Common Drug Review
Pharmacoeconomic Review Report

May 2017

Drug	sarilumab (Kevzara)
Indication	Treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to one or more biologic or non-biologic disease-modifying antirheumatic drugs
Listing request	As per indication
Dosage form(s)	Pre-filled syringe (150 mg/1.14 mL or 200 mg/1.14 mL)
NOC Date	January 12, 2017
Manufacturer	Sanofi Genzyme

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ABBREVIATIONS

CDR	CADTH Common Drug Review
DMARD	disease-modifying antirheumatic drugs
IV	intravenous
RA	rheumatoid arthritis
SC	subcutaneous
SEB	subsequent entry biologic

EXECUTIVE SUMMARY

Background

Sarilumab (Kevzara) for subcutaneous (SC) injection is a fully human immunoglobulin G1 monoclonal antibody that binds specifically to both soluble and membrane-bound interleukin-6 receptors inhibiting interleukin-6 mediated signalling. It is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to one or more biologic or non-biologic disease-modifying antirheumatic drugs (DMARDs).[1] Sarilumab is available in 150 mg and 200 mg single-use pre-filled syringes for SC injection. The recommended dose of sarilumab is 200 mg SC injection every two weeks, with a reduction to 150 mg every two weeks for management of neutropenia, thrombocytopenia, and elevated liver enzymes. Sarilumab should be given in combination with methotrexate or other conventional DMARD but may be used as monotherapy in cases of intolerance or contraindication to methotrexate or DMARDs.[1] The manufacturer has submitted a price of $700 per pre-filled syringe (for both 150 mg and 200 mg doses) resulting in an annual cost of $18,200 per patient.

Summary of the Economic Analysis Submitted by the Manufacturer

The manufacturer submitted a cost comparison[2] of sarilumab 200 mg to the monograph-recommended doses of other biologic DMARDs used for the treatment of RA in Canada (see Table 1).[3-14] Clinical similarity among biologics was assumed on the basis of head-to-head trials comparing sarilumab with adalimumab (MONARCH[15,16]) and tocilizumab (ASCERTAIN[17]) as well as an unpublished network meta-analysis.[18]

While the analysis was stated to be from the perspective of a public health care payer (e.g., a provincial Ministry of Health) only drug costs were included in the analysis; all other costs were assumed equal. Drug costs were considered over a three-year time horizon in order to account for dose titration in the first year and two years of maintenance therapy. Drug costs were derived primarily from the Ontario Drug Benefit Formulary and Exceptional Access Program list prices for comparators, the Saskatchewan Formulary for abatacept intravenous (IV) , and the manufacturer's submitted price for sarilumab. No discounting was applied in years 2 and 3. A patient weight of 75 kg was assumed for weight-based comparator dosing. A price for the subsequent entry biologic (SEB) etanercept (Brenzys) was not available at the time of the manufacturer's analysis, and thus results were not reported.

Key Limitations

Uncertainty in Assumption of Clinical Similarity

Head-to-head trials reported statistically significant and clinically relevant improvements in clinical response, clinical remission, and improvement in physical functioning when sarilumab monotherapy was compared with adalimumab monotherapy[15,16] [redacted].[17]

The manufacturer-provided network meta-analysis suggested that sarilumab [redacted] compared with other biologics, including tocilizumab IV and SC, [redacted] where biologics are used in combination with a conventional DMARD. [redacted] to other biologics within the network meta-analysis [redacted] patients with an inadequate response to conventional DMARDs using biologic monotherapy. The CADTH Common Drug Review (CDR) clinical reviewers determined that no conclusion could be drawn regarding the comparative efficacy and safety of

sarilumab versus biologics in patients with an inadequate response to an anti–tumour necrosis factor therapy (see CDR Clinical Report, Appendix 6).

In summary, CDR reviewers have higher confidence in the clinical similarity of sarilumab in combination with conventional DMARDs compared with other biologics plus conventional DMARDs in patients who have an inadequate response to conventional DMARDs alone. The assumption of clinical similarity is less certain between biologic monotherapies or in patients with an inadequate response to anti–tumour necrosis factor therapy.

Presentation of the Results

While an annual average cost of the first three years of therapy has been accepted by CDR in the past,[19] given the potential for biologic treatment for RA to either be discontinued or continue long term, CDR considered this method of presentation of results to be not easily generalized to variations in prescribing patterns in clinical practice. CDR reanalyses instead presented annual and incremental costs for the first year of therapy and then average subsequent years, allowing a better comparison of comparative drug costs, which highlights comparators with loading doses (most often IV therapies). This change had little impact on the cost of sarilumab relative to its comparators.

New Comparator Pricing Available

At the time of the manufacturer's analysis, no public price was available for SEB etanercept. However, a wholesale price of $305 per 50 mg pre-filled syringe of SEB etanercept ($15,860 per patient annually) was available at the time of the CDR review, which is $2,340 less expensive per patient per year than sarilumab.

Issues for Consideration

Monitoring Costs Excluded

Treatment with interleukin-6 inhibitors is associated with an increased risk of neutropenia, thrombocytopenia, elevated liver enzymes, and increased lipid levels; therefore, routine monitoring of neutrophils, platelets, and liver enzymes is recommended.[1,8,19] In contrast, anti–tumour necrosis factor biologic monographs recommend routine monitoring only for infection.[3,4] Should treatment with sarilumab (or tocilizumab) result in increased laboratory testing, this would increase incremental costs (or decrease incremental savings) relative to anti–tumour necrosis factor therapies.

Potential for Off-Label Escalated Dosing

While the sarilumab product monograph contains no approved dose escalation and a dose-ranging trial showed no additional benefit with 150 mg weekly dosing compared with 150 mg or 200 mg biweekly,[20] the expert consulted by CDR considered it possible that some patients who partially respond to initial sarilumab treatment might receive more frequent dosing, which would increase costs relative to biologics, which either are not typically escalated when treating RA in clinical practice according to experts consulted by CDR (e.g., adalimumab) or have already taken escalation into account (e.g., tocilizumab).

Publicly Available List Prices May Not Reflect Actual Costs to Public Plans

The actual costs paid by Canadian public drug plans for biologic treatments for RA are likely lower than those listed on publicly available formularies, which reduces the relative attractiveness of the submitted price of sarilumab.

Results / Conclusions

When compared with the most widely used biologics for the treatment of RA,[21,22] sarilumab ($18,200 per patient per year) is less expensive than adalimumab ($20,019 per patient per year) and branded etanercept (21,108 per patient per year), but more expensive than the newly introduced SEB etanercept ($15,860 per patient per year). A price reduction of 13% would be required for sarilumab to be cost-neutral to SEB etanercept.

When compared with tocilizumab, the other interleukin-6 inhibitor, sarilumab is more expensive than the tocilizumab IV formulation ($9,402 to $17,629 per patient per year) and biweekly tocilizumab SC use ($9,230 per patient per year) but similar to weekly tocilizumab SC use ($18,460 per patient per year). In order for sarilumab to be cost-neutral to a weighted average cost of tocilizumab SC, 97% of patients would need to be using weekly versus biweekly doses of tocilizumab. Where more than 3% of patients are receiving tocilizumab biweekly, price reductions for sarilumab would be required for cost neutrality (see APPENDIX 1).

Cost Comparison Table

Clinical experts have deemed the comparator treatments presented in Table 1 to be appropriate. Comparators may be recommended (appropriate) practice versus actual practice. Comparators are not restricted to drugs, but may be devices or procedures. Existing Product Listing Agreements are not reflected in Table 1 and as such may not represent the actual costs to public drug plans.

TABLE 1: COST COMPARISON TABLE OF BIOLOGIC TREATMENTS FOR RHEUMATOID ARTHRITIS IN ADULT PATIENTS

Comparators	Strength	Dose Form	Price ($)	Recommended Dose	Annual Drug Cost ($)
Sarilumab (Kevzara)	**150 mg/1.14 mL 200 mg/1.14 mL**	**Pre-filled syringe**	**700.0000[a]**	**200 mg SC every two weeks**	**18,200**
Abatacept SC (Orencia)	125 mg/mL	Pre-filled syringe	366.1000[b]	125 mg weekly[c]	19,037
Abatacept IV (Orencia)	250 mg/15 mL	Vial	490.0500[b]	Patients < 60 kg: 500 mg Patients 60 to 100 kg: 750 mg Patients > 100 kg: 1,000 mg 500 to 1,000 mg at weeks 0, 2, and 4 then every 4 weeks	Year 1: 20,582 Thereafter: 19,112
Adalimumab SC (Humira)	40 mg/0.8 mL	Pre-filled syringe or pen	769.9700	40 mg every other week	20,019
Anakinra (Kineret)	100 mg	Pre-filled syringe	48.0571	100 mg daily	17,493
Certolizumab pegol (Cimzia)	200 mg/mL	Pre-filled syringe	664.5100	400 mg at weeks 0, 2 and 4 then 200 mg every 2 weeks	Year 1: 19,271 Thereafter: 17,277
Etanercept (Enbrel)	25 mg	Vial	202.9300	50 mg weekly or two 25 mg doses on same day every week or every 3 or 4 days	21,105
	50mg/mL	Pre-filled syringe or auto-injector	405.9850		21,111
Entanercept (Brenzys)	50 mg/mL	Pre-filled syringe	305.0000[d]	50 mg weekly	15,860
Golimumab SC (Simponi)	50 mg/0.5 mL	Pre-filled syringe or auto-injector	1,555.17	50 mg monthly	18,662
Golimumab IV (Simponi)	50 mg/4 mL	Vial	849.5000[b]	2 mg/kg at weeks 0 and 4, then every 8 weeks thereafter	Year 1: 17,829 Thereafter: 16,565

Comparators	Strength	Dose Form	Price ($)	Recommended Dose	Annual Drug Cost ($)
Infliximab (Remicade)	100 mg	Vial	987.5600	3 mg/kg at weeks 0, 2, and 6, then every 8 weeks thereafter Depending on clinical response, dose can be increased to 10 mg/kg and/or up to every four weeks	Year 1: 23,701 Thereafter: 19,257 10 mg/kg every 4 weeks: $102,706 annually
Infliximab (Inflectra)	100 mg	Vial	525.0000		Year 1: 12,600[b] Thereafter: 10,238[b] 10 mg/kg every 4 weeks: $54,600 annually[b]
Rituximab (Rituxan)	100 mg/10 mL 500 mg/50 mL	Vial	466.3200 2,331.61	A course consists of 1,000 mg infusions at weeks 0 and 2. Reassess for retreatment at week 26, no sooner than 16 weeks after previous	18,653 assumes 2 courses Per course: 9,326
Tocilizumab SC (Actemra)	162 mg/ 0.9 mL	Pre-filled syringe	355.0000	Patients < 100 kg: 162 mg SC every two weeks, increasing to weekly based on clinical response. Patients ≥ 100 kg: 162 mg SC weekly	Every two weeks: 9,230 Weekly: 18,460
Tocilizumab IV (Actemra)	80 mg/4 mL 200 mg/10 mL 400 mg/20 mL	Vial	180.8100 452.0300 904.0600	4 mg/kg every 4 weeks followed by an increase to 8 mg/kg based on clinical response	4 mg/kg: 10,577[b] 8 mg/kg: 17,629[b]
Tofacitinib (Xeljanz)	5 mg	Tablet	23.5585	5 mg p.o. twice daily	17,151

IV = intravenous; p.o. = orally; SC = subcutaneous.
[a] Manufacturer's submitted price.
[b] Saskatchewan Formulary list price (January 2017).
[c] Abatacept-naive patients require a single weight-based loading dose of 500, 750, or 1,000 mg intravenous abatacept, with weekly SC injections to start within one day thereafter, not included in cost.
[d] IMS Quintiles Delta PA wholesale price (January 2017), also the price submitted to the CDR.[23]
Source: Ontario Drug Benefit Formulary or Exceptional Access Program (January 2017) list prices unless otherwise indicated. Patient weight assumed to be 75 kg. Excess medication in vials is assumed wasted. Annual period assumes 52 weeks, 26 × 2 weeks, 13 × 4 weeks, or 364 days per year.

APPENDIX 1: REVIEWER WORKSHEETS

TABLE 2: SUMMARY OF MANUFACTURER'S SUBMISSION

Drug Product	Sarilumab (Kevzara)
Treatment	Sarilumab 200 mg every 2 weeks with conventional DMARD therapy, 15% of patients reducing to 150 mg every 2 weeks for management of neutropenia, thrombocytopenia, and elevated liver enzymes
Comparators	With conventional DMARDs: • Anakinra • Abatacept IV or SC • Adalimumab • Certolizumab pegol • Etanercept (branded or SEB) • Golimumab IV or SC • Infliximab (branded or SEB) • Rituximab • Tocilizumab IV or SC • Tofacitinib
Study Question	From the perspective of a Canadian public payer, what is the incremental cost of sarilumab compared with other biologic DMARDs and targeted synthetic DMARD in patients with rheumatoid arthritis and who have an inadequate response or are intolerant to one or more biologic or non-biologic DMARDs?
Type of Economic Evaluation	Cost comparison
Target Population	Adults with rheumatoid arthritis who have an inadequate response or are intolerant to one or more biologic or non-biologic DMARDs
Perspective	Public payer
Outcome Considered	Average annual drug cost of first 3 years of therapy
Key Data Sources	
Cost	ODB list prices, Saskatchewan Formulary list prices
Clinical Efficacy	MONARCH and ASCERTAIN trials and manufacturer sponsored NMA
Harms	ASCERTAIN trial and NMA
Time Horizon	3 years (with 1 year equalling 364 days); no discount applied
Results for Base Case	Sarilumab had an average cost of $18,200 per year over three years of therapy, which was more expensive than that of anakinra, certolizumab, golimumab IV, standard doses of infliximab SEB, tocilizumab IV and standard dose SC, and tofacitinib, but less than abatacept, adalimumab, etanercept, golimumab SC, branded infliximab, high-dose SEB infliximab, and high-dose tocilizumab SC.

DMARD = disease-modifying antirheumatic drug; IV = intravenous; NMA = network meta-analysis; ODB = Ontario Drug Benefit Formulary; SC = subcutaneous; SEB = subsequent entry biologic.

Manufacturer's Results

In the manufacturer's base case, and at the submitted price of $700 per 150 mg or 200 mg syringe, the average annual cost of sarilumab over the first three years of therapy for rheumatoid arthritis (RA) was $18,200 per patient, while the average annual cost of the first three years of therapy with other biologics ranged from $9,326 to $21,108 per patient ($101,719 per patient if the highest recommended dose of infliximab is included). Thus, the incremental cost of sarilumab therapy ranged from a savings of $2,907 per patient per year to an additional cost of $8,874 per patient per year over the first three years of therapy. See Table 3 for details. The cost of subsequent entry biologic (SEB) etanercept was not available at the time of the manufacturer's analysis.

TABLE 3: MANUFACTURER'S RESULTS COMPARING THE AVERAGE ANNUAL COST OF THE FIRST THREE YEARS OF SARILUMAB THERAPY WITH THAT OF OTHER BIOLOGICS FOR THE TREATMENT OF RHEUMATOID ARTHRITIS

Comparator		3-Year Average Annual Cost ($)	Incremental Cost (Savings) of Sarilumab vs. Comparator ($)
Sarilumab (Kevzara)		18,200.00	Reference
Anakinra (Kineret)		17,492.78	707.22
Abatacept IV (Orencia IV)		19,602.00	(1,402.00)
Abatacept SC (Orencia SC)		19,509.82	(1,309.82)
Adalimumab (Humira)		20,019.22	(1,819.22)
Certolizumab (Cimzia)		18,163.27	36.73
Etanercept (Enbrel)		21,107.97	(2,907.97)
Etanercept SEB (Brenzys)		Price not available at time of analysis	Not available
Golimumab IV (Simponi IV)		16,540.00	1,660.00
Golimumab SC (Simponi SC)		18,662.04	(462.04)
Infliximab (Remicade)	3 mg/kg 10 mg/kg	19,751.20 101,718.68	(1,551.20) (83,518.68)
Infliximab SEB (Inflectra)	3 mg/kg 10 mg/kg	10,500.00 54,075.00	7,700.00 (35,875.00)
Rituximab (Rituxan)	1 course 2 courses	9,326.41 18,652.83	8,873.59 (452.83)
Tocilizumab IV (Actemra IV)	4 mg/kg 8 mg/kg	9,402.12 16,785.37	8,797.88 1,414.63
Tocilizumab SC (Actemra SC)	Q2W QW	9,230.00 18,460.00	8,970.00 (260.00)
Tofacitinib (Xeljanz)		17,150.59	1,049.41

IV = intravenous; Q2W = every two weeks; QW = weekly; SC = subcutaneous; SEB = subsequent entry biologic; vs. = versus.
Table 1 unit costs and dosing. Average annual cost includes the first three years of therapy divided by three and does not include dispensing fees, administration fees, markups, or discounting. Patient weight assumed to be 75 kg. Excess medication in vials was assumed to be wasted.

The manufacturer concluded that sarilumab for RA was more expensive than anakinra, certolizumab, golimumab intravenous (IV), infliximab SEB, rituximab, tocilizumab biweekly, and tofacitinib, but less expensive than abatacept, adalimumab, etanercept, golimumab subcutaneous (SC), tocilizumab weekly, and branded infliximab.

The manufacturer also provided results for patients weighing 50 kg and 100 kg. As sarilumab dosing and thus cost does not vary by weight, it became relatively more expensive when patients weighed 50 kg

and relatively less expensive when patients weighed 100 kg when compared with biologics with weight-based dosing such as abatacept IV, golimumab IV, infliximab, and tocilizumab IV.

In addition, the manufacturer conducted sensitivity analyses across all three assumed patient weights incorporating the World Health Organization Defined Daily Dose for each comparator, an annual compliance rate of 80%, the exclusion of drug wastage, and including markups and dispensing fees. These analyses altered the absolute costs of sarilumab and comparators but not the conclusion that the cost of sarilumab is within the range of biologic comparators for the treatment of adults with RA.

CADTH Common Drug Review Results

The CADTH Common Drug Review (CDR) reviewers considered the manufacturer's list of comparators to be appropriate with the addition of a newly available public price for etanercept SEB. However, rather than presenting an average annual drug costs over the first three years of therapy, given the unknown and potentially long-term length of therapy, CDR reviewers considered it more appropriate to present the comparative drug costs of the first and average subsequent years of therapy separately. Results remained similar to the manufacturer's (see Table 4), although as several IV comparators are less expensive in subsequent years than the first (which includes loading doses), the overall incremental drug cost of sarilumab is increased (or incremental savings decreased) the longer a patient remains on therapy.

The annual drug cost of sarilumab is $2,340 more per patient than that of SEB etanercept ($15,860 per patient.

TABLE 4: CDR'S RESULTS COMPARING THE AVERAGE ANNUAL COST OF THE FIRST AND SUBSEQUENT YEARS OF SARILUMAB THERAPY WITH THAT OF OTHER BIOLOGICS FOR THE TREATMENT OF RHEUMATOID ARTHRITIS

Comparator		First Year		Average Annual Cost Thereafter	
		Cost ($)	Incremental Cost (Savings) of Sarilumab vs. Comparator ($)	Cost ($)	Incremental Cost (Savings) of Sarilumab vs. Comparator ($)
Sarilumab (Kevzara)		18,200.00	Reference	18,200.00	Reference
Anakinra (Kineret)		17,492.78	707.22	17,492.78	707.22
Abatacept IV (Orencia IV)		20,582.10	(2,382.10)	19,111.95	(911.95)
Abatacept SC (Orencia SC)		20,455.05	(2,255.05)	19,037.20	(837.20)
Adalimumab (Humira)		20,019.22	(1,819.22)	20,019.22	(1,819.22)
Certolizumab (Cimzia)		19,935.30	(1,735.30)	17,277.26	922.74
Etanercept (Enbrel)		21,107.97	(2,907.97)	21,107.97	(2,907.97)
Etanercept SEB (Brenzys)		15,860.00	2,340.00	15,860.00	2,340.00
Golimumab IV (Simponi IV)		17,367.00	833.00	16,126.50	2,073.50
Golimumab SC (Simponi SC)		18,662.04	(462.04)	18,662.04	(462.04)
Infliximab (Remicade)	3 mg/kg 10 mg/kg	23,701.44 99,743.56	(5,501.44) (81,543.56)	17,776.08 102,706.24	423.92 (84,506.24)
Infliximab SEB (Inflectra)	3 mg/kg 10 mg/kg	12,600.00 53,025.00	5,600.00 (34,825.00)	9,450.00 54,600.00	8,750.00 (36,400.00)
Rituximab (Rituxan)	1 course 2 courses	9,326.42 18,652.84	8,873.58 (452.84)	9,326.42 18,652.84	8,873.58 (452.84)
Tocilizumab	4 mg/kg	9,402.12	8,797.88	9,402.12	8,797.88

Comparator		First Year		Average Annual Cost Thereafter	
		Cost ($)	Incremental Cost (Savings) of Sarilumab vs. Comparator ($)	Cost ($)	Incremental Cost (Savings) of Sarilumab vs. Comparator ($)
IV (Actemra IV)	8 mg/kg	15,097.77	3,102.23	17,629.17	570.83
Tocilizumab SC (Actemra SC)	Q2W QW	9,230.00 18,460.00	8,970.00 (260.00)	9,230.00 18,460.00	8,970.00 (260.00)
Tofacitinib (Xeljanz)		17,150.59	1,049.41	17,150.59	1,049.41

IV = intravenous; Q2W = every two weeks; QW = weekly; SC = subcutaneous; SEB = subsequent entry biologic; vs. = versus.
See Table 1 for unit costs and dosing. Average annual cost does not include dispensing fees, administration fees, markups, or discounting. Patient weight assumed to be 75 kg. Excess medication in vials was assumed to be wasted.

Of particular interest is the comparison of sarilumab to adalimumab and etanercept, the most prescribed anti–tumour necrosis factors for the treatment of RA,[21,22] and tocilizumab, an interleukin-6 inhibitor like sarilumab. Both adalimumab and tocilizumab IV were compared with sarilumab in head-to-head trials, in MONARCH[15,16] and ASCERTAIN,[17] respectively.

In MONARCH, sarilumab monotherapy showed a statistically significant and clinically meaningful clinical response, clinical remission, and improvement in physical functioning compared with adalimumab monotherapy, with a similar proportion of patients experiencing at least one serious adverse event and withdrawing due to adverse events (see CDR Clinical Report, sections 3.5 and 3.6). At the submitted price, sarilumab is less expensive than the list price of adalimumab.

ASCERTAIN was a small safety study comparing sarilumab plus conventional disease-modifying antirheumatic drugs (DMARDs) with tocilizumab IV plus conventional DMARDs in patients with an inadequate response or intolerance to anti–tumour necrosis factor therapy. Efficacy outcomes were considered exploratory, and statistical analyses were not conducted. There were higher rates of discontinuation due to adverse events in the sarilumab group (15.7%) compared with tocilizumab IV (3.9%), as well as [redacted], although given the small size of the trial, these conclusions are uncertain.

At the submitted price, sarilumab ($18,200 per patient per maintenance year) is more expensive than tocilizumab IV at either the 4 mg/kg or 8 mg/kg every four week dosing schedule ($9,402 to $17,629 per patient per maintenance year). Sarilumab is also more expensive than biweekly tocilizumab SC at the listed price ($9,230 per patient) but slightly less expensive than weekly tocilizumab SC ($18,460 per patient). Thus the relative cost of sarilumab compared with tocilizumab SC depends on the proportion of patients using weekly versus biweekly tocilizumab SC. In ASCERTAIN,[17] [redacted] of patients in the tocilizumab IV arm escalated treatment from 4 mg/kg to 8 mg/kg every four weeks, although the majority of them did so at [redacted], much earlier than escalation would be likely to occur in clinical practice. The proportion of patients escalating tocilizumab SC in clinical practice in Canada is unknown;[19] the clinical expert consulted by CDR roughly estimated that between 50% and 75% of patients continuing on tocilizumab SC eventually escalate to weekly dosing, though it would be unlikely to occur before 12 weeks of therapy in order to assess clinical response to initial dosing.

CDR conducted an exploratory analysis to compare the annual cost of sarilumab therapy with that of the weighted average cost of tocilizumab, assuming a varying proportion of patients using weekly as opposed to biweekly dosing. At the submitted price, sarilumab is more expensive than tocilizumab SC unless more than 97% or more of tocilizumab SC patients are using weekly dosing (see TABLE 5.) Additionally, CDR calculated the percentage price reduction required for sarilumab to be cost-neutral to tocilizumab SC across the all proportions of patients using weekly tocilizumab dosing. For example, if the approximately [redacted] of tocilizumab IV patients who escalated to 8 mg/kg dosing in the ASCERTAIN trial is assumed to be a reasonable proxy for tocilizumab SC escalation in clinical practice, then a price [redacted] would be necessary for the annual cost of sarilumab to be cost-neutral to the weighted average cost of tocilizumab SC.

While no head-to-head data exist comparing sarilumab with etanercept, the manufacturer's network meta-analysis [redacted] sarilumab and other biologics for the treatment of RA, although limitations exist (see CDR Clinical Report Appendix 6). At the submitted price, the annual cost of sarilumab is $2,908 less than that of branded etanercept but $2,340 per patient per year more than SEB etanercept. Should etanercept SEB displace branded etanercept in clinical practice, a price reduction of 13% would be necessary for the annual cost of sarilumab to be cost-neutral to etanercept.

TABLE 5: EXPLORATORY ANALYSIS COMPARING THE ANNUAL COST OF TOCILZUMAB SC WITH VARYING PROPORTIONS OF PATIENTS USING WEEKLY DOSING TO THAT OF SARILUMAB

Annual Maintenance Cost	Proportion of Tocilizumab SC Patients Using Weekly Dosing (vs. Biweekly)										
	0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%
Sarilumab	$18,200										
Weighted average cost tocilizumab	$9,230	$10,153	$11,076	$11,999	$12,922	$13,845	$14,768	$15,691	$16,614	$17,537	$18,460
Incremental cost (savings) of sarilumab compared with tocilizumab SC	$8,970	$8,047	$7,124	$6,201	$5,278	$4,355	$3,432	$2,509	$1,586	$663	($260)
Percentage price reduction for sarilumab to be cost-neutral to weighted average tocilizumab SC cost	49%	44%	39%	34%	29%	24%	19%	14%	9%	4%	Not applicable

SC = subcutaneous; vs. = versus.
Patients are assumed to be on the regular or escalated dose of tocilizumab SC for all 52 weeks of the calculated year.

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