



# Common Drug Review

## *Pharmacoeconomic Review Report*

August 2016

<b>Drug</b>	Secukinumab (Cosentyx)
<b>Indication</b>	For the treatment of adult patients with active psoriatic arthritis when the response to previous disease-modifying anti-rheumatic drug (DMARD) therapy has been inadequate. COSENTYX can be used alone or in combination with methotrexate.
<b>Reimbursement request</b>	[REDACTED]
<b>Dosage form(s)</b>	Pre-filled syringe or pen for subcutaneous injection, 150 mg/ml
<b>NOC date</b>	April 20, 2016
<b>Manufacturer</b>	Novartis Pharmaceuticals Canada Inc.

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## **ABBREVIATIONS**

<b>ACR</b>	American College of Rheumatology
<b>AS</b>	ankylosing spondylitis
<b>CDR</b>	CADTH Common Drug Review
<b>NMA</b>	network meta-analysis
<b>PASI</b>	Psoriasis Area Severity Index
<b>PsA</b>	psoriatic arthritis
<b>PsARC</b>	psoriatic arthritis response criteria
<b>SEB</b>	subsequent entry biologic
<b>TNF</b>	tumour necrosis factor

## SUMMARY

### Background

Secukinumab (Cosentyx) is an interleukin-17A inhibitor indicated for the treatment of active psoriatic arthritis (PsA) in adult patients.<sup>1</sup> The Health Canada recommended dose is 150 mg or 300 mg by subcutaneous injection at weeks 0, 1, 2 and 3, followed by once a month starting at week 4. The 300 mg dose is recommended for patients who are inadequate responders to anti-TNF alpha inhibitor or patients with concomitant moderate to severe plaque psoriasis; it is given as two subcutaneous injections of 150 mg.<sup>1</sup> At the manufacturer-submitted confidential price of [REDACTED] per 150 mg/mL pre-filled syringe or pen, or [REDACTED] per 2 × 150 mg/mL pre-filled syringe or pen (300 mg dose),<sup>2</sup> the cost of treatment is [REDACTED] per year in the first year and [REDACTED] per year in subsequent years for patients on the 150 mg dose; and [REDACTED] per year in the first year and [REDACTED] per year in subsequent years for patients on the 300 mg dose.

The manufacturer is requesting secukinumab be [REDACTED]

Secukinumab (150 mg) is also indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.<sup>1</sup> It was previously reviewed by the CADTH Canadian Drug Expert Committee for this indication and received a list recommendation with clinical criteria and conditions in October 2015;<sup>3</sup> the condition was that the drug plan cost of secukinumab should not exceed the cost of the least costly biologic reimbursed for the treatment of moderate to severe plaque psoriasis.<sup>3</sup> Additionally, secukinumab is concurrently being reviewed through the CADTH Common Drug Review (CDR) for the treatment of adult patients with active ankylosing spondylitis (AS).

### Summary of the Economic Analysis Submitted by the Manufacturer

The manufacturer submitted a cost comparison of secukinumab 150 mg and 300 mg to anti-TNF biologic drugs currently indicated and reimbursed for active PsA in Canada. These included the following: adalimumab 40 mg every other week; certolizumab pegol 400 mg at weeks 0, 2, and 4, followed by 200 mg every 2 weeks; etanercept 50 mg per week; golimumab 50 mg once a month; infliximab (Remicade) 5 mg/kg at weeks 0, 2, and 6, and then every eight weeks; and ustekinumab 45 mg at weeks 0 and 4, and then every 12 weeks thereafter.<sup>2</sup> As part of a sensitivity analysis, the manufacturer also included the phosphodiesterase-4 inhibitor apremilast titrated to 30 mg twice daily and subsequent entry biologic (SEB) infliximab (Inflectra) 5 mg/kg at weeks 0, 2, and 6, and then every eight weeks thereafter.<sup>2</sup> The analysis was conducted from the perspective of the publicly funded health care system, based on a time horizon of three years.<sup>2</sup> The manufacturer assumed that all other aspects of patient management were equivalent across treatments; therefore, only drug costs were considered. Drug costs were obtained from the Ontario Drug Benefit formulary or the Régie de l'assurance maladie du Québec.<sup>4,5</sup> All prices excluded markup and dispensing fees.

The assumption of similar efficacy and safety of secukinumab and other biologics was based on a manufacturer-submitted network meta-analysis (NMA), as no head-to-head comparative trials were available. The NMA assessed the following efficacy end points at weeks 12 to 16: the American College of Rheumatology (ACR) score, Psoriasis Area Severity Index (PASI), and the PsA response criteria (PsARC).<sup>2</sup> The analysis was conducted for two subpopulations: biologics-naïve and biologics-experienced

patients. In the biologics-naïve subpopulation, the results of the NMA suggested that secukinumab 150 mg was non-inferior to all comparator treatments based on the following end points: [REDACTED], PASI 75 (reduction from baseline of 75% or more), PASI 90 (reduction from baseline of 90% or more), ACR20 (improvement of 20% from baseline), [REDACTED]. In the biologics-experienced subpopulation, the NMA results suggested that secukinumab 300 mg was [REDACTED] to other comparators based on the following end points: ACR20 [REDACTED].<sup>2</sup> The NMA did not assess comparative safety.

### Key Limitations

- **Uncertain effectiveness compared with other biologics:** No head-to-head clinical evidence was provided to show that efficacy is similar among secukinumab, anti-TNF alpha biologic drugs, and phosphodiesterase-4 inhibitors. As noted in Appendix 7 of the CDR clinical report, heterogeneity in patient populations and methodological limitations of the NMA contribute to uncertainty regarding the conclusion that there are no significant differences in efficacy among secukinumab, anti-TNF alpha biologic drugs, and the phosphodiesterase-4 inhibitors.
- **Dosing of secukinumab:** The manufacturer assumed 15 administrations of secukinumab in the first year, leading to a conservative estimate of the treatment cost of secukinumab. To align with the dosing recommendation in the Health Canada product monograph,<sup>1</sup> the CDR analysis assumed 16 administrations of secukinumab in the first year and 12 to 13 administrations in subsequent years.
- **Exclusion of relevant comparator in the primary analysis:** The manufacturer did not include SEB infliximab (Inflectra) in the primary analysis, although it was included in a scenario analysis. SEB infliximab is a relevant comparator for the base-case analysis, as it is reimbursed by some public drug plans in Canada and may represent the least costly alternative biologic.
- **Uncertainty regarding long-term efficacy and discontinuation rates over time:** In the manufacturer's analysis, incremental costs were reported over a three-year time horizon; however, long-term discontinuation rates with different biologics are uncertain. Therefore, CDR presented drug costs separately for the first year (to reflect the different loading doses across biologics) and subsequent years.

### Issues for Consideration

- Etanercept SEB is currently being reviewed through CDR for AS and as a pre-Notice of Compliance (NOC) submission.<sup>6</sup> The introduction of this comparator may affect the cost savings associated with secukinumab predicted by the manufacturer's analysis.
- Secukinumab is concurrently being reviewed through CDR for the treatment of adult patients with active AS.
- In October 2015, the Canadian Drug Expert Committee recommended that secukinumab be listed under the condition that the cost not exceed the cost of the least costly biologic reimbursed for the treatment of moderate to severe plaque psoriasis.<sup>3</sup> Therefore, the actual cost to drug plans of secukinumab may be lower than the price submitted by the manufacturer in the current submission.

### Results/Conclusions

At the manufacturer-submitted confidential price of [REDACTED] per 150 mg/mL pre-filled syringe or pen, the annual cost of secukinumab (first year: [REDACTED] subsequent years: [REDACTED]) is less than that of anti-TNF alpha biologic drugs and apremilast, based on publicly available prices (see Appendix 1: Cost

Comparison). At the manufacturer-submitted price of [REDACTED], the annual cost secukinumab 300 mg dose (first year: [REDACTED], subsequent years: [REDACTED])<sup>2</sup> is less than that of infliximab (Remicade).

Secukinumab 300 mg is more expensive in the first year than adalimumab, etanercept, and ustekinumab, but less expensive in subsequent years. Secukinumab 300 mg is more expensive in the first year than golimumab and may be more or less expensive in subsequent years, depending on the number of administrations (i.e., 12 versus 13) of secukinumab. Additionally, secukinumab 300 mg is more expensive than SEB infliximab, certolizumab pegol, and apremilast in both the first and subsequent years. However, the cost impact of secukinumab may differ, should the actual prices paid by CDR-participating drug plans for anti-TNF alpha biologic drugs and apremilast be lower.

The manufacturer's cost analysis was based on the assumption of similar efficacy between secukinumab, anti-TNF alpha biologic drugs, and apremilast. An NMA was used to support this assumption; however, there was uncertainty regarding its conclusions because of methodological limitations and heterogeneity across included trials.

## APPENDIX 1: COST COMPARISON

The comparators presented in the subsequent table have been deemed to be appropriate by the clinical expert consulted by CDR. Existing Product Listing Agreements are not reflected in the table; as a result, the table may not represent the actual costs to public drug plans.

**TABLE 1: COST COMPARISON TABLE FOR PATIENTS WITH PSORIATIC ARTHRITIS**

Drug/ Comparator	Strength	Dosage Form	Price (\$)	Recommended Dose	Annual Drug Cost (\$)
Secukinumab (Cosentyx)	150 mg/mL	Pre-filled syringe or pen	██████ <sup>a</sup>	150 mg SC injection at weeks 0, 1, 2, 3, then monthly starting at week 4	First year: ██████ <sup>d</sup> Subsequent years: ██████ <sup>e</sup>
		2 × pre-filled syringes or pens	██████ <sup>b</sup>	or 300 mg SC injection at weeks 0, 1, 2, 3, then monthly starting at week 4 <sup>c</sup>	First year: ██████ <sup>d</sup> Subsequent years: ██████ <sup>e</sup>
<b>Biologic DMARDS</b>					
Adalimumab (Humira)	40 mg/0.8 mL	Pre-filled syringe or pen	769.9700	40 mg every other week SC injection	\$20,019
Certolizumab pegol (Cimzia)	200 mg/mL	Single-use pre- filled glass syringe	664.5100	400 mg SC injection at weeks 0, 2, and 4, then 200 mg every 2 weeks or 400 mg every 4 weeks	First year: \$19,271 <sup>f</sup> Subsequent years: \$17,277
Etanercept (Enbrel)	25 mg/vial	Vial	202.9300	50 mg weekly (one 50 mg injection or two 25 mg injections on the same day or 3 or 4 days apart)	\$21,105
	50 mg/mL	Pre-filled syringe or auto-injector	405.9850		\$21,111
Golimumab SC (Simponi)	50 mg/0.5 mL	Pre-filled syringe or auto-injector	1,555.17	50 mg SC injection once a month (on the same date)	\$18,662
Infliximab <sup>g</sup> (Remicade)	100 mg/vial	Vial	962.6800 <sup>h</sup>	5 mg/kg <sup>i</sup> initial dose followed with additional similar doses at 2 and 6 weeks after the first infusion, then every 8 weeks	5 mg/kg at weeks 0, 2, and 6, then every 8 weeks <sup>j</sup> First year: \$33,543 Subsequent years: \$27,254
SEB Infliximab <sup>g</sup> (Inflectra)	100 mg/vial	Vial	525.0000	5 mg/kg <sup>i</sup> initial dose followed with additional similar doses at 2 and 6 weeks after the first infusion, then every 8 weeks	5 mg/kg at weeks 0, 2 and 6 then every 8 weeks <sup>j</sup> First year: \$18,293 Subsequent years: \$14,863
Ustekinumab (Stelera)	45 mg/0.5 mL 90 mg/mL	Pre-filled syringe or vial	4,593.1400 (for both strengths)	Patients < 100 kg: 45 mg at weeks 0 and 4, then every 12 weeks	First year: \$22,966 <sup>k</sup> Subsequent years: \$20,669 <sup>l</sup>



**CDR PHARMACOECONOMIC REVIEW REPORT FOR COSENTYX**

Drug/ Comparator	Strength	Dosage Form	Price (\$)	Recommended Dose	Annual Drug Cost (\$)
				Patients > 100 kg: 90 mg at weeks 0 and 4, then every 12 weeks	
<b>Phosphodiesterase-4 inhibitors</b>					
Apremilast (Otezla)	10 mg 20 mg 30 mg	Tab	18.9041 <sup>l</sup>	30 mg twice daily, following titration period	First year: \$13,400 Subsequent years: \$13,419
<b>DMARDs</b>					
Methotrexate (generics)	2.5 mg 10 mg/mL 25mg/mL	Tab Injection Injection	0.6325 12.5000/2 mL 8.9200/2 mL	7.5 to 25 mg per week until adequate response is achieved  Dosage adjusted to achieve optimal clinical response; 30 mg/week should not ordinarily be exceeded	Oral: 1.900 to 6.325 per week until response. Then up to 7.590 per week.  Oral yearly cost for 30 mg per week: \$395
Methotrexate (generics)	10 mg	Tab	2.7000	Idem	Oral yearly cost for 30 mg per week: \$421
Leflunomide (generics)	10 mg 20 mg	Tab	2.6433 2.6433	Loading dose of 100 mg per day for 3 days. Maintenance therapy of 20 mg per day	First year: \$997 Subsequent years: \$965
Sulfasalazine (generics)	500 mg	Tab	0.1804	Titration: Week 1: 500 mg/day Week 2: 1,000 mg/day Week 3: 1,500 mg/day Maintenance dose: 2,000 mg/day	First year: \$255 Subsequent years: \$263

DMARD = disease-modifying antirheumatic drug; SC = subcutaneous; SEB = subsequent entry biologic.

Source: Ontario Drug Benefit Formulary, including the Exceptional Access Program (accessed March 2016) unless otherwise indicated.<sup>4</sup>

<sup>a</sup> Based on the manufacturer's confidential submitted price.<sup>2</sup>

<sup>b</sup> Based on the manufacturer's confidential submitted price. The price of the 300 mg dose is lower than twice the price of the 150 mg dose.

<sup>c</sup> 300 mg SC injection is for patients who are anti-TNF alpha inhibitor–inadequate responders or patients with concomitant moderate to severe plaque psoriasis. Each 300 mg dose is given as two subcutaneous injections of 150 mg.

<sup>d</sup> Assumes 16 administrations in the first year (five doses in the first month — at weeks 0, 1, 2, 3, and 4 — and 11 doses thereafter).

<sup>e</sup> The range of costs is based on 12 to 13 doses per year, depending on the frequency of dosing.

<sup>f</sup> Assumes 15 administrations in the first year (three doses in the first month, followed by 11 doses thereafter).

<sup>g</sup> Yearly drug costs were based on patients within the weight range of 61 kg to 80 kg.

<sup>h</sup> Source: Alberta Drug Benefit List.<sup>7</sup>

<sup>i</sup> Average of eight doses for the first year and 6.5 doses per year thereafter.

<sup>j</sup> Assumes five administrations in the first year.

<sup>k</sup> Source: Régie de l'assurance maladie du Québec.<sup>5</sup>

## APPENDIX 2: REVIEWER WORKSHEETS

TABLE 2: SUMMARY OF MANUFACTURER’S SUBMISSION

Drug Product	Secukinumab (Cosentyx)
<b>Treatment</b>	<ul style="list-style-type: none"> <li>• 150 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, and 3, followed by monthly maintenance dosing starting at week 4</li> <li>• 300 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2, and 3, followed by monthly maintenance dosing starting at week 4 for patients who are TNF alpha inhibitor–inadequate responders or patients with concomitant moderate to severe plaque psoriasis</li> </ul>
<b>Comparators</b>	<p>The main comparators in the base-case analysis included:</p> <ul style="list-style-type: none"> <li>• Adalimumab 40 mg every other week</li> <li>• Certolizumab pegol 400 mg at weeks 0, 2, and 4, followed by 200 mg every 2 weeks</li> <li>• Etanercept 50 mg per week</li> <li>• Golimumab 50 mg once a month</li> <li>• Infliximab (Remicade) 5 mg/kg at weeks 0, 2, and 6, then every 8 weeks thereafter</li> <li>• Ustekinumab 45 mg at weeks 0 and 4, then every 12 weeks thereafter</li> </ul> <p>The manufacturer also conducted a sensitivity analysis including the following comparators:</p> <ul style="list-style-type: none"> <li>• Apremilast 30 mg twice daily, following a titration period</li> <li>• Infliximab (Inflectra) 5 mg/kg at weeks 0, 2, and 6, then every 8 weeks thereafter</li> </ul>
<b>Study Question</b>	“From the perspective of the Canadian publicly funded health care system, what is the cost of treatment with Cosentyx compared with currently available biologics for the treatment of adult patients with active PsA?”
<b>Type of Economic Evaluation</b>	Cost analysis (drug costs only)
<b>Target Population</b>	Adults with psoriatic arthritis
<b>Perspective</b>	Canadian publicly funded health care system
<b>Outcomes Considered</b>	ACR, PASI, PsARC
<b>Cost</b>	<ul style="list-style-type: none"> <li>• Cost of secukinumab 150 mg and 300 mg was obtained from the manufacturer.</li> <li>• Cost of comparators were obtained from the Ontario Drug Benefit Formulary and the Régie de l’assurance maladie du Québec;<sup>4,5</sup> all costs excluded markup and dispensing fees.</li> <li>• Health care resource use and those associated with adverse events were not included.</li> </ul>
<b>Clinical Efficacy</b>	<ul style="list-style-type: none"> <li>• Two randomized, double-blind, placebo-controlled phase 3 studies (FUTURE-1 and FUTURE-2)</li> <li>• Published NMA</li> <li>• Manufacturer-conducted NMA</li> </ul>
<b>Harms</b>	Not considered
<b>Time Horizon</b>	3 years; a discount rate of 5% was applied to costs
<b>Results for Base Case</b>	<ul style="list-style-type: none"> <li>• For the biologics-naïve population, the total discounted cost of secukinumab 150 mg over 3 years is ██████; which results in approximately ██████ in cost savings compared with all other biologics</li> <li>• For the biologics-experienced population, the total discounted cost of secukinumab 300 mg over 3 years is ██████; this is ██████ more</li> </ul>

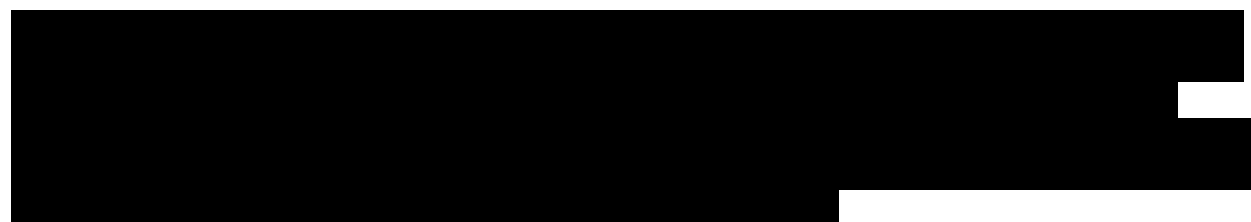
Drug Product	Secukinumab (Cosentyx)
	than the total costs for adalimumab, golimumab, and certolizumab pegol and [REDACTED] less than the total costs for etanercept, infliximab (Remicade), and ustekinumab.
<b>Results for Sensitivity Analysis</b>	The manufacturer conducted a deterministic sensitivity analysis on the following parameters: number of annual administrations of secukinumab; discount rate; time horizon; markups and dispensing fees; discontinuations; and the inclusion of SEB infliximab and apremilast. Varying these parameters did not change the rank order of treatments, with the exception of the time horizon and the inclusion of SEB infliximab.

ACR = American College of Rheumatology Score; NMA = network meta-analysis; PASI = Psoriasis Area Severity Index; PsA = psoriatic arthritis; PsARC = psoriatic arthritis response criteria; SEB = subsequent entry biologic; TNF = tumour necrosis factor.

**Manufacturer’s Results**

In the base case, the manufacturer submitted a cost analysis comparing the drug cost of secukinumab 150 mg/mL and 300 mg to anti-TNF alpha biologic drugs currently indicated and reimbursed for active PsA in Canada. These included the following: adalimumab 40 mg every other week; certolizumab pegol 400 mg at weeks 0, 2, and 4, followed by 200 mg every two weeks; etanercept 50 mg per week; golimumab 50 mg once a month; infliximab (Remicade) 5 mg/kg at weeks 0, 2, and 6, and then every eight weeks thereafter; and ustekinumab 45 mg at weeks 0 and 4, and then every 12 weeks thereafter.<sup>2</sup> The manufacturer also included apremilast 30 mg twice daily, following a titration period; and the subsequent entry biologic (SEB) infliximab (Inflectra) 5 mg/kg at weeks 0, 2, and 6, and then every eight weeks thereafter, as part of a sensitivity analysis.<sup>2</sup> The analysis was conducted from the perspective of the publicly funded health care system based on a time horizon of three years.<sup>2</sup>

Only drug costs were considered, as the manufacturer assumed that other resource use components were equivalent among all biologics. Drug costs were obtained from the Ontario Drug Benefit formulary or the Régie de l’assurance maladie du Québec.<sup>4,5</sup> All prices excluded markup and dispensing fees. The manufacturer presented the drug costs for year 1 (Table 3) and for two subsequent years (Table 4), with costs discounted at a rate of 5% annually.



For the biologics-naïve population, the total discounted cost of secukinumab 150 mg over three years was estimated at [REDACTED] (Table 5), resulting in approximately [REDACTED] in cost savings compared with all other biologics

For the biologics-experienced population, the manufacturer reported the total cost of secukinumab 300 mg over three years to be [REDACTED] (Table 5); this was [REDACTED] more costly than adalimumab, golimumab, and certolizumab pegol, and [REDACTED] less costly compared with etanercept, infliximab (Remicade), and ustekinumab.

**TABLE 3: MANUFACTURER'S RESULTS FOR BIOLOGIC-NAIVE AND -EXPERIENCED PATIENTS, YEAR 1**

Drug/Comparator	Strength	Unit Cost	Number of Administrations, Year 1	Total Cost, Year 1
<b>Included as part of manufacturer's base-case analysis</b>				
Secukinumab	150 mg	██████	15	██████
	300 mg	██████		██████
Adalimumab	40 mg	\$740.36	26	\$19,249
Certolizumab pegol	200 mg	\$664.51	29	\$19,271
Etanercept	50 mg	\$395.39	52	\$20,560
Golimumab	50 mg	\$1,555.17	12	\$18,662
Infliximab (Remicade) <sup>a</sup>	100 mg	\$987.56	8	\$34,410
Ustekinumab	45 mg/90 mg	\$4,593.14	6	\$27,559
<b>Included only as part of manufacturer's scenario analysis</b>				
Apremilast	30 mg	\$18.868	709	\$13,379
Infliximab (Inflectra)	100 mg	\$650.00	8	\$22,649

<sup>a</sup>Based on a mean weight of 87.11 kg from the FUTURE II trial.<sup>2</sup>  
 Source: Adapted from manufacturer's submission.<sup>2</sup>

**TABLE 4: MANUFACTURER'S RESULTS FOR BIOLOGIC-NAIVE AND -EXPERIENCED PATIENTS, YEARS 2 AND 3**

Drug/Comparator	Strength	Unit Cost	Number of Administrations in Year 2, Year 3	Total Cost in Year 2, Year 3	Total Cost in Year 2 (Discounted)	Total Cost in Year 3 (Discounted)
<b>Included as part of manufacturer's base-case analysis</b>						
Secukinumab	150 mg	██████	12	██████	██████	██████
	300 mg	██████		██████	██████	██████
Adalimumab	40 mg	\$740.36	26	\$19,249	\$18,333	17,460
Certolizumab pegol	200 mg	\$664.51	26	\$17,277	\$16,454	\$15,671
Etanercept	50 mg	\$395.39	52	\$20,560	\$19,581	\$18,649
Golimumab	50 mg	\$1,555.17	12	\$18,662	\$17,773	\$16,927
Infliximab (Remicade) <sup>a</sup>	100 mg	\$987.56	6.5	\$27,959	\$26,627	\$25,359
Ustekinumab	45 mg/90 mg	\$4,593.14	4.5	\$20,669	\$19,685	\$18,748
<b>Included only as part of manufacturer's scenario analysis</b>						
Apremilast	30 mg	\$18.868	710	Not reported	\$12,759	\$12,151
Infliximab (Inflectra)	100	\$650.00	6.5		\$17,526	\$16,691

<sup>a</sup>Based on a mean weight of 87.11 kg from the FUTURE 2 trial.<sup>2</sup>  
 Source: Adapted from manufacturer's submission.<sup>2</sup>

TABLE 5: TOTAL DISCOUNTED THREE-YEAR COSTS

Drug/Comparator		Total Cost Over 3 Years, Discounted	Incremental Cost vs. Secukinumab 150 mg	Incremental Cost vs. Secukinumab 300 mg
<b>Included as part of manufacturer's base-case analysis</b>				
Secukinumab	150 mg	████████	Reference	████████
	300 mg	████████		
Adalimumab		\$55,042	████████	████████
Certolizumab pegol		\$51,396	████████	████████
Etanercept		\$58,790	████████	████████
Golimumab		\$53,362	████████	████████
Infliximab (Remicade) <sup>a</sup>		\$86,397	████████	████████
Ustekinumab		\$65,991	████████	████████
<b>Included only as part of manufacturer's scenario analysis</b>				
Apremilast		38,288	████████	████████
Infliximab (Inflectra)		\$56,865	████████	████████

vs. = versus.

<sup>a</sup>Based on a mean weight of 87.11 kg from the FUTURE 2 trial.<sup>2</sup>

Source: Adapted from manufacturer's submission.<sup>2</sup>

The manufacturer conducted a deterministic sensitivity analysis on the following parameters: number of annual administrations of secukinumab (15 or 16 administrations in year 1), discount rate (0%, 3%), time horizon (10 years), markups and dispensing fees (markup of 6% to 8% and dispensing fee of \$8.83), discontinuation rates (30% for all treatments after year 1, and 10% from year 2 onwards), and the inclusion of SEBs infliximab and apremilast. Changes in these parameters did not change the rank order of treatments, with the exception of the time horizon and the inclusion of SEB infliximab.

### CADTH Common Drug Review Results

CDR compared the annual cost per patient of secukinumab with anti-TNF alpha biologic drugs (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, and SEB infliximab) and a phosphodiesterase-4 inhibitor (apremilast). Updated Ontario Drug Benefit list prices were used, as there were slight changes to the prices of some biologic drugs effective April 2016.<sup>4</sup> Given the uncertainty in long-term efficacy and discontinuation rates over time, annual drug costs were calculated for the first year (Table 6) and subsequent years (Table 7) to reflect different loading doses for particular biologic agents. SEB infliximab (Inflectra) was included as a primary comparator in the CDR analysis.

At the manufacturer-submitted price of ██████████, the annual cost of secukinumab 150 mg/mL pre-filled syringe or pen (first year: ██████████, subsequent years: ██████████),<sup>2</sup> is less than that of anti-TNF alpha biologic drugs (adalimumab ██████████, etanercept ██████████, infliximab [Remicade, first year: ██████████, subsequent years: ██████████], SEB infliximab [Inflectra, first year: ██████████, subsequent years: ██████████]), ustekinumab (first year: ██████████, second year: ██████████), and the phosphodiesterase-4 inhibitor, apremilast, based on publicly available prices (see APPENDIX 1: Cost Comparison).

At the manufacturer-submitted price of [REDACTED], the annual cost of secukinumab 300 mg (first year: [REDACTED], subsequent years: [REDACTED]) is less than that of infliximab (Remicade). Secukinumab 300 mg is more expensive in the first year than adalimumab, etanercept, and ustekinumab, but less expensive in subsequent years. Secukinumab 300 mg is more expensive in the first year than golimumab, and may be more or less expensive in the subsequent years, depending on the number of administrations (i.e., 12 versus 13) of secukinumab. Additionally, secukinumab 300 mg is more expensive than SEB infliximab, certolizumab pegol, and apremilast.

**TABLE 6: CDR RESULTS FOR BIOLOGIC-NAIVE AND -EXPERIENCED PATIENTS, YEAR 1**

Drug/ Comparator	Strength	Unit Cost	Number of Administrations, Year 1	Total Cost, Year 1	Incremental Cost vs. 150 mg	Incremental Cost vs. 300 mg
Secukinumab	150 mg	[REDACTED]	16	[REDACTED]	Reference	
	300 mg	[REDACTED]		[REDACTED]		
Adalimumab	40 mg	\$769.97	26	\$20,019	[REDACTED]	[REDACTED]
Certolizumab pegol	200 mg	\$664.51	29	\$19,271	[REDACTED]	[REDACTED]
Etanercept	50 mg	\$405.99	52	\$21,111	[REDACTED]	[REDACTED]
Golimumab	50 mg	\$1,555.17	12	\$18,662	[REDACTED]	[REDACTED]
Infliximab (Remicade) <sup>a</sup>	100 mg	\$962.68	8	\$33,543	[REDACTED]	[REDACTED]
Ustekinumab	45 mg/ 90 mg	\$4,593.14	5	\$22,966	[REDACTED]	[REDACTED]
Apremilast	30 mg	\$18.90	709	\$13,400	[REDACTED]	[REDACTED]
Infliximab (Inflectra)	100 mg	\$525.00	8	\$18,293	[REDACTED]	[REDACTED]

CDR = CADTH Common Drug Review; vs. = versus.

<sup>a</sup>Based on a mean weight of 87.11 kg from the FUTURE 2 trial.<sup>2</sup>

Markups and dispensing fees not included. Prices are the Ontario Drug Benefit list prices (May 2016),<sup>8</sup> with the exception of infliximab (Remicade) (Alberta Health Drug Benefit),<sup>7</sup> and secukinumab (manufacturer's list price).<sup>4</sup>

**TABLE 7: CDR RESULTS FOR BIOLOGIC-NAIVE AND -EXPERIENCED PATIENTS, SUBSEQUENT YEARS**

Drug/ Comparator	Strength	Unit Cost	Number of Administrations in Subsequent Years	Total Cost in Subsequent Years	Incremental Cost vs. 150 mg	Incremental Cost vs. 300 mg
Secukinumab	150 mg	██████	12-13	██████	Reference	
	300 mg	██████				
Adalimumab	40 mg	\$769.97	26	\$20,019	██████	██████
Certolizumab pegol	200 mg	\$664.51	26	\$17,277	██████	██████
Etanercept	50 mg	\$405.99	52	\$21,111	██████	██████
Golimumab	50 mg	\$1,555.17	12	\$18,662	██████	██████
Infliximab (Remicade) <sup>a</sup>	100 mg	\$962.68	6.5	\$27,254	██████	██████
Ustekinumab	45 mg/ 90 mg	\$4593.14	4.5	\$20,669	██████	██████
Apremilast	30 mg	\$18.90	710	\$13,419	██████	██████
SEB infliximab (Inflectra)	100	\$525.00	6.5	\$14,863	██████	██████

CDR = CADTH Common Drug Review; SEB = subsequent entry biologic; vs. = versus.

<sup>a</sup>Based on a mean weight of 87.11 kg from the FUTURE 2 trial.<sup>2</sup>

Markups and dispensing fees not included. Prices are the Ontario Drug Benefit list prices (May 2016)<sup>8</sup> with the exception of infliximab (Remicade) (Alberta Health Drug Benefit),<sup>7</sup> and secukinumab (manufacturer's list price).<sup>4</sup>

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