Common Drug Review
Pharmacoeconomic Review Report

August 2016

Drug	Secukinumab (Cosentyx)
Indication	For the treatment of adult patients with active ankylosing spondylitis who have inadequately responded to conventional therapy.
Reimbursement request	[redacted]
Dosage form	Pre-filled syringe or pen for subcutaneous injection, 150 mg/mL
NOC date	April 20, 2016
Manufacturer	Novartis Pharmaceuticals Canada Inc.

Redactions: Confidential information in this document has been redacted at the request of the manufacturer in accordance with the *CADTH Common Drug Review Confidentiality Guidelines.*

About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

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ABBREVIATIONS

AS	ankylosing spondylitis
ASAS	Assessment of SpondyloArthritis International Society
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
BASFI	Bath Ankylosing Spondylitis Functional Index
CDEC	Canadian Drug Expert Committee
CDR	CADTH Common Drug Review
NMA	network meta-analysis

SUMMARY

Background

Secukinumab (Cosentyx) is an interleukin-17A inhibitor indicated for the treatment of active ankylosing spondylitis (AS) in adult patients.[1] The recommended dose is 150 mg by subcutaneous injection at weeks 0, 1, 2 and 3, followed by once a month starting at week 4.[1] At the manufacturer-submitted confidential price of [redacted] per 150 mg/mL pre-filled syringe or pen,[2] the annual cost of treatment is [redacted] in the first year, and [redacted] in subsequent years, depending on whether 12 or 13 doses are administered.

The manufacturer is requesting secukinumab be listed as the first biologic of choice for adult patients with AS, with similar reimbursement criteria to currently prescribed biologics administered by subcutaneous injection indicated for the treatment of AS in adult patients.[2]

Secukinumab is also indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy. It was previously reviewed by CDEC for this indication, and a recommendation was made to list with clinical criteria or conditions in October 2015.[3] 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.[3] Secukinumab is also concurrently being reviewed through the CADTH Common Drug Review (CDR) for the treatment of adult patients with active psoriatic arthritis (PsA).

Summary of the economic analysis submitted by the manufacturer

The manufacturer submitted a cost analysis comparing the drug cost of secukinumab 150 mg/mL with anti-tumour necrosis factor (anti-TNF) biologics currently indicated and reimbursed for active AS in Canada. These included the following: adalimumab 40 mg every other week; etanercept 50 mg per week; golimumab 50 mg once a month; and infliximab (Remicade) 5 mg/kg at weeks 0, 2 and 6, and then every 8 weeks thereafter.[2] The manufacturer also included certolizumab pegol 400 mg at weeks 0, 2 and 4, followed by 200 mg every 2 weeks; and subsequent entry biologic (SEB) infliximab (Inflectra) 5 mg/kg at weeks 0, 2 and 6, and then every 8 weeks thereafter, as part of a scenario analysis.[2] The analysis was conducted from the perspective of the publicly funded health care system, based on a three-year time horizon.[2] The manufacturer assumed all other aspects of patient treatment were equivalent for all comparators; therefore, only drug costs were considered. Drug costs were obtained from the Ontario Drug Benefit formulary.[4] All prices excluded mark up and dispensing fees.

As no head-to-head trials were available, the assumption of similar efficacy and safety of secukinumab to other biologics was based on a manufacturer-submitted network meta-analysis (NMA). [redacted]

[redacted]

Key limitations

- **Uncertain comparative effectiveness of secukinumab with anti-TNF biologics:** No head-to-head evidence was provided to support that efficacy is similar between secukinumab and anti-TNF drugs. As noted in Appendix 6 of the CDR clinical report, heterogeneity in the baseline characteristics of patients across the included trials in the NMA contributes to uncertainty regarding its conclusion that there are [redacted] between secukinumab and anti-TNF biologics.
- **Dosing of secukinumab:** The manufacturer's cost analysis is based on 15 administrations of secukinumab in the first year, and 12 in subsequent years, which biases costs in favour of secukinumab. In the CDR reanalysis, it is assumed that patients will receive 16 administrations of secukinumab in the first year (in alignment with the dosing recommendations in the product monograph, which indicates administration at 0, 1, 2, and 3 weeks and then monthly beginning at week 4),[1] and 12 to 13 administrations in subsequent years.
- **Exclusion of relevant comparator in primary analysis:** The manufacturer's base case did not include SEB infliximab (Inflectra). While SEB infliximab was included within a scenario analysis presented by the manufacturer, given that it is reimbursed by some public drug plans in Canada and may represent the least costly alternative biologic, this is a relevant comparator for the base-case analysis.
- **Uncertainty regarding clinical effectiveness in treatment-experienced patients:** Potential differences in the clinical effectiveness of secukinumab between treatment-experienced and treatment-naive patients may exist. In the trials included in the manufacturer-submitted NMA, some trials enrolled both treatment-naive and treatment-experienced patients, and others only enrolled treatment-naive patients. As noted in the CDR clinical review, based on the results of the MEASURE 1 and MEASURE 2 trials, it appears that the efficacy of secukinumab may be [redacted] in treatment-experienced patients. Therefore, the conclusion of similar efficacy for secukinumab compared with anti-TNF biologic drugs is uncertain for treatment-experienced patients. This is an important limitation since patients with inadequate disease control on anti-TNF therapy may be switched to secukinumab due to its different mechanism of action, according to the clinical expert consulted by CDR.
- **Uncertainty regarding long-term efficacy and discontinuation rates over time:** The manufacturer reported incremental costs over a three-year time horizon; however, there is uncertainty regarding long-term efficacy and discontinuation rates with the use of different biologics. 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 as a pre-NOC submission; [5] 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 PsA.
- In October 2015, CDEC recommended that secukinumab be listed with the condition that the cost not exceed the cost of the least costly biologic reimbursed for the treatment of moderate to severe

plaque psoriasis.[3] 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 submitted unit price of [redacted], the annual cost of secukinumab (first year: [redacted], subsequent years: [redacted]) is less than that of all other anti-TNF biologics, based on publicly available prices (Appendix 1: Cost Comparison). However, the cost impact of secukinumab may differ should the actual prices paid by CDR-participating drug plans for anti-TNF biologics be lower.

The manufacturer's cost analysis was based on an assumption of similar efficacy between secukinumab and anti-TNF biologics. While the NMA used to support this assumption found [redacted], it was limited by heterogeneity across included trials and the lack of analysis of safety outcomes. Furthermore, there were no specific data from indirect comparisons provided for secukinumab in patients previously treated with an anti-TNF biologic; therefore, there is uncertainty regarding the conclusion of similar efficacy between secukinumab and anti-TNF biologics in this population, and the appropriateness of a cost (rather than cost-effectiveness) analysis is unclear.

APPENDIX 1: COST COMPARISON

The comparators presented in Table 1 have been deemed to be appropriate by the clinical expert consulted by CDR. Existing Product Listing Agreements are not reflected in the table and as such may not represent the actual costs to public drug plans.

TABLE 1: COST COMPARISON TABLE FOR PATIENTS WITH ANKYLOSING SPONDYLITIS

Drug	Strength	Dosage Form	Price ($)	Recommended Dose	Annual Drug Cost ($)
Secukinumab (Cosentyx)	**150 mg/mL**	**Pre-filled syringe or pen**	[redacted][a]	**150 mg SC injection at weeks 0, 1, 2, 3, then monthly starting at week 4**	**First year:** [redacted][b] **Subsequent years:** [redacted]
Biologic Disease Modifying Antirheumatic Drugs					
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[d] 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 autoinjector	405.9850		21,111
Golimumab SC (Simponi)	50 mg/0.5 mL	Pre-filled syringe or autoinjector	1,555.17	50 mg SC injection once a month (on the same date)	18,662
Infliximab[e] (Remicade)	100 mg/vial	Vial	962.6800[f]	5 mg/kg initial dose followed by additional 5 mg/kg doses at 2 and 6 weeks after the first infusion, then every 6 to 8 weeks thereafter	5 mg/kg at weeks 0, 2 and 6, then every 8 weeks[g] First year: 30,806 Subsequent years: 25,030 5 mg/kg at weeks 0, 2 and 6, then every 6 weeks[h] First year: 38,507 Subsequent years: 34,656
Infliximab SEB[e] (Inflectra)	100 mg/vial	Vial	525.0000	5 mg/kg initial dose followed by additional 5 mg/kg doses at 2 and 6 weeks after the first infusion, then every 6 to 8 weeks thereafter	5 mg/kg at weeks 0, 2 and 6, then every 8 weeks[g] First year: 16,800 Subsequent years: 13,650 5 mg/kg at weeks 0, 2 and 6, then every 6 weeks[h] First year: 21,000 Subsequent years: 18,900

SC = subcutaneously; SEB = subsequent entry biologic.
Source: Ontario Drug Benefit Formulary, including the Exceptional Access Program (accessed May 2016) unless otherwise indicated. [4]
[a] Based on the manufacturer's confidential submitted price. [2]
[b] Assumes 16 administrations in the first year (5 doses in the first month, at weeks 0, 1, 2, 3 and 4, and 11 doses thereafter).
[c] The range of costs is based on 12 to 13 doses per year, depending on the frequency of dosing.
[d] Assumes 14 administrations in the first year (3 doses in the first month, followed by 11 doses thereafter).
[e] Annual drug costs were based on patients within the weight range of 61 kg to 80 kg.
[f] Source: Alberta Drug Benefit List (May 2016).[6]
[g] Average of 8 doses for the first year and 6.5 doses per year thereafter.
[h] Average of 10 doses for the first year and 9 doses per year thereafter.

APPENDIX 1: REVIEWER WORKSHEETS

TABLE 2: SUMMARY OF MANUFACTURER'S SUBMISSION

Drug Product	Secukinumab (Cosentyx)
Treatment	150 mg by subcutaneous injection with initial dosing at weeks 0, 1, 2 and 3, followed by monthly maintenance dosing starting at week 4
Comparators	The main comparators in the base-case analysis included: • etanercept (Enbrel) 50 mg per week • adalimumab (Humira) 40 mg every other week • golimumab (Simponi) 50 mg once a month • infliximab (Remicade) 5 mg/kg at weeks 0, 2 and 6, then every 8 weeks thereafter. The manufacturer also conducted a scenario analysis including the following comparators: • certolizumab pegol (Cimzia) 400 mg at week 0, 2 and 4, followed by 200 mg every 2 weeks. • SEB infliximab (Inflectra) 5 mg/kg initially, followed by additional 5 mg/kg at weeks 2 and 6 after the first infusion, then every 8 weeks thereafter.
Study Question	"From the perspective of the Canadian publicly funded health care system, what is the cost of treatment with Cosentyx compared to etanercept, adalimumab, infliximab, and golimumab for the treatment of adult patients with AS?"
Type of Economic Evaluation	Cost comparison (drug costs only)
Target Population	Adult patients with ankylosing spondylitis
Perspective	Canadian publicly funded health care system
Outcomes Considered	ASAS response criteria, BASDAI score, and BASFI at week 12
Key Data Sources	
Cost	• Cost of secukinumab 150 mg was obtained from the manufacturer. • Costs of comparators were obtained from the Ontario Drug Benefit formulary;[4] all costs excluded mark up and dispensing fees. • Health care resource use and costs associated with adverse events were not included.
Clinical Efficacy	• Two phase 3 trials (Measure 1 and Measure 2) • Manufacturer conducted an NMA
Harms	Not considered
Time Horizon	3 years, as such a discount rate of 5% was applied to costs
Results for Base Case	Total discounted cost of secukinumab over 3 years is [redacted], which results in approximately [redacted] in cost savings compared to the least expensive comparator (golimumab; [redacted] over 3 years) and [redacted] in cost savings compared to the most expensive comparator (infliximab [Remicade]; [redacted] over 3 years).
Results for Sensitivity Analysis	The manufacturer presented sensitivity analysis around the yearly administrations of secukinumab, the average weight of patients taking infliximab, vial wastage in patients taking infliximab, and the dosing cycle of infliximab. Results of the sensitivity analysis showed that secukinumab continued to offer cost savings after varying each parameter.

ASAS = Assessment of Ankylosing Spondylitis; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; BASFI = Bath Ankylosing Spondylitis Functional Index; NMA = network meta-analysis.

Manufacturer's Results

In the base case, the manufacturer submitted a cost analysis comparing the drug cost of secukinumab 150 mg/mL with anti-tumour necrosis factor (anti-TNF) biologics; adalimumab 40 mg every other week; etanercept 50 mg per week; golimumab 50 mg once a month; and infliximab (Remicade) 5 mg/kg at weeks 0, 2 and 6, and then every 8 weeks thereafter.[2] The manufacturer also included certolizumab pegol 400 mg at weeks 0, 2 and 4, followed by 200 mg every 2 weeks; and SEB infliximab (Inflectra) 5 mg/kg at weeks 0, 2 and 6, and then every 8 weeks thereafter, as part of a scenario analysis.[2] The analysis was conducted from the perspective of the publicly funded health care system, based on a three-year time horizon.[2] The manufacturer presented the drug costs for the first year (Table 3) and for two subsequent years (Table 4), with costs discounted at a rate of 5% annually.

The manufacturer assumed all other aspects of patient management were equivalent for all comparators; therefore, only drug costs were considered. Drug costs were obtained from the Ontario Drug Benefit (ODB) formulary.[4] All prices excluded mark up and dispensing fees.

[redacted] Overall, the total discounted cost of secukinumab over 3 years was estimated to be [redacted] (Table 5), resulting in savings of approximately [redacted] compared with the least expensive comparator (golimumab; [redacted] over 3 years) and [redacted] in cost savings compared with the most expensive comparator (infliximab [Remicade]; [redacted] over 3 years).

TABLE 3: MANUFACTURER'S RESULTS, YEAR 1

Drug/Comparator	Strength	Unit Cost	# of Administrations, Year 1	Total Cost, Year 1
Included as part of manufacturer's base-case analysis				
Secukinumab	150 mg	[redacted]	15	[redacted]
Etanercept	50 mg	$395.39	52	$20,560
Adalimumab	40 mg	$740.36	26	$19,249
Golimumab	50 mg	$1,555.17	12	$18,662
Infliximab (Remicade)[a]	100 mg	$987.56	8	$31,602
Included only as part of manufacturer's scenario analysis				
Certolizumab pegol	200 mg	$664.51	29	$19,271
SEB Infliximab (Inflectra)	100 mg	$650.00	8	$20,800

[a] Assumes wastage and average body weight of 70 kg. During year 1, administered 3 times during the initiation phase and 5 times during the maintenance phase, based on an 8-week dosing schedule.
Adapted from manufacturer's pharmacoeconomic submission. [2]

TABLE 4: MANUFACTUER'S RESULTS, YEARS 2 AND 3

Drug/Comparator	Strength	Unit Cost	# of Administrations in Years 2 and 3	Total Cost in Years 2 and 3	Total Cost in Year 2 (discounted)	Total Cost in Year 3 (discounted)
Included as part of manufacturer's base-case analysis						
Secukinumab	150 mg	[redacted]	12	[redacted]	[redacted]	[redacted]
Etanercept	50 mg	$395.39	52	$20,560	$19,581	$18,649
Adalimumab	40 mg	$740.36	26	$19,249	$18,333	17,460
Golimumab	50 mg	$1,555.17	12	$18,662	$17,773	$16,927
Infliximab (Remicade)[a]	100 mg	$987.56	6.5	$25,676	$24,454	$23,289
Included only as part of manufacturer's scenario analysis						
Certolizumab pegol	200 mg	$664.51	26	$17,277	$16,454	$15,671
SEB Infliximab (Inflectra)	100 mg	$650.00	6.5	$16,900	$16,095	$15,329

[a] Assumes wastage and average body weight of 70 kg. Over years 2 and 3, administered 13 times during the maintenance phase based on an 8-week dosing schedule.
Adapted from manufacturer's pharmacoeconomic submission. [2]

TABLE 5: TOTAL DISCOUNTED THREE-YEAR COSTS

Drug/Comparator	Total Cost Over 3 Years, Discounted	Incremental Cost
Included as part of manufacturer's base-case analysis		
Secukinumab	[redacted]	Reference
Etanercept	$58,790	[redacted]
Adalimumab	$55,042	[redacted]
Golimumab	$53,362	[redacted]
Infliximab (Remicade)[a]	$79,345	[redacted]
Included only as part of manufacturer's scenario analysis		
Certolizumab pegol	$51,396	[redacted]
SEB infliximab (Inflectra)	$52,224	[redacted]

[a] Assumes wastage and average body weight of 70 kg. During year 1, administered 3 times during the initiation phase and 5 times during the maintenance phase. Over years 2 and 3, administered 13 times during the maintenance phase. All based on an 8-week dosing schedule.
Adapted from manufacturer's pharmacoeconomic submission.[2]

The manufacturer presented sensitivity analyses around the number of yearly administrations of secukinumab (16 doses in the first year, and 13 doses in years 2 and 3), the average weight of patients taking infliximab (+/- 20 kg from the base-case average of 70 kg), vial wastage in patients taking infliximab (exact recommended dose for patients at 70 kg corresponding to 3.5 vials), and the dosing cycle of infliximab (6-week dosing schedule). Results of the sensitivity analysis showed that secukinumab continued to offer cost savings after varying these parameters.

CADTH Common Drug Review Results

CDR compared the annual cost per patient of secukinumab with anti-TNF biologic drugs. Updated ODB list prices were used as there were slight changes to the prices effective April 2016.[4] Given the uncertainty in long-term efficacy and discontinuation rates over time, a three-year time horizon was not assumed, and annual drug costs were calculated for the first year (Table 6) and subsequent years (Table 7) to reflect loading doses across drugs. Certolizumab pegol and SEB infliximab were included as primary comparators in the CDR analysis to reflect the range of alternatives covered across jurisdictions in Canada.

At the submitted price of [redacted], the annual cost of secukinumab (first year: [redacted], subsequent years: [redacted]) is less than that of anti-TNF biologics: abalimumab ($20,019); certolizumab pegol (first year: $19,271, subsequent years: $17,277); etanercept ($21,112); golimumab ($18,662); infliximab (Remicade) (first year: $30,806 to $38,507, subsequent years: $25,030 to $34,656); SEB infliximab (Inflectra) (first year: $16,800 to $21,000, subsequent years: $13,650 to $18,900).

TABLE 6: CDR ANALYSIS, YEAR 1

Drug/Comparator	Strength	Unit Cost	# of Administrations, Year 1	Total Cost, Year 1	Incremental Cost
Secukinumab	150 mg	[redacted]	16	[redacted]	Reference
Etanercept	50 mg	$405.99	52	$21,112	[redacted]
Adalimumab	40 mg	$769.97	26	$20,019	[redacted]
Golimumab	50 mg	$1,555.17	12	$18,662	[redacted]
Infliximab (Remicade)[a]	100 mg	$962.68	8	$30,806	[redacted]
Certolizumab pegol	200 mg	$664.51	29	$19,271	[redacted]
SEB infliximab (Inflectra)	100 mg	$525.00	8	$16,800	[redacted]

[a] Assumes wastage and average body weight of 70 kg. During year 1, administered 3 times during the initiation phase and 5 times during the maintenance phase, based on an 8-week dosing schedule.
Mark ups and dispensing fees are not included. Prices are the ODB list prices (May 2016),[4] with the exception of infliximab (Remicade) (Alberta Health Drug Benefit)[6], and secukinumab (manufacturer's list price).[2]

TABLE 7: CDR ANALYSIS, SUBSEQUENT YEARS

Drug/Comparator	Strength	Unit Cost	# of Administrations in Subsequent Years	Total Cost in Subsequent Years	Incremental Cost
Secukinumab	150 mg	[redacted]	12 to 13	[redacted]	Reference
Etanercept	50 mg	$405.99	52	$21,112	[redacted]
Adalimumab	40 mg	$769.97	26	$20,019	[redacted]
Golimumab	50 mg	$1,555.17	12	$18,662	[redacted]
Infliximab (Remicade)[a]	100 mg	$962.68	6.5	$25,030	[redacted]
Certolizumab pegol	200 mg	$664.51	26	$17,277	[redacted]
SEB infliximab (Inflectra)	100 mg	$525.00	6.5	$13,650	[redacted]

[a] Assumes wastage and average body weight of 70 kg. Over years 2 and 3, administered 13 times during the maintenance phase based on an 8-week dosing schedule.
Mark ups and dispensing fees are not included. Prices are the ODB list prices (May 2016),[4] with the exception of infliximab (Remicade) (Alberta Health Drug Benefit)[6], and secukinumab (manufacturer's list price).[2]

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