periods with guselkumab were nasopharyngitis, upper respiratory tract infections, and headache.

In the NAVIGATE trial, a higher proportion of patients treated with guselkumab (64.4%) as compared with ustekinumab (55.6%) experienced AEs from week 16 to week 60; however, comparisons are difficult because patients in the randomized ustekinumab group had been receiving the drug from week 0 to 16 in addition to week 16 to 60 which allowed for more time for tolerance to develop or AEs to resolve, as compared with guselkumab-treated patients who initiated the drug at week 16.

In all three trials, SAEs occurred infrequently (i.e., ranging from 1.6% to 4.9% with guselkumab, 1.8% to 4.5% with adalimumab, and 1.2% to 1.7% with placebo), in VOYAGE-1 and VOYAGE-2, respectively, during the 16-week induction period. In the NAVIGATE trial, SAEs were reported in guselkumab- (6.7%) and ustekinumab- (4.5%) treated patients from week 16 to week 60.

In addition, WDAEs also occurred infrequently in all of the three trials regardless of the treatment period or treatment group, not exceeding 3.6% in any group at any time.

Treatment with guselkumab did not appear to be associated with increased mortality as there were only three deaths reported across the three trials (i.e., one death in VOYAGE-1 and two deaths in NAVIGATE) with no deaths reported in VOYAGE-2.

Notable harms (infections, injection-site reactions, serious hypersensitivity reactions, major cardiovascular events, and malignancy) were reported infrequently across all three trials, generally occurring in <1% of patients. The only exception was injection-site reactions in the VOYAGE-1 and VOYAGE-2 trials where the proportions of patients with injection-site reactions was higher with adalimumab (7.5% and 6.9%) compared to guselkumab (2.4% and 2.6%) from week 0 to week 16, which may be attributed to the higher frequency of injections with adalimumab, as necessitated by the dosing regimen.

Indirect Comparisons

A manufacturer-supplied IDC comparing guselkumab with currently available biologics, their biosimilars, and apremilast used in the treatment of plaque psoriasis was also considered by CDEC. A systematic review of RCTs up to January 2017 was conducted to identify studies that met the inclusion criteria for the IDC. Bayesian NMA methods were used to compare the effects of guselkumab with other biologics and apremilast on PASI outcomes (PASI 50, PASI 75, PASI 90, and PASI 100), DLQI, PGA/IGA, AEs, SAEs, and WDAEs. Fixed effects and random effects models using vague prior distributions for treatment effects and the between-study variance parameter were analyzed. Unadjusted analyses were preformed, as well as meta-regression analyses to adjust for heterogeneity across RCTs with respect to several patient and study characteristics. In addition, two other analyses were conducted but were not the focus of the CDEC discussion: a baseline risk-adjusted NMA of simultaneous (multinomial) PASI outcomes (i.e., PASI < 50, PASI 50 to 74, PASI 75 to 89, PASI 90 to 99, PASI 100); and a post hoc matching-adjusted IDC that compared guselkumab with ixekizumab only.

The results of the unadjusted and multiple adjusted NMAs conducted suggested that (in general) guselkumab 100 mg was superior to adalimumab, etanercept, and apremilast at helping patients with moderate-to-severe chronic plaque psoriasis achieve PASI 90 and PASI 100 responses, and at improving their DLQI response. The IDC also suggested that guselkumab was similar in efficacy versus other IL inhibitors and infliximab for these outcomes. In addition, guselkumab appeared to be superior to comparators (with the exception of secukinumab 300 mg and infliximab 5 mg/kg which were similar in efficacy, and ixekizumab 80 mg Q2W which was superior in all analyses except for the baseline risk-adjusted ones) for helping patients to achieve a PASI 75 response at the end of induction. When compared with most other biologics and apremilast, guselkumab also appeared to be more efficacious for patient's improvement in IGA/PGA response. There were no apparent differences in the number of AEs, SAEs, and WDAEs at the end of induction between biologics, with the exception of infliximab 5 mg/kg which was associated with an increase in AEs when compared with guselkumab.

A key limitation of the IDC was the underlying heterogeneity related to differences in cross-trial patients and study characteristics. Placebo response rate was used in the baseline risk-adjusted NMA as a proxy for cumulative differences in a number of patient and study characteristics. While for many outcomes the baseline risk-adjusted model appeared to be the best fit model statistically, it is unclear the extent to which placebo response was an adequate proxy for specific characteristics as clinically important potential effect modifiers.

When examined as a whole (including both the unadjusted and adjusted NMAs), the results of the IDC suggest that guselkumab 100 mg is another treatment option that appears to have similar efficacy as other IL inhibitors and infliximab.

Cost and Cost-Effectiveness

Guselkumab is available as a 100 mg/mL pre-filled syringe at a price of $3,060. At the recommended dose of 100 mg to be given as a subcutaneous injection at week 0 and week 4, followed by maintenance dosing every eight weeks thereafter, the first year cost of guselkumab is $21,418 with the price changing to $19,943 annually thereafter.

The manufacturer submitted a cost-utility analysis based on a Markov state-transition model comparing guselkumab with currently available treatments — adalimumab, etanercept, infliximab (based on a 93% biosimilar and 7% branded infliximab price), ixekizumab, ustekinumab, and secukinumab — for adult patients with plaque psoriasis, over a 10-year time horizon. Patients entering the model initiated on one of the treatments, as a first-line treatment. At the end of a treatment induction period patients were assigned to a health state based on PASI score. Patients with a PASI score < 75 moved to the next line of therapy, while patients with a PASI score ≥ 75 stayed in that state for the remainder of the time horizon unless they died or discontinued treatment. Second- and third-line therapies were considered and were hybrids of the therapies considered for first-line approach as comparators. After third-line, patients transition to best supportive care. Data on PASI scores were obtained from a manufacturer-commissioned unpublished NMA with results adjusted by placebo rates. Discontinuation rates were obtained from a published analysis for comparators, and it was assumed that the rate of discontinuation for would be the same as ustekinumab. Rates of AEs were obtained from a published study, and it was assumed that the average adverse evet rates rate for ustekinumab would reflect guselkumab.

Guselkumab was found to be less costly and more effective (more QALYs gained) compared with adalimumab, etanercept, infliximab, secukinumab, and ustekinumab. Ixekizumab was more effective and more costly compared with guselkumab — resulting in an incremental cost per QALY gained for ixekizumab of $121,255 compared with guselkumab.

CDR identified several key limitations with the model submitted by the manufacturer.

- The comparative clinical efficacy inputs relating to PASI score were obtained from a manufacturer-commissioned NMA. The main issue identified by CDR clinical reviewers was the use of an adjusted analysis for placebo response rates, which strongly favoured guselkumab over the unadjusted analysis. The clinical expert consulted for this review stated that the most important effect modifiers were weight, previous biologic use, and disease severity, which contradicts with the manufacturer's approach.
- Assumptions regarding duration of treatment effect were not realistic. Treatment effect at the end of the induction period was expected to be maintained for a patient's lifetime. The manufacturer indicated that applying discontinuation rates addresses this concern; however, this does not change the proportion of patients on active treatment as per PASI score category over time.
- There were no data available to inform AE and long-term discontinuation rates for guselkumab. The manufacturer assumed that the rates for ustekinumab could be applied to guselkumab. This was highly favourable for guselkumab. The CDR clinical expert suggested that assuming equal discontinuation rates for all therapies was more appropriate and using the average AE rates may be more appropriate.

CDR identified several other parameters of uncertainty, including health state utility values, time when patient response was assessed, and choice of second- and third-line therapies. These parameters were considered in combination with the key limitations in defining the CDR base case. However, given the overly complex nature of the model, it was not possible to incorporate alternative assumptions relating to continued treatment efficacy.

Based on CDR reanalyses, guselkumab is not a cost-effective treatment for adult patients with plaque psoriasis. Infliximab was the optimal therapy at a willingness-to-pay threshold of less than $219,387 per QALY gained. If a decision-maker's willingness to pay for a gain in QALY is greater than $219,387, then ixekizumab is the optimal therapy. Guselkumab was dominated by ixekizumab; and, the incremental cost per QALY gained for guselkumab versus infliximab was $1.6 million.

Results demonstrated a high degree of uncertainty with a probability that guselkumab was cost-effective at a willingness-to-pay threshold of $50,000 per QALY of 11.9%. A reduction in the submitted price of 5.4% or greater could result in an incremental cost-utility ratio of less than $50,000 per QALY for guselkumab. However, results would differ substantially if negotiated price reductions

for any of the comparators were considered because the price of comparators is a key driver of the results from the cost utility analysis.

CDEC Members:

Dr. James Silvius (Chair), Dr. Silvia Alessi-Severini, Dr. Ahmed Bayoumi, Dr. Bruce Carleton, Dr. Alun Edwards, Mr. Bob Gagne, Dr. Ran Goldman, Dr. Allan Grill, Dr. Peter Jamieson, Dr. Anatoly Langer, Mr. Allen Lefebvre, Dr. Kerry Mansell, Dr. Yvonne Shevchuk, and Dr. Adil Virani.

January 17, 2018 Meeting

Regrets:

None

Conflicts of Interest:

None