CADTH

CADTH Reimbursement Review

CADTH Reimbursement Recommendation

(Draft)

Deucravacitinib (Sotyktu)

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

Sponsor: Bristol-Myers Squibb

Recommendation: Do Not Reimburse

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Single Technology

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.

Recommendation

The CADTH Canadian Drug Expert Committee (CDEC) recommends that deucravacitinib not be reimbursed for the treatment of adult patients with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

Rationale for the Recommendation

The evidence considered by CDEC did not sufficiently demonstrate a therapeutic benefit of deucravacitinib relative to biologics that are available in Canada. Evidence from 2 double-blind, randomized controlled trials (RCTs), POETYK-1 (N=666) and POETYK-2 (N=1020), in adults with moderate to severe plaque psoriasis showed that deucravacitinib was associated with statistically significant improvements in skin clearance (Psoriasis Area and Severity Index [PASI] score reduced by 75% or 90%, or static Physician's Global Assessment [sPGA] of clear or almost clear) at week 16 versus apremilast and placebo. In the trials, 53% to 58% of patients in the deucravacitinib groups achieved a PASI 75 response, 27% to 36% achieved PASI 90 and 10% to 14% achieved PASI 100 response at week 16. However, the clinical relevance of these results within the Canadian treatment landscape is uncertain. Based on clinical expert input, although PASI 75 is accepted as clinically relevant minimal response threshold in clinical trials, in clinical practice, available biologics are expected to achieve a PASI 90 and PASI 100 response.

Direct evidence comparing newer interleukin (IL)-17 and IL-23 biologics and deucravacitinib was not identified by CADTH for this review. The only direct comparative evidence included deucravacitinib and apremilast. In clinical practice, apremilast is infrequently used in Canada and its relevance as a comparator is limited. Indirect evidence from 1 sponsor-submitted network meta-analysis (NMA) suggested that deucravacitinib was less effective in producing skin improvement than several biologics (including IL-17 and IL-23 biologics) available and reimbursed in Canada.

Patients expressed a need for treatments that improve skin clearance, symptoms of psoriasis, and health-related quality of life (HRQoL), as well as having access to treatments that are convenient to administer and have minimal adverse effects. CDEC concluded that there was insufficient evidence to demonstrate that deucravacitinib meets needs not already addressed by other available treatments.

Discussion Points

- CDEC discussed the potential benefit of the convenience of an oral therapy like deucravacitinib over injectable therapies. Cyclosporine and methotrexate are available oral alternatives funded in most jurisdictions. Furthermore, the clinical expert stated that many patients, including those that are needle-averse would prefer an infrequent subcutaneous injection of a more efficacious product, over a daily oral medication with lesser efficacy.
- In addition to putting a priority on skin clearance, patient groups also indicated the need for a treatment that would improve HRQoL with minimal adverse effects. CDEC discussed that the available data on Dermatology Life Quality Index (DLQI) suggest that deucravacitinib may be associated with short-term benefits in HRQoL versus placebo. However, the comparative benefit of deucravacitinib on HRQoL versus apremilast remains unknown, primarily because these HRQoL outcomes were not included in the statistical testing hierarchy in POETYK-1 or POETYK-2. In addition, the sponsor-submitted ITC did not assess comparative HRQoL or safety. Hence, it is uncertain whether deucravacitinib would improve HRQoL or have a lower rate of adverse events compared with other currently available biologics for the treatment of moderate to severe plaque psoriasis in adult patients.
- CDEC discussed that plaque psoriasis requires lifelong treatment and there is uncertainty regarding the long-term effectiveness and safety of deucravacitinib over other currently available treatment options for moderate to severe plaque psoriasis. There was no longer-term evidence identified by CADTH directly comparing deucravacitinib with any biologic. In addition, there were generalizability issues with the longer-term data in POETYK-2. The withdrawal period results of POETYK-2 were based on an enriched population who had responded to deucravacitinib. As a result, the 52-week skin response rate may be inflated relative to an unselected patient population. The available longer-term extension data were limited by selection bias, lack of a control group, and lack of blinding.

Background

Plaque psoriasis is a chronic inflammatory skin disease characterized by erythematous inflammatory plaques that may be itchy or painful and are usually covered by silver, flaking scales. In addition to the dermatological symptoms, plaque psoriasis is often associated with psychosocial symptoms and can impact self-esteem, interpersonal relationships and performance at school or work. Several comorbid conditions have been linked to psoriasis, such as depression, cardiovascular disease, and psoriatic arthritis. It is estimated that up to 1 million Canadians are living with a type of psoriasis, 90% of whom have plaque psoriasis.

Most patients with moderate to severe plaque psoriasis will require systemic therapies to control their symptoms. Traditional systemic drugs include cyclosporine, methotrexate and acitretin. Advanced therapy, which is usually reserved for patients who fail or are intolerant of traditional systemic therapies, include apremilast and biologic agents (tumor necrosis factor [TNF] alpha inhibitors, interleukin [IL]-23 inhibitors, IL-12/23 inhibitors, and IL-17 inhibitors).

Deucravacitinib is a tyrosine kinase 2 inhibitor that impedes the release of proinflammatory cytokines and chemokines. Deucravacitinib was approved by Health Canada for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy. It is available as a 6 mg oral tablet and the dosage recommended in the product monograph is 6 mg daily.

Sources of Information Used by the Committee

To make its recommendation, the committee considered the following information:

- a review of 2 randomized controlled clinical studies in adults with moderate to severe plaque psoriasis
- patients' perspectives gathered by patient groups, Canadian Psoriasis Network (CPN) and the Canadian Association of Psoriasis Patients (CAPP)
- input from public drug plans that participate in the CADTH review process
- one of clinical specialist with expertise diagnosing and treating patients with plaque psoriasis
- a review of the pharmacoeconomic model and report submitted by the sponsor

Stakeholder Perspectives

Patient Input

Two patient groups submitted a joint input: Canadian Psoriasis Network (CPN) and the Canadian Association of Psoriasis Patients (CAPP). The patient input was based on English and French surveys that received a total 22 responses and another survey entitled, "2022 Survey of People with Psoriatic Disease in Canada and their Caregivers" commissioned by the CPN that collected responses 502 from patients. The symptoms most frequently experienced by patients were flaking, itching, pain and burning, silvery scaly plaques, and dry skin that may crack or bleed. Many patients indicated that psoriasis negatively affected their mental health, self-esteem, social life, ability to exercise, and sleep. Further, some patients were financially impacted and missed work due to psoriasis.

The patient groups emphasized that the complexity and chronic nature of plaque psoriasis lead to a continuing need for treatment options that consider the needs of individual patients. Regarding patients' expectations for new medications, improved symptoms, better quality of life and reduced side effects were mentioned. Other responses included "affordable" and "easier to take, e.g., dosing schedule, route of administration."

Clinician input

Input from clinical experts consulted by CADTH

According to the clinical expert consulted by CADTH, the goals of treatment are to reduce signs and symptoms of psoriasis, improve quality of life and function. With available treatments, 80% to 90% of patients achieve a Psoriasis Area and Severity Index 90% (PASI 90) response and approximately 50% to 60% achieve a PASI 100 response. About 10% of patients may not respond to initial

induction therapy with a biologic (i.e., primary failure) or may lose response over time (secondary failure). The expert indicated that there is an unmet need for treatments that can be remittive and allow drug discontinuation or intermittent (rather than continuous) therapy, as well as for treatments that can modify the disease pathophysiology and have a beneficial effect on its natural history.

The clinical expert indicated that deucravacitinib does not address any of the unmet needs in plaque psoriasis and the expert did not anticipate that it would cause a shift in the current treatment paradigm. The expert stated that it would be difficult to define a role for deucravacitinib except as an oral alternative to the biologics for patients who prefer oral treatment.

Advanced therapy, such as deucravacitinib, should be reserved for patients who have failed first line traditional systemics (methotrexate, acitretin, cyclosporine), according to the clinical expert. Treatment response is usually assessed after 12 to 16 weeks and then at 1 year. Deucravacitinib should be discontinued if patients experience a significant adverse effect (e.g., hypersensitivity, serious infection). In addition, the expert stated that deucravacitinib ought to be discontinued if it fails to provide at least a PASI 75 response. Like biologics, the expert stated that deucravacitinib should be prescribed by dermatologists.

Clinician group input

No input was received from clinician groups.

Drug Program Input

Input was obtained from the drug programs that participate in the CADTH reimbursement review process. The following were identified as key factors that could potentially impact the implementation of a CADTH recommendation for deucravacitinib:

- relevant comparators
- considerations for initiation of therapy
- considerations for continuation or renewal of therapy
- considerations for discontinuation of therapy
- considerations for prescribing of therapy

The clinical experts consulted by CADTH provided advice on the potential implementation issues raised by the drug programs.

Clinical Evidence

Pivotal Studies and Protocol Selected Studies

Description of studies

Two 52-week double-blind, randomized controlled trials (RCTs) met the inclusion criteria for the systematic review. POETYK PSO-1 (N = 666) and POETYK PSO-2 (N = 1020) used a parallel study design, with POETYK-2 adding a randomized withdrawal design for responders at week 24. The studies enrolled adults (≥18 years) who had moderate to severe plaque psoriasis and were candidates for systemic psoriasis therapy and/or phototherapy. Patients were required to have a baseline PASI score of 12 or higher, with greater than 10% of body surface area (BSA) affected, and with a static Physician's Global Assessment (sPGA) score of at least 3 on a 5-point scale.

Both studies randomized eligible patients (2:1:1) to deucravacitinib 6 mg daily, apremilast 30 mg twice daily or placebo. All patients in the placebo groups switched to deucravacitinib at week 16. Both studies included a 24-week cross-over to deucravacitinib for patients in the apremilast group that did not show an adequate response to therapy (i.e., did not achieve a Psoriasis Area and Severity Index 50% (PASI 50) response in POETYK-1 or PASI 75 in POETYK-2). At week 24 in the POETYK-2 study, patients in the deucravacitinib group who achieved a PASI 75 response were re-randomized to placebo or to continue deucravacitinib, and patients in the apremilast group who achieved a PASI 75 response were switched to placebo.

The co-primary outcomes in both studies were the proportion of patients who achieved an sPGA score of 0 or 1 (with at least a 2-point change from baseline) and PASI 75 response at week 16, compared with placebo. The sPGA is a composite score of the physician's assessment of the overall severity of the patient's psoriatic lesions using a 5-point scale, described as clear (0), almost clear (1), mild (2), moderate (3) or severe (4). PASI grades the extent and severity of psoriatic lesions and combines an assessment of the BSA affected with the severity of desquamation, erythema, and plaque induration or infiltration. It is scored from 0 to 72, with higher scores representing more severe disease. A PASI response is the percentage improvement in PASI score, with PASI 75 considered the minimum clinically relevant change.

Key secondary outcomes included other PASI or sPGA response thresholds, health-related quality of life (HRQoL) and symptoms of psoriasis for deucravacitinib versus placebo or apremilast at week 16, 24 or 52. The POETYK-2 study also evaluated the time to relapse among patients in the deucravacitinib group that achieved a PASI 75 response at week 24.

The mean age of patients enrolled in the pivotal trials ranged from 44.7 years (standard deviation [SD] 12.1) to 47.9 (SD 14.0) per treatment group. The majority of patients were men (62% to 71%) and the minority were women (29% to 38%). Most patients were White (77% to 93%), with fewer patients who were Asian (3% to 21%) or Black (1% to 4%) or other races (≤2%). The patients enrolled had been diagnosed with psoriasis for a median of 13.4 years to 18.2 years, with a mean PASI score at baseline ranging from 20.7 (SD 8.0) to 21.8 (SD 8.6). The majority of patients had received prior systemic therapy for psoriasis (54% to 66%), including biologics (31% to 39%).

Efficacy Results

In the POETYK-1 study, 53.6%, 7.2% and 32.1% of patients in the deucravacitinib, placebo and apremilast groups, respectively, met the sPGA 0 or 1 response criteria at week 16. The between group differences favored deucravacitinib versus placebo (risk difference [RD] 46.7%, 95% confidence interval [CI] 40.2% to 53.2%, P<0.0001) and versus apremilast (RD 21.4%, 95% CI 12.7% to 30.1%, P<0.0001). The proportion of responders was 49.5%, 8.6% and 33.9% in the deucravacitinib, placebo and apremilast groups, respectively, of the POETYK-2 study. The between group risk difference was 40.9% (95% CI 35.4% to 46.4%) for deucravacitinib versus placebo, and 15.8% (95% CI 8.8% to 22.9%) versus apremilast. For both comparisons, the difference favored deucravacitinib with P values less than 0.0001.

The proportion of patients in POETYK-1 who achieved a PASI 75 response at week 16 was, 58.4%, 12.7% and 35.1% in the deucravacitinib, placebo and apremilast groups, respectively, with a risk difference of 46.1%, (95% CI 38.9% to 53.2%) for deucravacitinib versus placebo (P<0.0001), and 23.0% (95% CI 14.1% to 31.8%) versus apremilast (P<0.0001). The results were similar in the POETYK-2 study with 53.0%, 9.4% and 39.8% of patients in the deucravacitinib, placebo and apremilast groups, respectively, achieving a PASI 75 response at week 16. The risk difference was 43.7% (95% CI 38.0% to 49.3%, P<0.0001) for deucravacitinib versus placebo, and 13.4% (95% CI 6.2% to 20.7%, P = 0.0004) versus apremilast.

The results of the key secondary outcomes, PASI 90 and PASI 100 at week 16, favored deucravacitinib versus placebo in both studies. In addition, the PASI 90 response also favored deucravacitinib versus apremilast at week 16. The proportion of patients who achieved a PASI 90 response ranged from 27.0% to 35.5% in the deucravacitinib groups, 2.7% to 4.2% in the placebo groups and 18.1% to 19.6% in the apremilast groups. Few patients in any group achieved a PASI 100 response at week 16 (deucravacitinib: 10.2% to 14.2%, apremilast: 3.0% to 4.3%, placebo: 1%) and although numerically the proportion of PASI 100 responders was higher for deucravacitinib versus apremilast, this comparison was not controlled for type I error rate.

The Dermatology Life Quality Index (DLQI) was used to assess the impact of treatment on HRQoL. It is a patient-reported 10-item questionnaire that covers 6 domains: symptoms and feeling, daily activities, leisure, work and school, personal relationships, and bother with psoriasis treatment, each assessed over the past week. The overall DLQI score ranges from 0 to 30, with lower scores indicating better quality of life. A score of 0 or 1 may be interpreted as the disease has no impact on the patient's HRQoL. The proportion of patients who achieved a DLQI score of 0 or 1 at week 16 was 41.0%, 10.6% and 28.6% for POETYK-1 and 37.6%, 9.8% and 23.1% for POETYK-2 in the deucravacitinib, placebo and apremilast groups, respectively. The between group differences favored deucravacitinib versus placebo (POETYK-1: RD 30.5% [95% CI 23.4% to 37.6%]; POETYK-2: 27.9% [95% CI 22.2% to 33.7%]), with P values < 0.0001. Although numerically more patients reported a DLQI response in the deucravacitinib groups than in the apremilast groups (RD 12.3% and 14.6%), these comparisons were not controlled for type I error rate.

The patient reported Psoriasis Symptoms and Signs Diary (PSSD) was used to evaluate symptom severity in both studies. PSSD symptom score includes 5 symptoms (itch, pain, stinging, burning and skin tightness) and is scored from 0 to 100 with 0 indicating a complete absence of symptoms. Among patients who have a baseline PSSD symptom score of at least 1, the proportion of patients who had a symptom score of 0 at week 16 was 7.9%, 0.7% and 4.4% in POETYK-1 and 7.5%, 1.3% and 4.3% in POETYK-2 in the deucravacitinib, placebo and apremilast groups, respectively. In both studies, the differences favored deucravacitinib versus placebo (P<0.01), but with no statistically significant difference detected for deucravacitinib versus apremilast.

The trials were 52 weeks in duration and analyzed longer term outcomes for the randomized population (POETYK-1) and for the subgroup of patients who achieved a PASI 75 response at week 24 (POETYK-2). In the POETYK-1 study, [redacted] of patients achieved a PASI 75 response at week 24 and week 52, in comparison to [redacted] of patients who had received apremilast [redacted] Data from the POETYK-2 study indicate that patients who achieved a PASI 75 response with deucravacitinib, and who remained on treatment, were less likely to relapse than patients who were switched to placebo (P< 0.0001).

Harms Results

During the first 16 weeks of the pivotal trials (prior to any treatment switching), the frequency of adverse events was generally similar across groups with 53% and 58% of patients in the deucravacitinib groups, 42% and 54% of patients who received placebo, and 55% and 59% who received apremilast reporting 1 or more adverse events. The most commonly reported events in the deucravacitinib group were nasopharyngitis (6% to 11%), upper respiratory tract infection (5% to 6%), diarrhea and headache (each reported in 4% to 5%). The frequency of these events was comparable in the placebo and apremilast groups, except for gastrointestinal adverse events, which appeared to be more common among patients who received apremilast.

The frequency of serious adverse events was generally low during the trials, with 2% of patients in the deucravacitinib group, 1% to 5% in the placebo group and 0.4% to 2% in the apremilast group reporting an event during the first 16 weeks. Among patients who received deucravacitinib at any time during the 52-week trials, 3% to 6% of patients experienced a serious adverse event, compared with 1% to 4 % of those who received apremilast at any time. A total of 4 patients died during the studies. One patient in the placebo group (POETYK-1) died of hypertensive cardiovascular disease, 2 patients in the deucravacitinib group (POETYK-2) died of heart failure and sepsis, and hepatocellular carcinoma, and 1 patient in the apremilast group (POETYK-2) died of lung cancer and gastrointestinal hemorrhage.

The proportion of patients who stopped treatment due to adverse events was 2% and 3% for deucravacitinib, 4% for placebo and 5% and 6% for apremilast during the first 16 weeks of the trials.

During the first 16 weeks of the studies, infections and infestations were reported by 26% to 31% of patients in the deucravacitinib groups, 15% to 26% in the placebo groups and 18% to 25% in the apremilast groups. Few patients in any groups experienced an infection or infestation that was a serious adverse event, and there were no opportunistic infections or tuberculosis events reported in either study. The proportion of patients with at least a grade 2 increase in creatine kinase (CK) levels was 3% for the deucravacitinib groups, 1% to 4% in the placebo groups, and 0% to 4% in the apremilast groups during week 0 to 16. Over the 52-week study period, 6% of patients receiving deucravacitinib and 4% to 5% receiving apremilast reported ≥ grade 2 elevated CK levels. None of these events were considered serious adverse events. In both trials, the frequency of other adverse events which may be associated with drugs that work through the Janus kinase (JAK) pathway (major adverse cardiovascular events [MACE], thromboembolic events, malignancy, elevated liver enzymes, lymphopenia or neutropenia) was generally low.

Critical Appraisal

POETYK-1 and POETYK-2 studies appear to have a low risk of bias with regards to randomization, allocation concealment, and blinding. In general, the baseline characteristics of patients appeared to be balanced between groups within trials. The efficacy outcomes reported were relevant to patients (i.e., skin clearance, psoriasis symptoms and HRQoL), had evidence to support their validity, and key patient-reported outcomes were part of the statistical testing procedure to control the type I error rate. However, the co-primary outcome, PASI 75, may be considered the minimum clinically relevant response, whereas in clinical practice a PASI 90 response is generally the expected goal of therapy. Key skin clearance outcomes were analyzed based on the intention to treat population and using non-responder imputation for patients who stopped treatment or with missing data. This composite estimand

may be considered a conservative estimate of effects. However, up to 10% of patients were excluded from the DLQI or PSSD response endpoints (depending on the treatment group). The potential impact of these missing patients on the findings is unclear.

Overall, the clinical expert consulted for this review considered that the patients enrolled would represent patients with moderate to severe psoriasis who may be treated with advanced therapies in Canada, including those who had received with prior systemic or biologic therapy. The clinical expert identified some issues with apremilast as an active comparator, however. While apremilast is another oral advanced therapy, it is infrequently prescribed in Canada for the treatment of moderate to severe plaque psoriasis. The expert stated that efficacy of apremilast is considered to be low for an advanced therapy, and most dermatologists would select a biologic over apremilast. Thus, based on current practice, apremilast may not be as relevant a comparator as biologics for patients with moderate to severe disease.

Indirect Comparisons

Description of studies

The sponsor-submitted ITC conducted a systematic review and used a Bayesian NMA to evaluate the relative efficacy of deucravacitinib to other comparators for the treatment of patients with moderate-to-severe plaque psoriasis. The NMA was based on a systematic review of the literature and data from up to 84 trials were used to inform the analyses. The main efficacy outcome of interest was PASI response.

Efficacy Results

The sponsor-submitted ITC reported that in the short term (at 10 to 16 weeks) with 84 RCTs included, deucravacitinib was favored over [redacted]

The ITC reported that in the mid-term (at 24 to 28 weeks) with 48 trials included, deucravacitinib [redacted]

The sponsor-submitted ITC reported that in the long term (at 44 to 60 weeks) with 32 trials included, deucravacitinib was [redacted]

Critical Appraisal

The sponsor-submitted ITC involved a rich evidence base with a large network of RCTs and sample size, which strengthened the robustness of the NMA analyses. Nonetheless, the sponsor-submitted ITC had several limitations including heterogeneity present for many patient and study characteristics in the NMA analyses, incorporation of studies that included patients with mild disease, discordance between the sponsor's assumption of patient treatment adherence and true clinical practice, and lack of data for certain subgroup analyses. Given these limitations, the results from the sponsor-submitted ITC are at some risk of bias for the comparison of deucravacitinib with other treatments in patients with moderate to severe plaque psoriasis. Only one measure of efficacy was analyzed and no harms or quality of life endpoints were available.

Other Relevant Evidence

Description of studies

Interim data for a single-arm, open-label extension study, IM011075, was submitted by the sponsor. Patients who completed the POETYK-1 and POETYK-2 studies were eligible to enroll. A total of 1221 patients entered the extension study, which represented 72% of the patients randomized in the parent trials. All patients received deucravacitinib 6 mg daily. At the time of interim analysis, [redacted] of patients were ongoing in the study and receiving treatment, and [redacted] of patients provided data at [redacted] weeks, respectively.

Efficacy Results

In the total extension population, sPGA 0 or 1 response rates [redacted] PASI 75 response rates [redacted]

Harms Results

Adverse events were reported by [redacted] The most frequently reported events were COVID-19 [redacted]

Critical Appraisal

Limitations of the extension study include selection bias, lack of a control group, and lack of blinding. Reporting of harms and subjective measures (such as those included in the PASI score) may be biased by knowledge of treatment received. Since only descriptive statistics were published in this interim report, which were based on observed data with no imputation for missing data, and since there were no comparator groups, the interpretation of the results is limited. Moreover, there is potential for selection bias, as patients who discontinued the parent RCTs due to adverse events, lack of efficacy, or other reasons were excluded.

Economic Evidence

Cost and Cost-Effectiveness

Table 1: Summary of Economic Evaluation

Component	Description
Type of economic evaluation	Cost-utility analysis Markov model
Target population	Adult patients with moderate to severe PsO who are candidates for systemic therapy or phototherapy, which aligns with the reimbursement request
Treatment[a]	Deucravacitinib
Dose regimen	6 mg once daily
Submitted price	Deucravacitinib, 6 mg tablets: $39.45
Treatment cost	$14,409 per patient per year (365.25 days)
Comparators[a]	Adalimumab, apremilast, bimekizumab, brodalumab, certolizumab pegol, etanercept, guselkumab, infliximab, ixekizumab, risankizumab, secukinumab, tildrakizumab, ustekinumab
Perspective	Canadian publicly funded health care payer
Outcomes	QALYs, LYs
Time horizon	10 years
Key data source	A sponsor-commissioned NMA of 84 clinical trials was used to compare the ability of deucravacitinib to achieve PASI outcomes at 10 to 60 weeks compared to the other biologics. This network included two phase III clinical trials for deucravacitinib: POETYK PSO-1 and POETYK PSO-2.

Component	Description
Key limitations	• The indirect evidence is associated with some uncertainty, due to heterogeneity among trials included in the NMA. Direct evidence exists only for deucravacitinib compared to comparators of limited clinical relevance in Canadian practice. • The timepoint to assess deucravacitinib response (i.e., 24 weeks) was inconsistent with the timepoint for response assessment in the other treatment comparators within the indirect evidence (i.e., 10 to 16 weeks). Assessment at 24 weeks does not represent clinical practice. • Using a treatment-sequence specific basket of biologics to represent subsequent therapies may not appropriately represent clinical practice. The sponsor's approach resulted in differential efficacy and total costs associated with the specific sequencing of subsequent therapy, which impacted relative benefits and costs of the initial treatment in the sequence. • Long-term discontinuation rates after initial response are uncertain. • Treatment waning was not considered; patients achieving a certain PASI response were assumed to remain in that health state until treatment discontinuation, whereas in reality patient's symptoms may progress before switching therapies. • Tildrakizumab dosing was based on European rather than Canadian recommendations.
CADTH reanalysis results	In CADTH reanalyses, deucravacitinib response was assessed at 16 weeks, tildrakizumab was dosed as per its Health Canada's recommendation, and the basket of biologics representing subsequent therapy was assumed to be the same for all initial comparators. CADTH was unable to address the lack of direct evidence against relevant comparators, and uncertainty in discontinuation rates and long-term efficacy. • Deucravacitinib was less effective (fewer QALYs) than most comparators except apremiliast and etanercept. • Deucravacitinib was dominated by adalimumab, being associated with $5,512 in incremental costs, and 0.027 fewer QALYs. • Three treatments remained on the efficiency frontier in the CADTH reanalysis: adaliumamab, brodalumab, and bimekizumab.

ICER = incremental cost-effectiveness ratio; LY = life-year; NMA = network meta-analysis; PASI = psoriasis area severity index; PsO = plaque psoriasis; QALY= quality-adjusted life-year.

[a] All treatments were sequences which began with the noted comparator, followed by a basket of biologic comparators, followed by best supportive care.

Budget Impact

CADTH identified the following key limitations with the sponsor's analysis: the eligible patient population was inappropriately estimated by including the pediatric population of Canada, including the NIHB population in an inappropriate manner, and assuming all patients requiring biologic therapy are publicly funded; the model was poorly conceptualized and results did not meet face validity, substantially overestimating the costs associated with the treatment of plaque psoriasis in Canada; response rates and discontinuation assumptions have the same limitations as outlined in the pharmacoeconomic analysis; the use of the healthcare payer perspective was inappropriate; market uptake of deucravacitinib and its displacement of other comparators is uncertain; biosimilar use was underestimated; uncertainty in the modelling of the basket of biologics used to represent subsequent therapies; and the analysis assumes only patients who would otherwise receive a biologic will access deucravacitinib.

CADTH was unable to fully mitigate conceptual limitations associated with the model due to structural inflexibility and non-intuitive programming. As deucravacitinib is less expensive per treatment year than most biologic therapies currently being reimbursed, its use is likely to result in cost-savings to jurisdictional drug plans over the short term (i.e., within a 3-year time horizon) as more expensive therapies would be displaced. However, due to its lower efficacy (as suggested in the sponsor's NMA), it is likely that the use of deucravacitinib will delay rather than prevent the use of more expensive and more effective therapies, and thus reimbursement may result in an overall increase in costs over the course of each patients' life.

CADTH conducted reanalyses to adjust the eligible patient population to include only adults with plaque psoriasis, to mitigate overcounting the number of patients initiating new therapy each year, to assume deucravacitinib response would be assessed at 16 weeks, to exclude costs not within drug plan program budgets, to decrease the assumed uptake of deucravacitinib, to assume 100%

biosimilar use where available, to equalize subsequent therapies between comparators, and to dose tildrakizumab according to its Health Canada recommendation.

CADTH exploratory analyses suggest that if deucravacitinib is reimbursed in a similar manner to biologics available for the treatment of moderate-to-severe plaque psoriasis, its reimbursement might be associated with budgetary savings of $2,469,191 in Year 1, $9,227,095 in Year 2, and $12,766,452 in Year 3, for a 3-year incremental savings of $24,462,738.

CDEC Information

Members of the Committee:

Dr. James Silvius (Chair), Dr. Sally Bean, Mr. Dan Dunsky, Dr. Alun Edwards, Mr. Bob Gagne, Dr. Ran Goldman, Dr. Allan Grill, Dr. Christine Leong, Dr. Kerry Mansell, Dr. Alicia McCallum, Dr. Srinivas Murthy, Ms. Heather Neville, Dr. Danyaal Raza, Dr. Emily Reynen, and Dr. Peter Zed.

Meeting date: February 22, 2023

Regrets:

1 expert committee member did not attend

Conflicts of interest:

None