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CADTH Reimbursement Recommendation

Secukinumab (Cosentyx)

Indication: For the treatment of adult patients with moderate to severe hidradenitis suppurativa (acne inversa) who have responded inadequately to conventional systemic hidradenitis suppurativa therapy

Sponsor: Novartis Pharmaceuticals Canada Inc.

Final recommendation: Reimburse with conditions

Summary

What Is the Reimbursement Recommendation for Cosentyx?

It is recommended that Cosentyx be reimbursed by public drug plans for the treatment of adult patients with moderate to severe hidradenitis suppurativa (HS) (acne inversa) who have responded inadequately to conventional systemic HS therapy only if certain conditions are met.

Which Patients Are Eligible for Coverage?

Cosentyx should only be covered to treat patients who have moderate to severe HS (Hurley stage II or III), a total abscess and nodule count of 5 or greater, and lesions in at least 2 separate areas of the body. Additionally, these are patients whose HS did not adequately respond to conventional therapy.

What Are the Conditions for Reimbursement?

Cosentyx should only be reimbursed if prescribed by a physician experienced in the management of HS but should not be reimbursed if used in combination with other biologic therapies for HS. Cosentyx should be reimbursed for ongoing treatment if there is improvement in HS after starting treatment with Cosentyx. The price of Cosentyx should be negotiated so that its total drug cost does not exceed the total drug cost of treatment with the lowest-cost adalimumab.

Why Did Canada's Drug Agency Make This Recommendation?

- Evidence from 2 clinical trials showed that treatment with Cosentyx reduced severity and improved symptoms of HS after 16 weeks of treatment compared with placebo.
- The treatment effect of Cosentyx on HS, compared with adalimumab, after 12 to 16 weeks of treatment was uncertain based on the evidence from 1 indirect treatment comparison.
- Cosentyx likely meets the unmet needs identified by patients, including a safe and effective treatment that controls HS and manages symptoms of HS. Patients also identified a need for a treatment that works long term, but the evidence for a treatment effect of Cosentyx up to 52 weeks was uncertain.
- Based on the Canada's Drug Agency review team's assessment of the health economic evidence, Cosentyx does not represent good value to the health care system at the public list price. The committee determined there is not enough evidence to justify a greater cost for Cosentyx compared with adalimumab over the duration of treatment.

Summary

- Based on public list prices, Cosentyx is estimated to cost the public drug plans approximately $9,547,349 over the next 3 years. However, the actual budget impact is uncertain.

Additional Information

What Is Hidradenitis Suppurativa?

HS is a skin condition characterized by abscesses that lead to tissue destruction and scarring on the skin. Key symptoms of HS are pain, itch, malodourous discharge, burning sensations, and local warmth. The estimated prevalence of HS in North America and Europe is approximately 1% of the population.

Unmet Needs in Hidradenitis Suppurativa

Patients identified the following unmet needs in the treatment of HS: a safe and effective treatment that controls HS through a reduction in lesions, nodules, or draining fistulas; a treatment that works long term; and a treatment that can reduce the severity of symptoms of HS.

How Much Does Cosentyx Cost?

Treatment with Cosentyx is expected to cost $50,465 for the first year and $46,052 for the second year onward when administered every 2 weeks. Costs will be different for different administration schedules.

Recommendation

The Canadian Drug Expert Committee (CDEC) recommends that secukinumab be reimbursed for the treatment of adult patients with moderate to severe hidradenitis suppurativa (HS) (acne inversa) who have responded inadequately to conventional systemic HS therapy only if the conditions listed in Table 1 are met.

Table 1: Reimbursement Conditions and Reasons

Reimbursement condition	Reason	Implementation guidance
Initiation		
1. In patients with moderate to severe HS only if the following criteria are met: 1.1. the patient currently has a total abscess and nodule count of 5 or greater 1.2. lesions are in at least 2 distinct anatomical areas 1.3. at Hurley stage II or III.	The SUNNY trials demonstrated that treatment with secukinumab likely resulted in clinical benefit in patients with moderate to severe HS, defined as patients with a total of at least 5 inflammatory lesions (i.e., abscesses and/or inflammatory nodules) affecting at least 2 distinct anatomical areas. Additionally, most patients (94% to 98% of patients across treatment groups) enrolled in the SUNNY trials had HS at Hurley stage II or III at baseline.	—
2. In patients with an inadequate response to conventional therapy.	At baseline in the SUNNY trials, most patients ([redacted] across treatment groups) had prior experience with at least 1 therapy for HS. As such, there is limited evidence to support the use of secukinumab as a first-line therapy before conventional therapy options.	An inadequate response may be defined as an inability to maintain a minimum 50% reduction in the sum of AN count with no increase in abscess count or draining fistula count relative to baseline. Conventional therapy typically refers to systemic antibiotic therapy. An adequate trial was defined as 12 weeks of treatment with systemic antibiotic therapy.
3. The physician must provide a baseline assessment of AN count, abscess count, and draining fistula count at the time of initial request for reimbursement.	Patients in the SUNNY trials were required to have a total of at least 5 inflammatory lesions (i.e., abscesses and/or inflammatory nodules) affecting at least 2 distinct anatomical areas. Further, response to treatment as per the HiSCR50 response was informed by the number of AN and draining fistulas.	—
4. The maximum duration of initial authorization is 12 months.	The primary end point used to demonstrate efficacy in the SUNNY trials was HiSCR50 response assessed at week 16. Given that patients may need additional time for dose optimization and the availability of evidence of treatment with secukinumab up to 52 weeks in the SUNNY trials, a 12-month initial authorization was considered appropriate.	Within the secukinumab submission, guidance on dosage escalation from monthly dosing to biweekly dosing is limited to clinical expert input. The clinical experts suggested that based on the anticipated time to improvement in HS with treatment with biologics (i.e., adalimumab), if there was not a response to monthly dosing, a request to increase to biweekly dosing would likely occur at 16 to 24 weeks.

Reimbursement condition	Reason	Implementation guidance
Renewal		
5. For renewal after initial authorization, the physician must provide proof of beneficial clinical effect when requesting continuation of reimbursement, defined by HiSCR50 response (i.e., at least a 50% reduction in AN count with no increase in abscess or draining fistula count) 12 months after initiation of treatment with secukinumab.	The primary end point used to demonstrate efficacy in the SUNNY trials was achievement of HiSCR50 response, defined as at least a 50% reduction in AN count with no increase in the number of abscesses and/or in the number of draining fistulas from baseline to week 16. As noted for condition 4, renewal up to 12 months was considered reasonable because there is evidence of treatment with secukinumab up to 52 weeks in the SUNNY trials that did not suggest any new safety concerns.	—
6. For subsequent renewal, the initial HiSCR50 response must at least be maintained to continue receiving secukinumab. Subsequent renewals should be assessed every 6 months.	There is no evidence to support long-term maintenance of treatment effect after 52 weeks. Further, the outcomes reported at 52 weeks were associated with uncertainty. Subsequent assessment for renewal is recommended to ensure patients continue to benefit from treatment. Based on clinical expert input, subsequent assessment of renewal every 6 months was considered reasonable and aligned with what occurs in clinical practice.	CDEC noted that jurisdictions may wish to consider criteria for subsequent renewal that is aligned with adalimumab or that requires assessment at least every 12 months.
Prescribing		
7. Prescribed by a practitioner with expertise in the management of patients with HS.	To ensure secukinumab is appropriately prescribed for patients with HS.	—
8. Secukinumab should not be prescribed in combination with other biologics.	There is no evidence to support the use of secukinumab in combination with other biological therapies for HS.	—
Pricing		
9. Secukinumab should be negotiated so that it does not exceed the drug program cost of treatment with the least costly form of adalimumab reimbursed for the treatment of HS.	Cost-effectiveness of secukinumab relative to adalimumab is uncertain given the lack of direct head-to-head evidence and uncertainty with indirect comparisons. To ensure cost-effectiveness regardless of administration frequency, the total drug cost of secukinumab should also not exceed the total drug cost of the lowest-cost adalimumab.	—
Feasibility of adoption		
10. The feasibility of adoption of secukinumab must be addressed.	At the submitted price, the magnitude of uncertainty in the budget impact must be addressed to ensure the feasibility of adoption because of the difference between the sponsor's estimate and the estimates by Canada's Drug Agency.	—

AN = abscesses and inflammatory nodules; CDEC = Canadian Drug Expert Committee; HiSCR50 = > 50% response in Hidradenitis Suppurativa Clinical Response; HS = hidradenitis suppurativa.

Rationale for the Recommendation

Evidence from 2 phase III, double-blind, randomized controlled trials (RCTs), SUNSHINE (N = 541) and SUNRISE (N = 543) (SUNNY trials), demonstrated that treatment with secukinumab resulted in added clinical benefit compared to placebo for adult patients living with moderate to severe HS. Evidence of added clinical benefit compared to placebo was demonstrated based on the proportion of patients with at least a 50% decrease in abscesses and inflammatory nodules (AN count) with no increase in the number of abscesses and/or in the number of draining fistulas according to the Hidradenitis Suppurative Clinical Response (HiSCR50) after 16 weeks of treatment. The SUNNY trials also demonstrated that secukinumab results in a decrease in AN count, a decrease in the proportion of patients experiencing disease worsening as measured by flares, and an increase in the proportion of patients with at least a 30% reduction and at least 2 units reduction from baseline in skin pain at its worst as measured by a Numerical Rating Scale (NRS30) compared with placebo. Because there was no direct evidence comparing secukinumab to other biologics for the treatment of adults with moderate to severe HS, the sponsor provided a network meta-analysis (NMA) that assessed short-term efficacy (12 to 16 weeks) versus adalimumab; however, the results of the NMA were inconclusive, showing 95% credible intervals (CrIs) that were wide and included the null for all outcomes tested (HiSCR50, AN count, skin pain, flares, and health-related quality of life [HRQoL]).

Patient groups identified the following unmet needs in the treatment of patients living with HS: a safe and effective treatment that controls HS through a reduction in lesions, nodules, or draining fistulas; a treatment that can lead to disease remission; and a treatment that can manage symptoms of HS (e.g., reduces pain). CDEC concluded that secukinumab likely meets each of these needs, with the exception of disease remission because longer-term (52-week) outcomes were associated with uncertainty.

Using the sponsor-submitted price for secukinumab and the publicly listed price for biosimilar adalimumab, secukinumab was determined to be more costly than adalimumab. Because there is insufficient evidence to suggest secukinumab is more effective than adalimumab, the total drug cost of secukinumab should not exceed the total drug cost of the lowest-cost adalimumab.

Discussion Points

- CDEC discussed whether it is appropriate for patients to switch from adalimumab to secukinumab. Although the SUNNY trials were not designed to evaluate a switch in biologic therapies for HS, based on experience with prior HS therapies reported at baseline in the SUNNY trials, approximately 20% or more of patients in each group had prior experience with adalimumab, with most patients also discontinuing due to lack of efficacy. Additionally, the results of a subgroup analysis of the primary end point by previous use of systemic biologics was not adjusted for multiple testing and was limited by a small sample size. Although the effectiveness of secukinumab after failure of adalimumab is uncertain, the clinical experts consulted by Canada's Drug Agency anticipated that a trial of secukinumab following adalimumab may occur in clinical practice.

- In the absence of other effective treatment options for HS, dosage escalation beyond the recommended dosage approved by Health Canada is considered for some patients in clinical practice. Based on input from clinical experts, clinicians rely on experience with biologics in other conditions for safety information. Despite this, CDEC discussed that there is no evidence to support dosage escalation of secukinumab in patients with HS that goes beyond the recommended dosage and dosage adjustment outlined in the product monograph. Further, as noted by the clinical experts, dosage escalation of other treatments, such as adalimumab, does not consistently result in an adequate treatment response based on their clinical experience.
- CDEC discussed the challenges of treating a chronic, debilitating skin condition such as HS and the impact on a patient's HRQoL. In the SUNNY trials, HRQoL was assessed using the Dermatology Life Quality Index (DLQI) and EQ-5D health state assessment. These outcomes were considered exploratory in the trials and yielded discordant results. More specifically, secukinumab resulted in little to no clinically important difference between groups in change from baseline in DLQI score, but likely results in a clinically important improvement in EQ-5D health state assessment. As such, there was limited evidence to support an improvement in HRQoL based on the DLQI and ED-5D outcomes studied in the trials.
- CDEC discussed the use of adalimumab in clinical practice in Canada. Feedback from clinical experts indicated that for certain patients, adalimumab does not have the desired effectiveness. Despite this, some of these patients may continue treatment with adalimumab. Therefore, the financial impact of switching these patients to secukinumab would be minimal if the annual cost of secukinumab is not higher than the annual cost of adalimumab. However, CDEC noted that although the effectiveness of secukinumab after failure of adalimumab is uncertain, if secukinumab is used in patients who are no longer receiving adalimumab, this will add additional costs to drug budgets.
- The review of secukinumab was accepted as a pre–Notice of Compliance (NOC) submission, and the clinical report that informed the initial committee deliberation (September 2023) was drafted based on the submitted draft product monograph. The final product monograph that was approved by Health Canada (May 17, 2024) differed in that it recommends patients start with monthly maintenance dosing (every 4 weeks); based on clinical response, the maintenance dosage can be increased to 300 mg every 2 weeks. Monthly maintenance dosing and related evidence was not included in the original clinical review report (CRR); however, the CRR was updated, reviewed, and discussed by a subpanel of CDEC members. During the subpanel discussion (July 2024), CDEC noted there is no evidence included in the submission that would support a decision to use monthly over biweekly dosing or, conversely, biweekly over monthly dosing. Further, there is no evidence included in the submission to support a dosage escalation from every 4 weeks to every 2 weeks; therefore, whether patients who did not respond to monthly dosing would respond to biweekly dosing is highly uncertain. As such, guidance for changes to the maintenance dosing is based on clinical expert opinion.
- During the subpanel discussion (July 2024), the committee also acknowledged that the analysis of the primary end point, HiSCR50 response, in the SUNSHINE trial was not statistically significant in the

treatment group that received maintenance dosing of secukinumab 300 mg every 4 weeks, which is a notable limitation of the overall body of evidence. In contrast, the results of other outcomes reported for the monthly maintenance dosage included in the CRR were generally aligned with the results reported with biweekly dosing.

- The economic review was based on the proposed dosage regimen that was initially submitted to Canada's Drug Agency (secukinumab 300 mg per week for 5 weeks followed by 300 mg every 2 weeks). In addition, the sponsor notified Canada's Drug Agency that the submitted price had been updated during the review. The appraisal by Canada's Drug Agency was undertaken based on the information included in the initial application package and was not revised after the NOC or revised price was received. CDEC concluded that the updated dosage regimen and price has no impact on the conclusions draw upon the original economic appraisal.

Background

HS is a chronic, debilitating skin condition characterized by abscesses that lead to tissue destruction and scarring on the skin, particularly in the skin folds such as the axillae, groin, and perineum. HS is thought to involve a combination of factors including immune and endocrine dysregulation, genetics, and bacterial infection. Key symptoms of HS are pain, itch, malodourous discharge, burning sensations, and local warmth. The onset of HS typically occurs after puberty, mostly occurring in the second or third decade of life. The estimated prevalence of HS in North America and Europe is approximately 1% of the population. A study of patients with HS living in Canada suggested that approximately 44% of patients have stage II disease and 12% of patients have stage III disease.

The clinical experts consulted by Canada's Drug Agency for this review indicated that systemic antibiotics are the first-line systemic therapies in the treatment of HS. The experts indicated that the tetracyclines are the most commonly used antibiotic class, with prescriptions for doxycycline and tetracycline exceeding those for minocycline. The experts further indicated that clindamycin combined with rifampin and IV ertapenem are used much less frequently than the tetracyclines. In general, the North American clinical management guidelines for HS (published in 2019) indicate that systemic antibiotics are used as adjunctive therapy in advanced disease due to lower response rates and increased recurrence. The clinical experts indicated that patients with moderate to severe HS that has failed to respond to systemic antibiotic therapy would be eligible for adalimumab, the only biologic therapy currently with Health Canada approval for use in HS. This is aligned with the guidelines that reference treatment with adalimumab in patients with moderate to severe disease. Other biologics without approval for use in HS discussed in the guidelines for moderate to severe HS include infliximab, anakinra, and ustekinumab. The experts indicated that topical therapy may be continued as adjunct therapy in a patient with moderate to severe HS who partially responded to the topical therapy before starting systemic therapy. More specifically, the guidelines reference treatment with topical clindamycin and resorcinol.

Secukinumab has been approved by Health Canada for the treatment of adult patients with moderate to severe HS. Secukinumab is a human IgG1k monoclonal antibody that selectively binds to interleukin (IL)-17A, a naturally occurring cytokine involved in inflammatory and immune responses. It is available as a solution for injection and the dosage recommended in the product monograph is 300 mg of secukinumab by subcutaneous (SC) injection with initial dosing at weeks 0, 1, 2, 3, and 4, followed by a maintenance dosage of 300 mg every 4 weeks. Based on clinical response, the maintenance dosage can be increased to 300 mg every 2 weeks. Each 300 mg dose is given as 1 SC injection of 300 mg or as 2 SC injections of 150 mg.

Sources of Information Used by the Committee

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

- a review of 2 phase III, multicentre, randomized, double-blind, placebo-controlled, parallel group clinical studies in adult patients (≥ 18 years) with moderate to severe HS
- patients' perspectives gathered by patient groups, the Canadian Skin Patient Alliance (CSPA), HS Heroes, and Hidradenitis and Me Support Group
- input from public drug plans that participate in the Canada's Drug Agency review process
- input from 2 clinical specialists with expertise diagnosing and treating patients with HS
- input from 1 clinician group, the Canadian Hidradenitis Suppurativa Foundation
- a review of the pharmacoeconomic model and report submitted by the sponsor.

Perspectives of Patients, Clinicians, and Drug Programs

The information in this section is a summary of input provided by the patient and clinician groups who responded to call by Canada's Drug Agency for input and from clinical experts consulted by Canada's Drug Agency for the purpose of this review.

Patient Input

The CSPA, HS Heroes, and Hidradenitis and Me Support Group collaboratively provided input for this review. Patient input was gathered from the 2020 National Report of Patients' Experiences Living with HS survey (N = 547) and a patient survey hosted by the patient groups between March 28 to May 23, 2023 (N = 15). Of note, 4 patients from the 2023 patient survey reported prior experience with secukinumab. All respondents indicated their HS lesions are chronic, with the majority being active lesions.

More than 80% of respondents to the 2020 survey reported HS negatively impacted their work performance, social interactions, and intimacy with their partner. Respondents to the 2020 survey reported being worried about odour, staining of clothes, and the unpredictable onset of painful disease flares. Nearly all respondents to the 2020 survey reported experiencing some degree of moderate pain daily; only 11% of all survey respondents considered their pain well-controlled and 46% considered their pain poorly controlled. Similarly,

respondents to the 2023 survey reported severe impact of HS (drainage, severe pain, and lesions) on their day-to-day life. Respondents to the 2023 survey highlighted the high costs associated with wound care and treatment for HS and the high level of anxiety and irritation due to living with HS. When considering unmet needs, 1 respondent to the 2020 survey described their experience with HS as "so painful, so disgusting, and so life-altering."

In the 2020 survey, respondents reported trying an average of 15 different medications, surgical procedures, home treatments, and lifestyle modifications to manage symptoms, with only a few reporting any significant improvement. Of the survey respondents, 82% reported receiving a long course of antibiotics, with 11% reporting improvement in symptoms; 27% of survey respondents reported using biologics, with 38% reporting symptomatic improvement. Other treatments reported by the survey respondents were corticosteroid injections, CO_2 lasers, radiotherapy, incision and drainage, and surgical intervention. Overall, 13% of survey respondents reported satisfaction with their current treatments. Respondents reported the following side effects with currently available treatments: back pain, headache, intestinal problems, and fatigue.

The main treatment goals described by the 2020 survey respondents were to achieve symptom control, cure HS, and be able to enjoy personal relationships. Moreover, based on input from the patient groups, patients expressed that they would derive emotional, physical, and daily life benefits with effective therapy. In describing their experience with the current drug under review, 2 of 4 respondents indicated secukinumab to be effective in reducing HS lesions, pain, and the need for wound care. One respondent reported achieving complete resolution of HS lesions and disease remission, while 1 reported treatment discontinuation due to ineffectiveness.

Clinician Input

Input From Clinical Experts Consulted by Canada's Drug Agency

The clinical experts indicated that not all patients respond to currently available treatment options, including adalimumab. The experts estimated 40% to 60% of patients would have partial response to adalimumab and 20% of patients would have a good response to adalimumab. The experts also indicated that patients become refractory to systemic therapies, including adalimumab. The experts anticipated secukinumab to be an alternative treatment option to adalimumab as a second-line systemic drug used after failure of systemic antibiotics. The experts anticipated secukinumab to be offered to patients whose HS did not respond to treatment or who developed adverse events (AEs) to or have contraindications to adalimumab. The experts indicated that secukinumab can be offered as the patient's first biologic therapy. As such, the experts concluded that it may cause a slight shift in the current treatment paradigm. According to the experts, the patient population best suited for treatment with secukinumab are patients with moderate to severe HS who are eligible for adalimumab (i.e., as an alternative to adalimumab) and whose HS has not previously responded to systemic antibiotic therapy or antibiotic therapy and adalimumab.

The clinical experts identified the following as outcomes used in clinical practice to assess response to treatment: lesion count (abscess, nodule, and fistula), pain scale, number of sites involved, extent of disease, and patient-reported outcomes, such as DLQI, activities of daily living, and HRQoL. The experts

highlighted the importance of the number of sites involved — a reduction in lesion count with new sites of involvement would likely be interpreted as treatment failure from the patient's perspective. The experts indicated that outcomes are typically assessed every 3 to 6 months. When deciding to discontinue treatment with secukinumab, the experts indicated that they would consider the following: disease progression, less than 50% improvement after 6 months of treatment, and severe AEs to secukinumab, such as severe inflammatory bowel disease.

Clinician Group Input

One clinician group, Canadian Hidradenitis Suppurativa Foundation, provided input for this review, with 2 clinicians contributing to this input. When considering unmet needs, the clinician group indicated that current management options are not able to completely control the disease and are not effective in inducing remission; some patients may also lose benefit with treatment. The clinician group further indicated that a higher dose of medication (i.e., adalimumab) may be required in patients with severe disease to maintain efficacy. The clinician group noted that adalimumab is the only approved biologic option in Canada for the treatment of HS. According to the clinician group, off-label alternative biologics include infliximab, ustekinumab, IL-17 inhibitors, and IL-1 inhibitors; however, these alternative treatments are offered to patients depending on coverage and compassionate programs.

The clinician group suggested that secukinumab may be an alternative treatment option for patients who would have not demonstrated efficacy with the current standard of care (i.e., secukinumab should be offered as a biologic alternative to patients whose HS has failed to respond to systemic antibiotics for 12 weeks). When considering patients who would be best suited for treatment with the drug under review, the clinician group identified patients with moderate to severe HS (i.e., Hurley stage II and III).

To determine response to treatment, the clinician group suggested achievement of a 50% reduction in abscesses and sinuses with no new lesions after initiation of therapy with secukinumab. The clinician group further suggested patient-reported outcomes, such as pain, odour, and drainage management, as alternative outcome measures.

Drug Program Input

The clinical experts consulted by Canada's Drug Agency provided advice on the potential implementation issues raised by the drug programs.

Table 2: Responses to Questions From the Drug Programs

Implementation issues	Response
Relevant comparators	
In the context of currently available treatment options for moderate to severe HS in Canada, is placebo an appropriate comparator?	The experts noted that the ideal comparator would be other biologics, in particular, adalimumab. As standard of care for HS includes adalimumab, CDEC indicated that placebo would not be considered an appropriate comparator; instead, a comparative trial would be considered more appropriate.

Implementation issues	Response
Patients in the antibiotic strata were allowed to enter the SUNSHINE and SUNRISE trials on a stable dose of permitted antibiotics. Could this have affected results? Should antibiotics be considered a relevant comparator?	The clinical experts agreed that patients in the antibiotic strata entering the trials on a stable dose of permitted antibiotic would have an impact on the results. The clinical experts agreed that antibiotics should be considered a relevant comparator. CDEC noted that antibiotics may be used in conjunction with biologics and are part of SOC. CDEC indicated that antibiotics within SOC are a valid comparator before or after failure of biologics.
Adalimumab received a positive recommendation for the indication under review and has established criteria in its recommendation. Adalimumab is listed for this indication (as well as some biosimilars) in most jurisdictions.	Comment from the drug programs to inform CDEC deliberations.
Considerations for initiation of therapy	
Should patients need to fail a conventional treatment, such as oral antibiotics, as was included in the adalimumab recommendation, before starting secukinumab?	The clinical experts indicated that it would be reasonable to recommend at least 1 adequate trial of systemic antibiotic therapy before initiating treatment with secukinumab. CDEC noted there is limited evidence to support the use of secukinumab as a first-line therapy before conventional therapy options. CDEC further noted that the majority of patients in the SUNNY trials had HS that failed to respond or who were intolerant to systemic antibiotics.
Should 1 biologic be preferred over other biologics in the treatment of HS?	In the absence of direct treatment comparison with relevant comparators, the clinical experts suggested that the decision to use 1 biologic over another should be based on clinician judgment. CDEC suggested that both secukinumab and adalimumab should be available with no cost premium for either drug and that reimbursement of secukinumab and adalimumab is appropriate if the total drug costs of the treatment regimen for secukinumab and adalimumab is the same.
Considerations for continuation or renewal of therapy	
Consider alignment with criteria for adalimumab.	Comment from the drug programs to inform CDEC deliberations.
Considerations for prescribing of therapy	
How does both secukinumab and adalimumab fit into therapy?	In terms of place in therapy, the clinical experts anticipated that secukinumab will be a second-line systemic drug, like adalimumab, used after failure of conventional therapy (e.g., systemic antibiotics). The clinical experts indicated that secukinumab may be offered if adalimumab failed or if patients have contraindications to or developed adverse events related to adalimumab. Additionally, the clinical experts suggested secukinumab may be offered before adalimumab as the patient's first biologic therapy. CDEC defers to the expertise of the clinical experts.

Implementation issues	Response
There may be interest in combining secukinumab with other biologics because of different mechanisms of action. Would this be a concern?	The clinical experts indicated that, in practice, it is highly unlikely that 2 biologics would be combined in the treatment of HS. CDEC further noted that in the absence of supportive evidence, combining secukinumab with other biologics should not be permitted due to efficacy and safety concerns.
Should prescribing of secukinumab be consistent with adalimumab or managed separately?	The clinical experts suggested that secukinumab should be prescribed by a dermatologist. CDEC suggested that prescriber criteria should be based on how patients with HS are managed in clinical practice, whether it be by dermatologists or general practitioners.
There may be limited access to specialists in some regions.	Comment from the drug programs to inform CDEC deliberations.
Generalizability	
The inclusion criteria in the trials included the following: • Diagnosis of HS ≥ 1 year prior to baseline • Patients with moderate to severe HS, defined as a total of ≥ 5 inflammatory lesions affecting ≥ 2 distinct anatomic areas The exclusion criteria in the trials included the following: • Total fistulae count ≥ 20 at baseline • Active ongoing inflammatory diseases other than HS that require treatment with prohibited medications or the use of or planned use of prohibited treatment Should patients with these characteristics be considered for treatment with secukinumab as well?	The clinical experts noted that patients with fewer than 5 inflammatory lesions who have a history of numerous lesions may be candidates for treatment in clinical practice because HS fluctuates in disease severity independent of treatment. CDEC considered the experts' opinion in their deliberation but noted that there is uncertainty regarding the efficacy of treatment with secukinumab in a population that was not studied because of the exclusion criteria related to disease severity (i.e., the exclusion of patients with fewer than 5 inflammatory lesions). Regarding the use of prohibited medications in the SUNNY trials, the clinical experts anticipated that patients would remain on topical antibiotic therapy while on treatment with secukinumab if the patient experienced partial response to the topical antibiotic therapy before receiving secukinumab. The clinical experts also noted that opioid analgesics can be occasionally prescribed for patients with HS. Additionally, the clinical experts noted that patients with previous exposure to any IL-17 inhibitors would be candidates for treatment in clinical practice. CDEC defers to the expertise of the clinical experts regarding the exclusion criteria described here.
Care provision issues	
Patients were allowed to continue antibiotic and topical therapy in the studies. Is this a required or recommended practice? Are antibiotic and topical therapy considered adjunctive therapy?	The clinical experts indicated that the drugs considered as concomitant and/or adjunctive therapy in the treatment of HS would depend on the clinician. CDEC defers to the expertise of the clinical experts.
System and economic issues	
If secukinumab is recommended as a first-line option, this will have significant budget impact.	Comment from the drug programs to inform CDEC deliberations.
Adalimumab and its biosimilars have achieved confidential negotiated prices.	Comment from the drug programs to inform CDEC deliberations.

CDEC = Canadian Drug Expert Committee; HS = hidradenitis suppurativa; IL = interleukin; SOC = standard of care.

Submission Update Provided by the Sponsor (April 24, 2024)

The review of secukinumab was accepted as a pre-NOC submission and the clinical report was drafted based on the draft product monograph. In consideration of the revisions included in the final product monograph, specifically the indication and dosage and administration sections for HS, additional information relevant to the updated product monograph was extracted from the SUNSHINE and SUNRISE studies (collectively referred to as the SUNNY trials) and ITC submitted by the sponsor. This included results on the comparison between the secukinumab 300 mg every 4 weeks dosage group versus the placebo group from the SUNNY trials and versus the adalimumab group from the ITC for the outcomes of interest to this review.

Systematic Review Evidence on the Monthly Maintenance Dosage of Secukinumab

Results

Period 1: 16-Week Placebo-Controlled Treatment

Overall, the direction of treatment effect based on the key efficacy results was consistent between the biweekly and monthly maintenance dosing of secukinumab versus placebo. Statistical significance cannot be claimed for the primary analysis results of AN count and NRS30 skin pain response at week 16 in the SUNSHINE trial for the secukinumab monthly maintenance dosage group versus the placebo group despite the P value being less than 0.005. This is because the result for the primary end point (HiSCR50 response), a prior end point in the testing hierarchy, was not statistically significant. Results for these end points should be considered supportive evidence. Overall, no notable differences in the frequency of AEs between study drug groups were identified in each study.

Entire Study Period

The entire study period consisted of the 16-week placebo-controlled treatment period 1, a 36-week treatment period 2, and an 8-week follow-up. The results at week 52 were noncomparative and presented descriptively. Overall, the direction of treatment effect based on the key efficacy results was consistent between the biweekly and monthly maintenance dosing of secukinumab. Additionally, no notable differences in the frequency of AEs between study drug groups were identified in each study.

Critical Appraisal

In general, no notable differences in the study population between study drug groups (secukinumab 300 mg every 2 weeks, secukinumab 300 mg every 4 weeks, and placebo groups) were identified in each study. As such, the limitations discussed for the primary and exploratory efficacy analyses at week 16 and week 52 of the biweekly maintenance dosing are applicable to the corresponding analyses of the monthly maintenance dosing. Overall, no serious risk of bias concerns and no major issues with the generalizability of the results to the target population and Canadian practice were identified in the appraisal of the SUNNY trials. Notably, there was not an active or placebo comparator group for the assessments made at week 52. As such, the inability to draw causal conclusions about the 52-week results is because the noncomparative design does not facilitate distinguishing between the effect of treatment, placebo effects, and natural history.

Network Meta-Analyses on the Monthly Maintenance Dosage of Secukinumab

The primary evidence network was informed by 4 studies (PIONEER 1, PIONEER 2, SUNSHINE, and SUNRISE) and was limited to patients who were biologic naive. All results were based on the induction phase of the trials (12 to 16 weeks). Overall, the results for the secukinumab every 4 weeks dosage group were similar to the secukinumab every 2 weeks dosage group. The findings were inconclusive, showing 95% CrI that were wide and included the null for secukinumab versus adalimumab in patients who were biologic naive as well as the sensitivity analyses that included both patients with and without experience with biologics. These analyses shared the same limitations as discussed for the secukinumab every 2 weeks comparison.

Summary of Clinical Evidence Before Submission Update

The following summary on clinical evidence reflects the draft product monograph before the previously mentioned revisions were made, hence the focus on the maintenance dosage of 300 mg of secukinumab administered every 2 weeks unless otherwise specified. Detailed information regarding the maintenance dosage of 300 mg of secukinumab administered every 4 weeks is included in the Appendix 2 of the CRR.

Clinical Evidence

Systematic Review

Description of Studies

Two phase III, randomized, double-blind, placebo-controlled, parallel group trials, SUNSHINE (N = 541) and SUNRISE (N = 543), assessed whether 2 SC secukinumab dosage regimens improved HiSCR50 response from baseline compared with placebo after 16 weeks of treatment in adult patients (≥ 18 years) with moderate to severe HS. The outcomes measured in the trials and selected for Grading of Recommendations, Assessment, Development and Evaluation (GRADE) assessment were response to treatment and disease severity (HiSCR50 and AN count), disease worsening (patients experiencing flares), symptoms (NRS30 skin pain), HRQoL (DLQI and EQ-5D health state assessment), and notable harms (infections and infestations; *Candida* infections; malignant or unspecified tumours; neoplasms benign, malignant, and unspecified [including cysts and polyps]; squamous cell carcinoma of HS-affected area; and inflammatory bowel disease).

Baseline characteristics were generally similar between groups and across trials. Across trials, the mean age of patients ranged from 35.5 years (standard deviation [SD] = 10.75 years) in the placebo group in SUNSHINE to 37.3 years (SD = 11.48 years) in the secukinumab group in SUNRISE. Across trials, most patients were categorized with Hurley stage II disease severity at baseline, ranging from 51.1% (92 of 180 patients) in the secukinumab group in SUNRISE to 67.2% (121 of 180 patients) in the placebo group in SUNSHINE. At baseline, patients with Hurley stage III disease severity ranged from 28.3% (51 of 180 patients) in the placebo group in SUNSHINE to 45.6% (82 of 180 patients) in the secukinumab group in SUNRISE. The proportions of patients with 1 to 11 anatomic regions with at least 1 total fistula, inflammatory nodule, or abscess were generally well balanced between groups and across trials. The mean baseline AN count across trials ranged

from 12.8 (SD = 8.15) in the placebo group in SUNSHINE to 13.9 (SD = 9.93) in the secukinumab group in SUNRISE.

Note that 2 different dosage regimens were assessed in both trials, however, only the maintenance dosage of 300 mg of secukinumab administered every 2 weeks is included in the Health Canada indication. Therefore, only the results of the dosage regimen of every 2 weeks are summarized in this report.

Efficacy Results

Response to Treatment and Disease Severity

Hidradenitis Suppurativa Clinical Response

Both the SUNSHINE and SUNRISE studies met the primary end point — achievement of HiSCR50 response at week 16 — for the secukinumab 300 mg every 2 weeks dosage regimen. In SUNSHINE, the marginal risk difference in HiSCR50 response at week 16 between secukinumab and placebo was [redacted] (96% confidence interval [CI], [redacted]) (odds ratio [OR] = 1.75; 96% CI, [redacted]; P value = 0.0070), in favour of secukinumab. In SUNRISE, the marginal risk difference in HiSCR50 response at week 16 between secukinumab and placebo was [redacted] (96% CI, [redacted]) (OR = 1.64; 96% CI, [redacted]; P value = 0.0149), also in favour of secukinumab. The sensitivity analysis, supplementary analysis, and tipping point analysis results of HiSCR50 response at week 16 were generally consistent with and supportive of the primary analysis results for secukinumab 300 mg every 2 weeks dosage regimen in both studies. The results of the subgroup analysis by the key subgroups (concomitant antibiotic use, body weight stratum, previous use of systemic biologics, Hurley stage, and baseline AN count) are generally consistent with the primary analysis, with the exception of the results from patients with Hurley stage I in SUNRISE.

The proportion of patients achieving HiSCR50 response observed at week 52 was an exploratory end point in both studies. In SUNSHINE, [redacted] ([redacted] of 117 patients; 95% CI, [redacted]) in the secukinumab group and [redacted] ([redacted] of 58 patients; 95% CI, [redacted]) in the placebo to secukinumab group achieved HiSCR50 response at week 52. In SUNRISE, [redacted] ([redacted] of 137 patients; 95% CI, [redacted]) in the secukinumab group and [redacted] ([redacted] of 64 patients; 95% CI, [redacted]) in the placebo to secukinumab group achieved HiSCR50 response at week 52.

Abscesses and Inflammatory Nodules Count

Both the SUNSHINE and SUNRISE studies met the secondary end point — percentage change from baseline in AN count at week 16 — for the secukinumab 300 mg every 2 weeks dosage regimen; this secondary end point was tested in a hierarchical manner to control for type I error rate. In SUNSHINE, the least squares [LS] mean difference in percentage change from baseline in AN count at week 16 between secukinumab and placebo was −23.05 (96% CI, [redacted]; P < 0.0001), in favour of secukinumab. In SUNRISE, the LS mean difference in percentage change from baseline in AN count at week 16 between secukinumab and placebo was −16.33 (96% CI, [redacted]; P = 0.0051), also in favour of secukinumab. The sensitivity analysis and tipping point analysis results of AN count at week 16 were generally consistent with and supportive of the primary analysis results for secukinumab 300 mg every 2 weeks dosage regimen in both studies.

The percentage change from baseline in AN count observed at week 52 was an exploratory end point in both studies. In SUNSHINE, the mean percentage change from baseline in AN count at week 52 was [redacted] (95%

CI, [redacted]) in the secukinumab group and [redacted] (95% CI, [redacted]) in the placebo to secukinumab group. In SUNRISE, the mean percentage change from baseline in AN count at week 52 was [redacted] (95% CI, [redacted]) in the secukinumab group and [redacted] (95% CI, [redacted]) in the placebo to secukinumab group.

Remission

Disease remission was not measured in the SUNSHINE and SUNRISE trials.

Disease Worsening

Flare

Only the SUNSHINE study met the secondary end point — experience of any flares at week 16 — for the secukinumab 300 mg every 2 weeks dosage regimen; this secondary end point was tested in a hierarchical manner to control for type I error rate. In SUNSHINE, the marginal risk difference in flares at week 16 between secukinumab and placebo was [redacted] (96% CI, [redacted]) (OR = 0.42; 96% CI, [redacted]; P value = 0.0010), in favour of secukinumab. In SUNRISE, the marginal risk difference in flares at week 16 between secukinumab and placebo was [redacted] (96% CI, [redacted]) (OR = 0.68; 96% CI, [redacted]; P value = 0.0732). The sensitivity analysis and tipping point analysis results of flares at week 16 were generally consistent with and supportive of the primary analysis results for secukinumab 300 mg every 2 weeks dosage regimen in both studies.

The proportion of patients experiencing any flares observed at week 52 was an exploratory end point in both studies. In SUNSHINE, [redacted] ([redacted] of 138 patients) (95% CI, [redacted]) in the secukinumab group and [redacted] ([redacted] of 65 patients; 95% CI, [redacted]) in the placebo to secukinumab group experienced any flares at week 52. In SUNRISE, [redacted] ([redacted] of 151 patients; 95% CI, [redacted]) in the secukinumab group and [redacted] ([redacted] of 67 patients; 95% CI, [redacted]) in the placebo to secukinumab group experienced any flares at week 52.

Symptoms

Skin Pain

The secondary end point achievement of NRS30 (skin pain at its worst) at week 16 was met by the secukinumab 300 mg every 2 weeks dosage regimen based on pooled data from the SUNSHINE and SUNRISE studies in patients with baseline NRS of 3 or more; this secondary end point was tested in a hierarchical manner to control for type I error rate. The marginal risk difference in NRS30 (skin pain) at week 16 between secukinumab and placebo was [redacted] (96% CI, [redacted]) (OR = [redacted]; 96% CI, [redacted]; P value = 0.0003), in favour of secukinumab. The tipping point analysis results of NRS30 (skin pain) at week 16 were supportive of the primary analysis results for secukinumab 300 mg every 2 weeks dosage regimen in both studies.

The proportion of patients achieving NRS30 (skin pain) observed at week 52 was an exploratory end point based on pooled data from both trials in patients with baseline NRS of 3 or more. Based on the pooled data, [redacted] ([redacted] of [redacted] patients; 95% CI, [redacted]) in the secukinumab group and [redacted] ([redacted] of [redacted] patients; 95% CI, [redacted]) in the placebo to secukinumab group achieved NRS30 (skin pain) at week 52.

Health-Related Quality of Life

Dermatology Life Quality Index

The proportion of patients achieving DLQI response observed at week 16 was an exploratory end point in both studies. In SUNSHINE, the risk difference in DLQI response at week 16 between secukinumab and placebo was [redacted] (95% CI, [redacted]) (OR = [redacted]; 95% CI, [redacted]; P value = [redacted]). In SUNRISE, the risk difference in DLQI response at week 16 between secukinumab and placebo was [redacted] (95% CI, [redacted]) (OR = [redacted]; 95% CI, [redacted]; P value = [redacted]).

The proportion of patients achieving DLQI response observed at week 52 was an exploratory end point in both studies. In SUNSHINE, 51.0% (49 of 96 patients; 95% CI, [redacted]) in the secukinumab group and 50.0% (25 of 50 patients; 95% CI, [redacted]) in the placebo to secukinumab group achieved DLQI response at week 52. In SUNRISE, 55.2% (64 of 116 patients; 95% CI, [redacted]) in the secukinumab group and 47.5% (29 of 61 patients; 95% CI, [redacted]) in the placebo to secukinumab group achieved DLQI response at week 52.

The change from baseline in DLQI total score observed at week 16 was an exploratory end point in both studies. In SUNSHINE, the mean difference in absolute change from baseline in DLQI total score at week 16 between secukinumab and placebo was [redacted] (95% CI, [redacted]). In SUNRISE, the mean difference in absolute change from baseline in DLQI total score at week 16 between secukinumab and placebo was [redacted] (95% CI, [redacted]).

The change from baseline in DLQI total score observed at week 52 was an exploratory end point in both studies. In SUNSHINE, the mean absolute change from baseline in DLQI total score at week 52 was [redacted] (95% CI, [redacted]) in the secukinumab group and [redacted] (95% CI, [redacted]) in the placebo to secukinumab group. In SUNRISE, the mean absolute change from baseline in DLQI total score at week 52 was [redacted] (95% CI, [redacted]) in the secukinumab group and [redacted] (95% CI, [redacted]) in the placebo to secukinumab group.

EQ-5D Health State Assessment (Visual Analogue Scale)

The change from baseline in EQ-5D health state assessment (VAS) observed at week 16 was an exploratory end point in both studies. In SUNSHINE, the mean difference in absolute change from baseline in EQ-5D VAS score at week 16 between secukinumab and placebo was [redacted] (95% CI, [redacted]). In SUNRISE, the mean difference in absolute change from baseline in EQ-5D VAS score at week 16 between secukinumab and placebo was [redacted] (95% CI, [redacted]).

The change from baseline in EQ-5D VAS score observed at week 52 was an exploratory end point in both studies. In SUNSHINE, the mean absolute change from baseline in EQ-5D VAS score at week 52 was [redacted] (95% CI, [redacted]) in the secukinumab group and [redacted] (95% CI, [redacted]) in the placebo to secukinumab group. In SUNRISE, the mean absolute change from baseline in EQ-5D VAS score at week 52 was [redacted] (95% CI, [redacted]) in the secukinumab group and [redacted] (95% CI, [redacted]) in the placebo to secukinumab group.

Harms Results

Adverse Events

In treatment period 1, the proportion of patients with any AE was generally similar between groups and across trials, ranging from 62.8% (113 of 180 patients) in the secukinumab group in SUNRISE to 67.4% (122 of 181 patients) in the secukinumab group in SUNSHINE. The most common AEs (frequency ≥ 5% in any group) reported in the secukinumab and placebo groups in SUNSHINE were nasopharyngitis (11.0% [20 of 181 patients] and 7.2% [13 of 180 patients], respectively), headache (9.4% [17 patients] and 7.8% [14 patients], respectively), hidradenitis (6.1% [11 patients] and 13.3% [24 patients], respectively), and diarrhea (2.8% [5 patients] and 5.0% [9 patients], respectively). The most common AEs (frequency ≥ 5% in any group) reported in the secukinumab and placebo groups in SUNRISE were headache (11.7% [21 of 180 patients] and 8.2% [15 of 183 patients], respectively), nasopharyngitis (7.2% [13 patients] and 8.7% [16 patients], respectively), hidradenitis (5.6% [10 patients] and 7.7% [14 patients], respectively), upper respiratory tract infection (5.0% [9 patients] and 3.8% [7 patients], respectively), and diarrhea (4.4% [8 patients] and 7.1% [13 patients], respectively).

Over the entire study period, the proportion of patients with any AE continued to be generally similar across trials, ranging from 80.1% (209 of 261 patients) in the any secukinumab group (comprising the secukinumab every 2 weeks and placebo to secukinumab every 2 weeks groups) in SUNRISE to 85.1% (154 of 181 patients) in the secukinumab group in SUNSHINE. The most common AEs (frequency ≥ 10% in any group) reported in both trials were headache, nasopharyngitis, and hidradenitis.

Serious Adverse Events

In treatment period 1, the proportion of patients with any serious AE (SAE) was generally similar between groups and across trials, ranging from 1.7% (3 of 181 patients) in the secukinumab group to 3.3% (6 of 180 patients) in the placebo group in SUNSHINE. The most common SAE (frequency ≥ 1% in any group in both trials) reported was hidradenitis in 0.6% (1 of 181 patients) in the secukinumab group and 1.1% (2 of 180 patients) in the placebo group in SUNSHINE, and 0.6% (1 of 180 patients) in the secukinumab group and no patients in the placebo group in SUNRISE.

Over the entire study period, the proportion of patients with any SAE was generally similar across trials, ranging from 6.8% (18 of 266 patients) in the any secukinumab group in SUNSHINE to 10.6% (19 of 180 patients) in the secukinumab group in SUNRISE. The most common SAE (frequency ≥ 1% in any group) in both trials reported was hidradenitis in 1.7% (3 of 181 patients) in the secukinumab group and 1.5% (4 of 266 patients) in the any secukinumab group in SUNSHINE, and 2.2% (4 of 180 patients) in the secukinumab group and 1.9% (5 of 261 patients) in the any secukinumab group in SUNRISE. In SUNRISE, each SAE, acute kidney injury and pyrexia, was reported in 1.1% (2 of 180 patients) in the secukinumab group and 0.8% (2 of 261 patients) in the any secukinumab group.

Withdrawals Due to Adverse Events

In treatment period 1, the proportion of patients who stopped treatment due to any AE was generally similar between groups and across trials, ranging from 0.6% (1 of 180 patients) in the placebo group to 2.8% (5 of

181 patients) in the secukinumab group in SUNSHINE. There was no AE that led to treatment discontinuation reported in 1% or more of patients in any group in both trials.

In the entire study period, the proportion of patients who stopped treatment due to any AE was generally similar across trials, ranging from 3.4% (9 of 261 patients) in the any secukinumab group in SUNRISE to 5.5% (10 of 181 patients) in the secukinumab group in SUNSHINE. Similar to treatment period 1, no AE that led to treatment discontinuation was reported in 1% or more of patients in any group in both trials.

Mortality

In treatment period 1 and the entire study period, no deaths were reported in both trials.

Notable Harms

In general, AEs of special interest (notable harms) were similar between secukinumab and placebo groups and across trials in treatment period 1. For infections and infestations (system organ class), the risk difference was [redacted] (95% CI, [redacted]) in SUNSHINE and [redacted] (95% CI, [redacted]) in SUNRISE. For *Candida* infections (high-level term), the risk difference was [redacted] (95% CI, [redacted]) in SUNSHINE and [redacted] (95% CI, [redacted]) in SUNRISE. For malignant and unspecified tumour (standardized MedDRA query), the risk difference was [redacted] (95% CI, [redacted]) in SUNSHINE and [redacted] (95% CI, [redacted]) in SUNRISE. For neoplasms benign, malignant, and unspecified (including cysts and polyps), the risk difference was [redacted] (95% CI, [redacted]) in SUNSHINE and [redacted] (95% CI, [redacted]) in SUNRISE. No patients were reported with squamous cell carcinoma of HS-affected area or inflammatory bowel disease in treatment period 1.

Over the entire study period, patients with any notable harms continued to be generally similar across trials. Patients reported with infections and infestations (system organ class) ranged from 51.7% (93 of 180 patients) in the secukinumab group in SUNRISE to 58.6% (106 of 181 patients) in the secukinumab group in SUNSHINE. Patients reported with *Candida* infections (high-level term) ranged from 5.4% (14 of 261 patients) in the any secukinumab group to 6.7% (12 of 180 patients) in the secukinumab group in SUNRISE. The proportion of patients reported with malignant and unspecified tumour (standardized MedDRA query) or neoplasm benign, malignant, and unspecified (including cysts and polyps) was less than 5% of patients in each group for both trials. Similar to treatment period 1, no patients were reported with squamous cell carcinoma of HS-affected area or inflammatory bowel disease in the entire study period.

Critical Appraisal

The SUNSHINE and SUNRISE trials were randomized, double-blind, and placebo controlled. Randomization was stratified by region, concomitant antibiotic use, and body weight. The proportions of patients with the relevant medical history and disease characteristics (effect modifiers) at baseline were generally well balanced between the secukinumab and placebo groups in both trials. There were slightly more patients with Hurley stage III disease in the secukinumab group than in the placebo group. The experts indicated that Hurley stage III disease is more severe and difficult to treat and, as such, potential bias against secukinumab may have been introduced in analyses that were unadjusted for this characteristic; however, the magnitude is unclear and could be small. Of note, there was no active or placebo comparator group for the assessments

made at week 52; therefore, the ability to draw definitive conclusions about the 52-week results is limited due to the potential for confounding.

A statistical testing strategy was implemented in both trials to control for type I error rate at the level of the individual studies and at the level of the pooled dataset of both studies. Exploratory end point analyses, including DLQI, EQ-5D health state assessment, and efficacy outcomes at week 52, were not adjusted for multiple comparisons and are therefore at an increased risk of false-positive results. Subgroup analyses were not adjusted for multiple testing; moreover, the ability to draw definitive conclusions about the results is limited due to the relatively small sample size of most subgroups.

There is evidence in the literature to support the measurement properties of HiSCR as a measure of response to treatment and the clinical importance of HiSCR50 in patients with HS. There is also evidence in the literature to support the validity of the patient-reported outcomes, NRS30, DLQI, and EQ health state assessment, as a measure of skin pain and HRQoL in patients with HS. Furthermore, there is evidence to support the clinical importance of NRS30 skin pain (albeit, only a 30% threshold was suggested and not in patients with HS) and DLQI response (estimated minimal important difference of 5 points in patients with HS) as defined in the trials. Note that a minimal important difference in EQ-5D health state assessment has not been estimated in patients with HS.

According to the experts, the inclusion and exclusion criteria used in the trials were considered standard in HS. Although some potential candidates for treatment (identified by the experts) were excluded from the trials, the experts indicated the results would likely be applicable in those patients (e.g., patients with fewer than 5 inflammatory lesions). The experts agreed that the criteria for use of rescue therapy and options for rescue therapy used in the trials generally reflected clinical practice. According to feedback from the experts, aside from minocycline that is used less commonly in practice in Canada, the concomitant use of antibiotics in the antibiotic strata and nonopioid analgesics in the trials were consistent with clinical practice and aligned with the guidelines. Although topical antibiotic therapy was prohibited in the trials, the experts anticipated that patients would continue topical antibiotic therapy while on treatment with secukinumab if they previously experienced partial response to the topical antibiotic therapy.

GRADE Summary of Findings and Certainty of the Evidence

Methods for Assessing the Certainty of the Evidence

For pivotal studies and RCTs identified in the sponsor's systematic review, GRADE was used to assess the certainty of the evidence for outcomes considered most relevant to inform the expert committee deliberations, and a final certainty rating was determined as outlined by the GRADE Working Group.

- **For RCTs:** Following the GRADE approach, evidence from RCTs started as high-certainty evidence and could be rated down for concerns related to study limitations (which refers to internal validity or risk of bias), inconsistency across studies, indirectness, imprecision of effects, and publication bias.
- **For single arms of trials (not presented in the Summary of Findings table):** Although GRADE guidance is not available for noncomparative studies, the Canada's Drug Agency review team assessed the noncomparative (52 weeks) outcomes for study limitations (which refers to internal

validity or risk of bias), inconsistency across studies, indirectness, imprecision of effects, and publication bias to present these important considerations. Because the lack of a comparator arm does not allow for a conclusion to be drawn on the effect of the intervention versus any comparator, the certainty of evidence for single-arm trials started at very low certainty with no opportunity for rating up.

When possible, certainty was rated in the context of the presence of an important (nontrivial) treatment effect; if this was not possible, certainty was rated in the context of the presence of any treatment effect (i.e., the clinical importance is unclear). In all cases, the target of the certainty of evidence assessment was based on the point estimate and where it was located relative to the threshold for a clinically important effect (when a threshold was available) or to the null.

The reference points for the certainty of evidence assessment for HiSCR50 response, AN count, flares, NRS30 skin pain, DLQI response, and EQ-5D health state assessment was set according to the presence or absence of an important effect based on thresholds informed by the clinical experts consulted for this review. The reference point for the certainty of evidence assessment for DLQI total score was set according to the presence or absence of an important effect based on the threshold identified in the literature. The reference points for the certainty of evidence assessment for notable harms was set according to the presence or absence of an important effect based on thresholds informed by the clinical experts.

For the GRADE assessments, findings from the SUNSHINE and SUNRISE studies were considered together and summarized narratively per outcome because these studies were similar in population, interventions, design, and outcome measures.

The selection of outcomes for GRADE assessment was based on the sponsor's Summary of Clinical Evidence, consultation with clinical experts, and input received from patient and clinician groups and public drug plans. The following list of outcomes was finalized in consultation with expert committee members:

- response to treatment and disease severity — HiSCR50 and AN count
- disease worsening — flares
- symptoms — NRS30 skin pain
- HRQoL — DLQI and EQ-5D health state assessment
- notable harms — infections and infestations; *Candida* infections; malignant or unspecified tumours; neoplasms benign, malignant, and unspecified (including cysts and polyps); squamous cell carcinoma of HS-affected area; and inflammatory bowel disease.

Results of GRADE Assessments

Secukinumab Versus Placebo

Table 3 presents the GRADE summary of findings for secukinumab 300 mg every 2 weeks versus placebo as well as secukinumab 300 mg every 4 weeks versus placebo. Note that data presented in the table on GRADE summary of findings is based on data provided by the sponsor following the submission update dated April 24, 2024.

Table 3: Summary of Findings for Secukinumab Versus Placebo for Patients With Hidradenitis Suppurativa

Outcome and follow-up	Dosage N (studies)	Relative and absolute effects	Certainty	What happens
Response to treatment and disease severity				
HiSCR50 response, proportion of patients with ≥ 50% decrease in AN count with no increase in the number of abscesses and/ or in the number of draining fistulas (96% CI for every 2 weeks dosing and 99% CI for every 4 weeks dosing) Follow-up: 16 weeks	**Secukinumab 300 mg every 2 weeks:** 724 (2 RCTs)	**SUNSHINE** **Odds ratio**: 1.75 • Secukinumab: • Placebo: • **Difference**: **SUNRISE** **Odds ratio**: 1.64 • Secukinumab: • Placebo: • **Difference**:	Moderate[a]	Secukinumab 300 mg every 2 weeks likely results in a clinically meaningful increase in the proportion of patients with HiSCR50 response compared with placebo.
	Secukinumab 300 mg every 4 weeks: 723 (2 RCTs)	**SUNSHINE** **Odds ratio**: 1.48 • Secukinumab| • Placebo: • **Difference**: **SUNRISE** **Odds ratio**: 1.90 • Secukinumab: • Placebo: • **Difference**:	Low[b]	Secukinumab 300 mg every 4 weeks may result in a clinically meaningful increase in the proportion of patients with HiSCR50 response compared with placebo.
AN count, LS mean percentage change from baseline (96% CI for every 2 weeks dosing and 99% CI for every 4 weeks dosing) Follow-up: 16 weeks	**Secukinumab 300 mg every 2 weeks:** 724 (2 RCTs)	**SUNSHINE** • Secukinumab: −46.8 (NR)	Moderate[c]	Secukinumab 300 mg every 2 weeks likely results in a clinically meaningful reduction in AN count compared with placebo.

Outcome and follow-up	Dosage N (studies)	Relative and absolute effects	Certainty	What happens
		• Placebo: −24.3 (NR) • **Difference**: [redacted]		
		SUNRISE • Secukinumab: −39.3 (NR) • Placebo: −22.4 (NR) • **Difference**: [redacted]		
	Secukinumab 300 mg every 4 weeks: 723 (2 RCTs)	**SUNSHINE** • Secukinumab: −42.4 • Placebo: −24.3 (NR) • **Difference**: [redacted]	Moderate[c]	Secukinumab 300 mg every 4 weeks likely results in a clinically meaningful reduction in AN count compared with placebo.
		SUNRISE • Secukinumab: −45.5 • Placebo: −22.4 (NR) • **Difference**: [redacted]		
Disease worsening				
Flares, proportion of patients with ≥ 25% increase in AN count with a minimum increase of 2 AN relative to baseline (96% CI for every 2 weeks dosing and 99% CI for every 4 weeks dosing) Follow-up: 16 weeks	**Secukinumab 300 mg every 2 weeks:** 724 (2 RCTs)	**SUNSHINE** **Odds ratio**: 0.42 [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]	Low[d]	Secukinumab 300 mg every 2 weeks may result in a clinically meaningful decrease in the proportion of patients experiencing flares compared with placebo.
		SUNRISE **Odds ratio**: 0.68 [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]		

Outcome and follow-up	Dosage N (studies)	Relative and absolute effects	Certainty	What happens
	Secukinumab 300 mg every 4 weeks: 723 (2 RCTs)	**SUNSHINE** **Odds ratio**: 0.71 [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]	Low[e]	Secukinumab 300 mg every 4 weeks may result in a clinically meaningful decrease in the proportion of patients experiencing flares compared with placebo.
		SUNRISE **Odds ratio**: 0.49 [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]		
Symptoms				
NRS30 skin pain (0 [no skin pain] to 10 [skin pain as bad as you can imagine]), proportion of patients with ≥ 30% reduction and ≥ 2-unit reduction in the patient's global assessment of skin pain (96% CI for every 2 weeks dosing and 99% CI for every 4 weeks dosing) Follow-up: 16 weeks	**Secukinumab 300 mg every 2 weeks:** 724 (2 RCTs)	**SUNSHINE and SUNRISE (pooled data)** **Odds ratio**: [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]	Moderate[f]	Secukinumab 300 mg every 2 weeks likely results in a clinically meaningful increase in the proportion of patients with NRS30 skin pain response compared with placebo.
	Secukinumab 300 mg every 4 weeks: 723 (2 RCTs)	**SUNSHINE and SUNRISE (pooled data)** **Odds ratio**: [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]	Moderate[f]	Secukinumab 300 mg every 4 weeks likely results in a clinically meaningful increase in the proportion of patients with NRS30 skin pain response compared with placebo.
Health-related quality of life				
DLQI response, proportion of patients with ≥ 5-point reduction in DLQI total score	**Secukinumab 300 mg every 2 weeks:** 551 (2 RCTs)	**SUNSHINE** **Odds ratio**: [redacted] • Secukinumab: [redacted]	Moderate[g]	Secukinumab 300 mg every 2 weeks likely results in a clinically meaningful increase in

Outcome and follow-up	Dosage N (studies)	Relative and absolute effects	Certainty	What happens
(95% CI) Follow-up: 16 weeks		• Placebo: [redacted] • **Difference**: [redacted]		the proportion of patients with DLQI response compared with placebo.
		SUNRISE **Odds ratio**: [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]		
	Secukinumab 300 mg every 4 weeks: 607 (2 RCTs)	**SUNSHINE** **Odds ratio**: [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]	High[h]	Secukinumab 300 mg every 4 weeks results in a clinically meaningful increase in the proportion of patients with DLQI response compared with placebo.
		SUNRISE **Odds ratio**: [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference:** [redacted]		
DLQI total score (0 [no effect at all on patient's life] to 30 [extremely large effect on patient's life]), mean absolute change from baseline (95% CI) Follow-up: 16 weeks	**Secukinumab 300 mg every 2 weeks:** 590 (2 RCTs)	**SUNSHINE** • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]	High[i]	Secukinumab 300 mg every 2 weeks results in little to no clinically meaningful difference in the DLQI total score compared with placebo.
		SUNRISE • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]		

Outcome and follow-up	Dosage N (studies)	Relative and absolute effects	Certainty	What happens
	Secukinumab 300 mg every 4 weeks: 588 (2 RCTs)	**SUNSHINE** • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted] **SUNRISE** • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]	High[i]	Secukinumab 300 mg every 4 weeks results in little to no clinically meaningful difference in the DLQI total score compared with placebo.
EQ-5D health state assessment (VAS score) (0 [worst imaginable health state] to 100 [best imaginable health state]), mean absolute change from baseline (95% CI) Follow-up: 16 weeks	**Secukinumab 300 mg every 2 weeks:** 585 (2 RCTs)	**SUNSHINE** • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted] **SUNRISE** • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]	Low[j]	Secukinumab 300 mg every 2 weeks may result in a clinically meaningful improvement in the EQ-5D health state assessment when compared with placebo.
	Secukinumab 300 mg every 4 weeks: 586 (2 RCTs)	**SUNSHINE** • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted] **SUNRISE** • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]	Moderate[k]	Secukinumab 300 mg every 4 weeks likely results in little to no clinically meaningful difference in the EQ-5D health state assessment when compared with placebo.

Outcome and follow-up	Dosage N (studies)	Relative and absolute effects	Certainty	What happens
Notable harms				
Infections and infestations (system organ class), n (95% CI) Follow-up: 16 weeks	**Secukinumab 300 mg every 2 weeks:** 724 (2 RCTs)	**SUNSHINE** **Relative risk**: • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted] **SUNRISE** **Relative risk**: • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]	Low[l]	Secukinumab 300 mg every 2 weeks may result in little to no difference in infections and infestations compared with placebo.
	Secukinumab 300 mg every 4 weeks: 723 (2 RCTs)	**SUNSHINE** **Relative risk**: • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted] **SUNRISE** **Relative risk**: • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]	Low[l]	Secukinumab 300 mg every 4 weeks may result in little to no difference in infections and infestations compared with placebo.
***Candida* infections (HLT)**, n (95% CI) Follow-up: 16 weeks	**Secukinumab 300 mg every 2 weeks:** 724 (2 RCTs)	**SUNSHINE** **Relative risk**: • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]	Low[m]	Secukinumab 300 mg every 2 weeks may result in little to no difference in *Candida* infections compared with placebo.

Outcome and follow-up	Dosage N (studies)	Relative and absolute effects	Certainty	What happens
		SUNRISE **Relative risk**: [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]		
	Secukinumab 300 mg every 4 weeks: 723 (2 RCTs)	**SUNSHINE** **Relative risk**: [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]	Low[m]	Secukinumab 300 mg every 4 weeks may result in little to no difference in *Candida* infections compared with placebo.
		SUNRISE **Relative risk**: [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]		
Malignant or unspecified tumours (SMQ), n (95% CI) Follow-up: 16 weeks	**Secukinumab 300 mg every 2 weeks:** 724 (2 RCTs)	**SUNSHINE** **Relative risk**: [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]	Very low[n]	The evidence is very uncertain about the effect of secukinumab 300 mg every 2 weeks on malignant or unspecified tumours compared with placebo.
		SUNRISE **Relative risk**: [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]		

Outcome and follow-up	Dosage N (studies)	Relative and absolute effects	Certainty	What happens
	Secukinumab 300 mg every 4 weeks: 723 (2 RCTs)	**SUNSHINE** **Relative risk**: [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted] **SUNRISE** **Relative risk**: [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]	Very low[o]	The evidence is very uncertain about the effect of secukinumab 300 mg every 4 weeks on malignant or unspecified tumours compared with placebo.
Neoplasms benign, malignant, and unspecified (including cysts and polyps) (system organ class), n (95% CI) Follow-up: 16 weeks	**Secukinumab 300 mg every 2 weeks:** 724 (2 RCTs)	**SUNSHINE** **Relative risk**: [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted] **SUNRISE** **Relative risk**: [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]	Very low[n]	The evidence is very uncertain about the effect of secukinumab 300 mg every 2 weeks on neoplasms benign, malignant, and unspecified (including cysts and polyps) compared with placebo.
	Secukinumab 300 mg every 4 weeks: 723 (2 RCTs)	**SUNSHINE** **Relative risk**: [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]	Very low[o]	The evidence is very uncertain about the effect of secukinumab 300 mg every 4 weeks on neoplasms benign, malignant, and unspecified (including cysts and polyps) compared with placebo.

Outcome and follow-up	Dosage N (studies)	Relative and absolute effects	Certainty	What happens
		SUNRISE **Relative risk**: [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]		
Squamous cell carcinoma of HS-affected area (preferred term), n (95% CI) Follow-up: 16 weeks	**Secukinumab 300 mg every 2 weeks:** 724 (2 RCTs)	**SUNSHINE** **Relative risk**: [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]	Very low[n]	The evidence is very uncertain about the effect of secukinumab 300 mg every 2 weeks on squamous cell carcinoma of HS-affected area compared with placebo.
		SUNRISE **Relative risk**: [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]		
	Secukinumab 300 mg every 4 weeks: 723 (2 RCTs)	**SUNSHINE** **Relative risk**: [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]	Very low[n]	The evidence is very uncertain about the effect of secukinumab 300 mg every 4 on squamous cell carcinoma of HS-affected area compared with placebo.
		SUNRISE **Relative risk**: [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference**: [redacted]		

Outcome and follow-up	Dosage N (studies)	Relative and absolute effects	Certainty	What happens
Inflammatory bowel disease (NMQ), n (95% CI) Follow-up: 16 weeks	**Secukinumab 300 mg every 2 weeks:** 724 (2 RCTs)	**SUNSHINE** **Relative risk:** [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference:** [redacted] **SUNRISE** **Relative risk:** [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference:** [redacted]	Very low[n]	The evidence is very uncertain about the effect of secukinumab 300 mg every 2 weeks on inflammatory bowel disease compared with placebo.
	Secukinumab 300 mg every 4 weeks: 723 (2 RCTs)	**SUNSHINE** **Relative risk:** [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference:** [redacted] **SUNRISE** **Relative risk:** [redacted] • Secukinumab: [redacted] • Placebo: [redacted] • **Difference:** [redacted]	Very low[n]	The evidence is very uncertain about the effect of secukinumab 300 mg every 4 weeks on inflammatory bowel disease compared with placebo.

AN = abscesses and inflammatory nodules; CI = confidence interval; DLQI = Dermatology Life Quality Index; HiSCR = Hidradenitis Suppurativa Clinical Response; HRQoL = health-related quality of life; HS = hidradenitis suppurativa; LS = least squares; NA = not applicable; NMQ = standardized MedDRA query, narrow; NR = not reported; NRS = numeric rating scale; OR = odds ratio; RCT = randomized controlled trial; RR = risk ratio; SMQ = standardized MedDRA query.

Notes: Data presented in this table are based on data provided by the sponsor following the submission update dated April 24, 2024 (details in Appendix 2).

Study limitations (which refers to internal validity or risk of bias), inconsistency across studies, indirectness, imprecision of effects, and publication bias were considered when assessing the certainty of the evidence. All serious concerns in these domains that led to the rating down of the level of certainty are documented in the table footnotes.

Applicable to all outcomes of importance in the Table 3 — Although some potential candidates for treatment with secukinumab were excluded from the SUNNY trials, in consultation with the 2 clinical experts consulted by Canada's Drug Agency for the purpose of this review, it was concluded that the results are likely generalizable to those patients and as such, did not rate down for indirectness.

Applicable to the primary and secondary end points in the SUNNY trials — The analysis of the secondary end point, flares at week 16, on the secukinumab every 2 weeks dosing group failed to meet statistical significance in the statistical hierarchy in the SUNRISE trial. The analysis of the primary end point, HiSCR50 response at week 16, on the secukinumab every 4 weeks dosing group failed to meet statistical significance in the statistical hierarchy in the SUNSHINE trial; as such, all subsequent tests of the secondary end points were considered not statistically significant. These can be considered as supportive evidence only.

Applicable to the patient-reported outcomes (NRS30 skin pain and HRQoL measures) — Analysis of these outcomes was not adjusted for multiplicity; as such, results are considered supportive evidence. Although the outcome measures were subjective, in consideration of the low rates of discontinuation and the double-blind trial design, the risk of bias was not rated down.

Applicable to outcomes for which the analysis did not adjust for Hurley stage (DLQI total score and EQ-5D health state assessment [VAS score]) — Because of the small baseline imbalance in Hurley stage III (effect modifier identified by the clinical experts) between groups, the risk of bias was not rated down.

[a]Rated down 1 level for serious imprecision; data from both trials show secukinumab may provide benefit or little to no benefit based on a conservative threshold of 100 more per 1,000 patients (50 per 1,000 to 100 per 1,000 was suggested by clinical experts).

[b]Rated down 1 level for serious inconsistency; although the 99% confidence intervals are largely overlapping, there is large variability in the point estimates; SUNSHINE results suggest little to no important difference whereas SUNRISE suggest a clinically important benefit. Rated down 1 level for serious imprecision; data from both trials show secukinumab may provide benefit or little to no benefit based on a conservative threshold of 100 more per 1,000 patients (50 per 1,000 to 100 per 1,000 was suggested by clinical experts). Although the boundaries of the 99% confidence intervals least favourable to the intervention include the possibility of harm, it was concluded that it did not considerably cross the null (i.e., not a substantial harm); therefore, imprecision was rated down by 1 level only.

[c]Rated down 1 level for serious imprecision; data from both trials show secukinumab may provide benefit or little to no benefit based on a conservative threshold of 10% difference (5% to 10% difference was suggested by clinical experts).

[d]Rated down 1 level for serious inconsistency; although the 96% confidence intervals are largely overlapping, there is large variability in the point estimates; SUNSHINE results suggest a clinically important benefit whereas SUNRISE suggest little to no difference. Rated down 1 level for serious imprecision. Data from both trials show secukinumab may provide benefit or little to no benefit based on a conservative threshold of 100 fewer per 1,000 patients (50 per 1,000 to 100 per 1,000 was suggested by clinical experts).

[e]Did not rate down for inconsistency; although there is some variability in the point estimates, the 99% confidence intervals are largely overlapping and the following concerns in imprecision that led to the rating down of the level of certainty in the evidence was felt to sufficiently reflect the level of certainty in the evidence. Rated down 2 levels for very serious imprecision based on a conservative threshold of 100 fewer per 1,000 patients (50 per 1,000 to 100 per 1,000 was suggested by clinical experts), data from the trials show secukinumab may provide benefit or little to no benefit and includes the possibility of harm. The boundary of the 99% confidence interval least favourable to the intervention includes the possibility of harm and it was concluded that it did considerably cross the null (i.e., a substantial harm); therefore, imprecision was rated down by 2 levels.

[f]Rated down 1 level for serious imprecision. Data from the pooled results show secukinumab may provide benefit or little to no benefit based on a conservative threshold of 100 more per 1,000 patients (50 per 1,000 to 100 per 1,000 was suggested by clinical experts).

[g]Rated down 1 level for serious imprecision; data from the trials show secukinumab may provide benefit or little to no benefit based on a conservative threshold of 50 more per 1,000 patients (as suggested by clinical experts).

[h]Data from the trials show secukinumab may provide benefit based on a conservative threshold of 50 more per 1,000 patients (as suggested by clinical experts).

[i]A treatment difference of at least 5 points is considered clinically meaningful (based on literature findings and aligned with clinical expert input); data from both trials show secukinumab may provide a trivial (or no) effect.

[j]Rated down 1 level for serious inconsistency. Minimal overlap of the 95% confidence intervals was considered. Rated down 1 level for serious imprecision. Based on a conservative threshold of 5 points (as suggested by clinical experts), data from both trials show secukinumab may provide benefit or little to no benefit.

[k]Rated down 1 level for serious imprecision. Based on a conservative threshold of 5 points (as suggested by clinical experts), data from both trials show secukinumab may provide benefit or little to no benefit.

[l]In absence of a threshold for clinical importance, the null was used. Rated down 2 levels for very serious imprecision. Based on the null, data from both trials show secukinumab may provide benefit and harm.

[m]In absence of a threshold for clinical importance, the null was used. Rated down 2 levels for very serious imprecision. There were very few events; ratio of the upper to the lower bound of the 95% CIs associated with the relative risk from both trials are greater than 3.0; therefore, the number of events is likely far from meeting the optimal information size.

[n]In absence of a threshold for clinical importance, the null was used. Rated down 1 level for serious indirectness. Follow-up was not sufficiently long to observe events. Rated down 2 levels for very serious imprecision. Little to no events observed due to insufficient follow-up.

[o]In absence of a threshold for clinical importance, the null was used. Rated down 1 level for serious indirectness. Follow-up was not sufficiently long to observe events. Rated down 2 levels for very serious imprecision. Little to no events observed due to insufficient follow-up. The ratio of the upper to the lower bound of the 95% confidence interval associated with the relative risk from the trial is greater than 3.0; therefore, the number of events is likely far from meeting the optimal information size.

Source: SUNSHINE Clinical Study Report, SUNRISE Clinical Study Report, and sponsor response to June 19, 2023, July 5, 2023, and May 22, 2024, Canada's Drug Agency requests for additional information regarding the Canada's Drug Agency secukinumab review.

Long-Term Extension Study

The extension study, NCT04179175, assessed the effects of noninterrupted versus interrupted and long-term treatment of 2 dosage regimens of secukinumab in patients with HS. The study is ongoing, and no results were available at the time of this report.

Indirect Comparisons

Description of Studies

The sponsor submitted an NMA that assessed the short-term efficacy (12 to 16 weeks) of secukinumab versus adalimumab for the treatment of adults with moderate to severe HS. The base case Bayesian NMA was informed by 4 RCTs and limited to patients who were biologic naive (N = 1,462).

Efficacy Results

For secukinumab 300 mg every 2 weeks versus adalimumab 40 mg weekly, the results of the NMA were inconclusive, showing 95% CrIs that were wide and included the null for HiSCR50, skin pain NRS30 response, the proportion of patients with flares or who achieved a DLQI score of 0 or 1. The change from baseline in AN count and DLQI total score, and the multinomial model that examined HiSCR25, HiSCR50, and HiSCR75 response thresholds, also showed 95% CrIs that included the null. The sensitivity analyses that included patients with and without biologic experience showed similar findings.

Harms Results

No safety end points were analyzed in the NMA.

Critical Appraisal

No major issues were identified by Canada's Drug Agency on the methods used to conduct the systematic review or the statistical methods used in the NMA. The evidence networks were sparse, and the analyses were limited to short-term efficacy outcomes at the end of the induction period. There was heterogeneity present for some patient characteristics (e.g., the distribution of males, people who smoke, and Hurley stage), as well as study characteristics (treatment duration, definition of NRS30 response, and imputation methods for missing study data). Most effect estimates lacked precision, showing 95% CrIs that included the null. Thus, it is unclear if secukinumab is superior, inferior, or had comparable efficacy to adalimumab 40 mg once daily. The comparative safety is unknown because no safety end points were analyzed in the NMA.

Studies Addressing Gaps in the Evidence From the Systematic Review

No additional studies were submitted by the sponsor for this review.

Economic Evidence

Submission Update Provided by the Sponsor (April 24, 2024)

Pharmacoeconomic Review on the Monthly Maintenance Dosage of Secukinumab

Economic Impact

The original economic review compared secukinumab dosage of 300 mg every 2 weeks to standard of care and adalimumab. At the committee meeting, it was noted that the comparison to adalimumab was more relevant, and this informed the pricing condition. Because no robust evidence was provided that indicated secukinumab produced better health outcomes than adalimumab, the pricing condition was "Secukinumab should be negotiated so that it does not exceed the drug program cost of treatment with the least costly form of adalimumab reimbursed for the treatment of HS." This statement is not unique to 2-week dosing. The same pricing condition would apply to the new draft monograph, which also allows for 4-week dosing.

Budget Impact

The budget impact analysis (BIA) was conducted assuming a secukinumab dosage of 300 mg every 2 weeks. If monthly maintenance dosing was implemented, this would reduce drug costs associated with secukinumab and therefore lower the BIA. However, it is unclear how many patients would be placed on this dosing schedule and how many would remain on this schedule. It is also uncertain if a less frequent dosing schedule would increase the size of the market of patients willing to try a biologic; if so, this would increase the budget impact. Overall, there was considerable uncertainty around the size of the original BIA, with the Canada's Drug Agency estimates being substantially lower than the sponsor's submitted BIA (Canada's Drug Agency 3-year BIA: $9,547,349; sponsor-submitted 3-year BIA: $76,542,993). As such, a reimbursement condition was added to the recommendation text stating that uncertainty associated with the BIA must be addressed (refer to reimbursement condition 10). The presence of a different dosing schedule would further increase the uncertainty associated with the BIA.

Summary of Pharmacoeconomic Evidence Before Submission Update

The sponsor's application was filed on a pre-NOC basis and the pharmacoeconomic submission is reflective of the proposed dosage regimen that was initially submitted to Health Canada and Canada's Drug Agency. The sponsor's submission included a recommended dosage for secukinumab of 300 mg per week for 5 weeks followed by 300 mg every 2 weeks. The final product monograph that was approved by Health Canada recommended that patients start with monthly maintenance dosing (every 4 weeks) and, based on clinical response, the maintenance dosage can be increased to 300 mg every 2 weeks. The monthly maintenance dosing and related evidence was not included in the original economic report. In addition, the sponsor notified Canada's Drug Agency that the submitted price had been updated during the review. The appraisal by Canada's Drug Agency was undertaken based on the information included in the initial application package and was not revised after the NOC or revised price was received.

Cost and Cost-Effectiveness

Table 4: Summary of Economic Information

Component	Description
Type of economic evaluation	Cost-utility analysis Markov model
Target population	Adults with moderate to severe HS that has not responded to conventional therapy
Treatment	Secukinumab
Dosage regimen	300 mg every week for 5 weeks and 300 mg every 2 weeks thereafter
Submitted price	Secukinumab, 75 mg/0.5 mL: $772.50 per prefilled syringe Secukinumab, 150 mg/mL, $882.59 per prefilled glass syringe or pen ($1,765.18 per 2-unit pack)
Treatment cost	At the recommended dosage, the annual cost of secukinumab is $50,465 for the first year and $46,052 for the second year onward
Comparators	Adalimumab SOC (defined as a basket of antibiotics, retinoids, and immunosuppressants)
Perspective	Canadian publicly funded health care payer
Outcomes	Life-years, QALYs
Time horizon	Lifetime (44 years)
Key data sources	SUNRISE and SUNSHINE trials (for secukinumab and SOC) PIONEER trials (for adalimumab, with efficacy lowered and discontinuation increased to "adjust" for the use of biosimilars)
Submitted results	Sequential results: ICER (secukinumab versus adalimumab) = $254,840 per QALY gained (incremental costs: $116,119; incremental QALYs: 0.46)
Key limitations	• Comparative clinical efficacy of secukinumab versus adalimumab is uncertain because there are no direct head-to-head studies comparing them. Although the sponsor conducted an indirect treatment comparison, this evidence was not used in the economic evaluation; instead, the sponsor relied on a naive comparison of adalimumab versus secukinumab. This was inappropriate because it does not account for potential confounding, which was evident by differing placebo response rates across the trials. The sponsor also assumed biosimilar adalimumab was worse than originator adalimumab; the experts consulted by Canada's Drug Agency noted evidence to support this assumption was too uncertain to draw strong conclusions. • The sponsor assumed the efficacy of secukinumab did not wane over time based on a study examining discontinuation rates of biologics in patients with ankylosing spondylitis. However, data on patients with HS receiving adalimumab show potential waning of efficacy over time, at least between 12 and 24 months after treatment initiation. • Cost-effectiveness by biologic exposure is uncertain. Secukinumab is indicated for use in both patients who have yet to receive a biologic and those who are biologic exposed; however, the model does not allow for the examination of secukinumab in different lines of treatment. • The model was not programmed to explore the impact of relevant scenarios that may occur after treatment discontinuation. For example, once a patient fails secukinumab, they may be

Component	Description
	switched to adalimumab given there are no approved alternatives. Likewise, patients whose HS does not respond to adalimumab may have their dose titrated up to 80 mg weekly.
CDA-AMC reanalysis results	• Canada's Drug Agency incorporated the following changes to address the identified limitations for the base case: assuming equivalent response rates between adalimumab and secukinumab, increasing rates of treatment discontinuation after 1 year to account for potential treatment waning (4.61% per 4-week cycle). • Based on a sequential analysis, secukinumab is compared to adalimumab on the cost-effectiveness frontier. A pairwise comparison of secukinumab versus SOC is also presented because SOC is the only relevant comparator for patients whose HS has not responded to adalimumab. • ICER (secukinumab versus adalimumab) = $2,884,183 per QALY gained (incremental costs: $25,558; incremental QALYs: < 0.01) • ICER (secukinumab versus SOC) = $321,446 per QALY gained (incremental costs: $47,026; incremental QALYs: 0.15)

HiSCR = Hidradenitis Suppurativa Clinical Response; HS = hidradenitis suppurativa; ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life-year; SOC = standard of care.

Budget Impact

Based on the Canada's Drug Agency reanalysis, the estimated budget impact from the reimbursement of secukinumab would be $1,717,030 in year 1, $3,091,377 in year 2, and $4,738,942 in year 3, for a 3-year total of $9,547,349. This was considerably lower than the sponsor's submitted estimate (3-year total budget impact of $76,542,993) due to a substantial decrease in the size of the population currently receiving a biologic for HS as well as a smaller expectation in the proportion of patients switching from adalimumab to secukinumab.

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, Mr. Morris Joseph, 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.

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Conflicts of interest: None

Subpanel meeting date: July 24, 2024

Regrets: None

Conflicts of interest: None

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