Common Drug Review
Pharmacoeconomic Review Report

July 2015

Drug	golimumab (Simponi) IV
Indication	To be used in combination with methotrexate (MTX), for the treatment of adult patients with moderately to severely active rheumatoid arthritis.
Listing request	Golimumab (Simponi IV), in combination with methotrexate (MTX), be listed for the treatment of adult patients with moderately to severely active rheumatoid arthritis following failure of MTX or other disease modifying antirheumatic drugs (DMARDs).
Manufacturer	Janssen Inc.

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ABBREVIATIONS

bDMARD	biologic disease-modifying antirheumatic drug
CADTH	Canadian Agency for Drugs and Technologies in Health
CDR	CADTH Common Drug Review
IV	intravenous
RA	rheumatoid arthritis
SC	subcutaneous
TNF-alpha	tumour necrosis factor-alpha

SUMMARY

Simponi IV (intravenous golimumab) is a tumour necrosis factor-alpha (TNF-alpha) inhibitor that is indicated, in combination with methotrexate, for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA). IV golimumab is available as 50 mg vials for intravenous infusion as 2 mg/kg at Weeks 0 and 4, then every eight weeks thereafter. The manufacturer has submitted a price of $826.86 per vial. A subcutaneous (SC) form of golimumab is currently reimbursed by several public plans for patients with RA.

The manufacturer submitted a cost-minimization analysis in which only the drug costs of IV golimumab were compared with those of SC golimumab, IV infliximab, and IV abatacept based on an average patient weight of 75 kg. Indirect health care costs, such as routine patient care, serious adverse events (SAEs), hospitalization, and drug administration were assumed to be the same for the three drugs. The manufacturer's analysis had several limitations, the most significant of which was assuming an average patient weight of 75 kg for the analysis rather than using a range of plausible patient weights. Recalculations by the Canadian Agency for Drugs and Technologies in Health (CADTH), accounting for wastage as well as including other relevant comparators, updated drug prices, and a range of patient body weights, suggested that when used in patients who weigh between 70 kg and 75 kg, the three-year treatment cost of IV golimumab ($41,982) is $4,489 to $13,122, which is 8% to 20% less costly than SC golimumab, IV infliximab, IV abatacept, SC adalimumab, IV etanercept, or SC certolizumab. However, IV golimumab is more costly than all other treatment options in patients who weigh between 75 kg and 90 kg, and is frequently the most costly treatment option in patients who weigh more than 90 kg.

REVIEW OF THE PHARMACOECONOMIC SUBMISSION

1. INTRODUCTION

Simponi IV (golimumab) is a tumour necrosis factor-alpha (TNF-alpha) inhibitor that is indicated, in combination with methotrexate, for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA). The approved dose for IV golimumab is 2 mg/kg given as a 30-minute intravenous (IV) infusion at Weeks 0 and 4, then every eight weeks thereafter. The product is available as vials of 50 mg/4.0 mL solution at a price of $826.86 per vial.

Golimumab is also available as a subcutaneous (SC) injection, which is reimbursed by several public plans in Canada. In 2010, the Canadian Expert Drug Advisory Committee (CEDAC) recommended that SC golimumab be listed in a similar manner to other TNF-alpha inhibitors for the management of moderately to severely active RA.

1.1 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. Costs are manufacturers' list prices, unless otherwise specified.

TABLE 1: COST COMPARISON TABLE FOR BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS

Comparators	Strength	Dose Form	Price ($)	Average Dose	Yearly Drug Cost ($)
IV Golimumab (Simponi IV)	**50 mg**	**Vial[a]**	**826.8600[b]**	**Year 1: 2 mg/kg Weeks 0 and 4, then every 8 weeks thereafter[c]**	Year 1:[d] 23,152.08 Thereafter:[d] 21,498.36
SC Golimumab (Simponi SC)	50 mg	Pre-filled syringe	1520.2100	50 mg monthly	18,243
Adalimumab (Humira)	40 mg	Pre-filled syringe	740.3600	40 mg every other week	19,249
Certolizumab pegol (Cimzia)	200 mg	Pre-filled syringe	664.5100	Year 1: 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	194.2500[e]	50 mg weekly; 25 mg doses can also be administered every 3 or 4 days	20,202
	50 mg	Pre-filled syringe	388.6100[e]		20,208
Infliximab (Remicade)	100 mg/vial	Vial[a]	987.5600	Year 1: 3 mg/kg at Weeks 0, 2, and 6, then every 8 weeks[f] thereafter[c] Thereafter: every 8 weeks[c] Depending on clinical response, dose can be increased to 10 mg/kg and/or treatment can be given as often as every 4 weeks	3 mg/kg at Weeks 0, 2, and 6, then every 8 weeks thereafter. Year 1:[g] 23,701.44 Thereafter:[g] 19,257.42 10 mg/kg at Weeks 0, 2, and 6, then every 4 weeks thereafter (13 doses/year) Yearly: $102,706.24
Tocilizumab (Actemra)	80 mg/4 mL 200 mg/10 mL 400 mg/20 mL	Vial[a]	179.2000 448.0000 896.0000	Depending on clinical response, 4 mg/kg every 4 weeks; dose can be increased to 8 mg/kg[c]	4 mg/kg:[h] 10,483.20 8 mg/kg:[h] 18,636.80
IV Abatacept (Orencia IV)	250 mg	Vial	480.4100	Year 1: Dose at Weeks 0, 2, and 4, then every 4 weeks thereafter	Year 1:[i] 20,177 Thereafter:[h] 18,736
SC Abatacept (Orencia SC)	125 mg	Pre-filled syringe	351.8625	125 mg weekly[j]	18,297[j]
Anakinra (Kineret)	100 mg	Pre-filled syringe	47.5800[e]	100 mg daily	17,367
Rituximab	100 mg/	Vial	453.1000	A course consists of 1,000 mg	9,062 per course

Comparators	Strength	Dose Form	Price ($)	Average Dose	Yearly Drug Cost ($)
(Rituxan)	10 mL 500 mg/ 50 mL		2265.5000	infusions at Weeks 0 and 2	

IV = intravenous; SC = subcutaneous.
Note: Prices were based on average patient weights of > 75 kg to ≤ 80 kg. (For detailed prices for other patients' weights see Table 2 and Figure 1.)
[a] Single-use product; the prepared infusion solution of tocilizumab should be used immediately although it is stable for 24 hours.
[b] Manufacturer's submitted price.
[c] Including wastage of any unused proportion of opened vial.
[d] Average of seven doses for the first year and 6.5 doses per year thereafter.
[e] Saskatchewan Formulary (accessed January 2014).
[f] In the case of incomplete response, dosing can be increased up to 10 mg/kg and/or treatment can be given as often as every four weeks.
[g] Average of eight doses for the first year and 6.5 doses per year thereafter.
[h] Average of 13 doses per year.
[i] Assumes 14 doses in Year 1 (one dose every four weeks with an additional dose at Week 2).
[j] Abatacept-naive patients require a single, weight-based loading dose of 500 mg, 750 mg, or 1,000 mg IV abatacept, with weekly SC injections to start within one day thereafter.
Source: Ontario Drug Benefit Formulary Exceptional Access Program (accessed January 2014) unless otherwise indicated.

2. SUMMARY OF PHARMACOECONOMIC SUBMISSION

The manufacturer submitted a cost-minimization analysis from the perspective of the public drug plan over a time horizon of three years. The manufacturer justified the cost-minimization approach based on the results of an indirect treatment comparison that reported similar efficacy and safety for IV golimumab compared with SC golimumab, IV infliximab, and IV abatacept).[1] Health Canada approved the use of IV golimumab for patients with moderately to severely active RA. However, the submitted analysis targeted only those who had failed to achieve responses with methotrexate.

In the base-case analysis, the manufacturer considered only drug costs reimbursed by the drug plans. The costs of IV infusions were not included, since the manufacturers cover the administration costs of the IV infusion for IV golimumab and IV infliximab, and the manufacturer assumed that this would probably also be the case for IV abatacept. In the base case, a 5% discount rate was used and a mark-up of 8% and a dispensing fee of $8 were included. The results suggested that, for patients with an average weight of 75 kg, IV golimumab was cost saving compared with SC golimumab, IV infliximab, or IV abatacept over the first three years of treatment, representing savings of $4,208 (7.6%), $16,056 (23.9%), and $9,982 (16.3%), respectively.

The results of the sensitivity analyses provided by the manufacturer were similar to the results of the base-case analysis.

3. KEY LIMITATIONS

3.1 Comparators

The manufacturer considered only IV abatacept, IV infliximab, and SC golimumab as comparators. Given that there are other bDMARDs indicated for RA, the CADTH Common Drug Review (CDR) reanalysis included additional comparators that were included in the submitted indirect treatment comparison and that were shown to have efficacy and safety profiles similar to that of IV golimumab. The included comparators were SC abatacept, IV tocilizumab, SC adalimumab, IV etanercept, and SC certolizumab (Table 2 and Figure 1). Of note, both IV abatacept and IV tocilizumab can be used in different doses, and because the indirect treatment comparison included the lowest dose for one of these drugs, the CDR reanalysis was limited to these doses.

3.2 Drug Costs

The treatments costs were based on outdated product prices (dated August 2013). CDR updated the prices to January 2014 (see Table 1), and CDR reviewers used the updated prices for their reanalysis. (Table 2 and Figure 1).

Another limitation was that the model assumed that the costs related to IV administration would be covered by the manufacturers of the included IV drugs; however, this assumption may not be operationalized by all plans, especially federal plans for patients in remote areas who would still need to travel. These plans would incur additional costs associated with IV treatment administration, which were not accounted for in the analysis.

3.3 Dosing

The manufacturer calculated an annual cost for IV abatacept based on 15 doses in the first year; however, the suggested dosing for the first year of IV abatacept is at Weeks 0, 2, and 4, then every four weeks thereafter (i.e., the first treatment year requires 14 doses rather than 15 doses). The correct dosing schedule was used in the CDR reanalysis (see Table 2 and Figure 1).

3.4 Weight-Based Dosing for IV Drugs

IV golimumab is dosed according to the patient's weight. The analysis in the manufacturer's submission assumed an average patient weight of 75 kg for the analysis, based on the average weight of patients in the GO-FURTHER trials.[2,3] However, the use of an average weight does not reflect the variation in patients' weights seen in clinical practice. Therefore, CDR reviewers recalculated the treatment costs over a range of patient weights (see Table 2 and Figure 1).

4. ISSUES FOR CONSIDERATION

4.1 CADTH Common Drug Review Reanalysis

CDR carried out a reanalysis of the relative treatment costs of IV golimumab over three years using the correct dosing schedules and updated product costs, and including wastage for all appropriate comparators over a range of body weights. The results of these analyses are presented in Table 2 and Figure 1. These analyses showed that whether IV golimumab is cost saving depends on body weight. When used in patients who weigh between 70 kg and 75 kg, IV golimumab is $4,489 to $13,122 less costly compared with SC golimumab, IV infliximab, IV abatacept, SC adalimumab, IV etanercept, or SC certolizumab. This concurs with the conclusions of the manufacturer's analysis that IV golimumab will likely be cost saving in patients with an average weight of 75 kg. However, IV golimumab is consistently more costly than low-dose IV tocilizumab, irrespective of body weight. In addition, IV golimumab is more costly than all other treatment options in patients who weigh between 75 kg and 90 kg, and is frequently the most costly treatment option in patients who weigh more than 90 kg (see Table 2 and Figure 1).

TABLE 2: CADTH COMMON DRUG REVIEW CALCULATION OF THREE-YEAR TREATMENT COSTS FOR IV GOLIMUMAB RELATIVE TO OTHER BDMARDS, BY BODY WEIGHT

Weight (kg)	SC Golimumab [$] (% difference)	IV Infliximab[a] [$] (% difference)	IV Abatacept [$] (% difference)	IV Tocilizumab[b] [$] (% difference) (Low-dose)	SC Adalimumab [$] (% difference)	IV Etanercept [$] (% difference)	SC Certolizumab [$] (% difference)
40	22,313 (40)	8,751 (20)	5,631 (14)	–19,533 (–134)	25,414 (43)	28,350 (45)	21,493 (39)
> 40, ≤ 50	22,313 (40)	8,751 (20)	5,631 (14)	–15,945 (–88)	25,414 (43)	28,350 (45)	21,493 (39)
> 50, ≤ 55	5,309 (9)	–8,253 (–19)	–11,373 (–29)	–25,772 (–101)	8,410 (14)	11,346 (18)	4,489 (8)
> 55, ≤ 60	5,309 (9)	–8,253 (–19)	8,386 (14)	–25,772 (–101)	8,410 (14)	11,346 (18)	4,489 (8)
> 60, ≤ 65	5,309 (9)	–8,253 (–19)	8,386 (14)	–25,772 (–101)	8,410 (14)	11,346 (18)	4,489 (8)
> 65, ≤ 70	5,309 (9)	13,122 (20)	8,386 (14)	–25,772 (–101)	8,410 (14)	11,346 (18)	4,489 (8)
> 70, ≤ 75	5,309 (9)	13,122 (20)	8,386 (14)	–18,595 (–57)	8,410 (14)	11,346 (18)	4,489 (8)
> 75, ≤ 80	–11,695 (–21)	–3,882 (–6)	–8,618 (–14)	–35,599 (–109)	–8,594 (–14)	–5,658 (–9)	–12,515 (–22)
> 80, ≤ 90	–11,695 (–21)	–3,882 (–6)	–8,618 (–14)	–35,599 (–109)	–8,594 (–14)	–5,658 (–9)	–12,515 (–22)
> 90, ≤ 95	–11,695 (–21)	–3,882 (–6)	–8,618 (–14)	–32,011 (–89)	–8,594 (–14)	–5,658 (–9)	–12,515 (–22)
> 95, ≤ 100	–11,695 (–21)	17,493 (20)	–8,618 (–14)	–32,011 (–89)	–8,594 (–14)	–5,658 (–9)	–12,515 (–22)
> 100, ≤ 110	–28,699 (–51)	489 (1)	–5,863 (–7)	–41,838 (–97)	–25,598 (–43)	–22,662 (–36)	–29,519 (–53)
> 110, ≤ 120	–28,699 (–51)	489 (1)	–5,863 (–7)	–41,838 (–97)	–25,598 (–43)	–22,662 (–36)	–29,519 (–53)

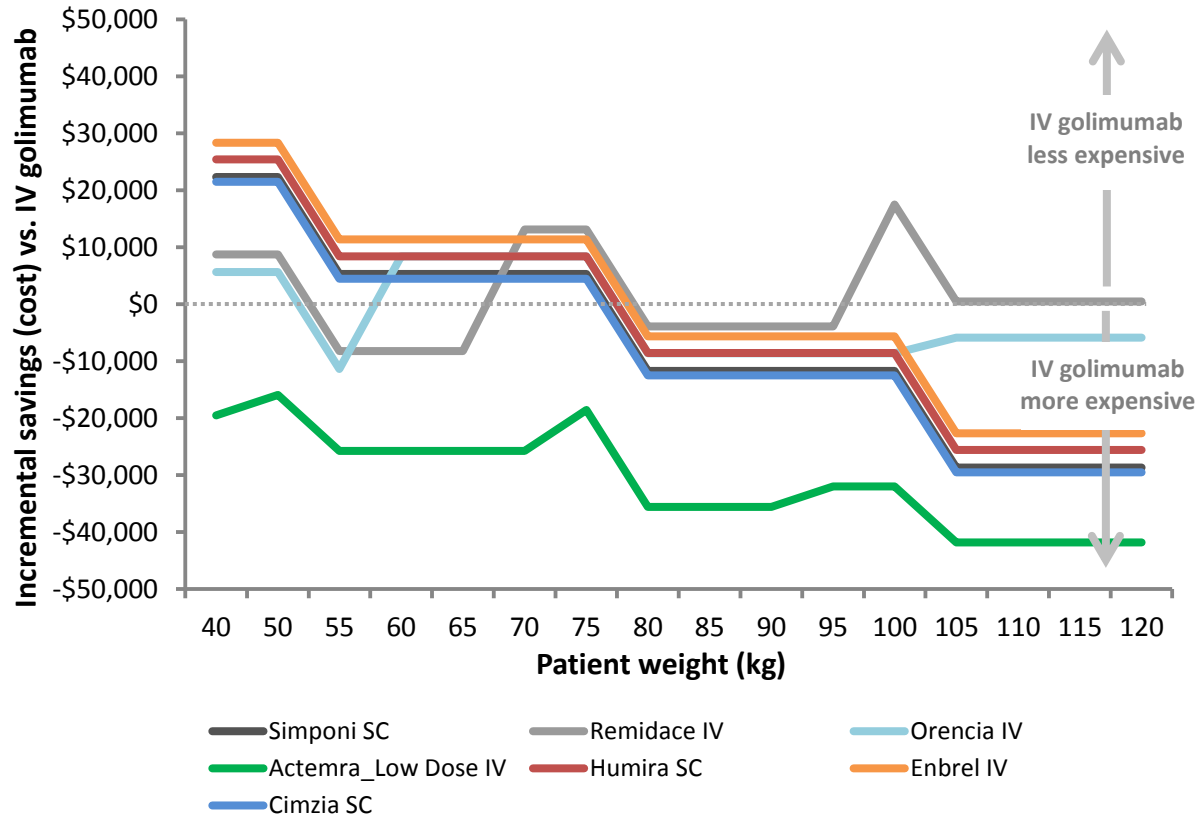
bDMARD = biologic disease-modifying antirheumatic drug; IV = intravenous; SC = subcutaneous.

Note: Values were calculated as the cost of treatment for the comparator versus the cost of treatment with IV golimumab. Negative values indicate a cost burden associated with IV golimumab; positive values indicate cost savings associated with IV golimumab.

[a] The reanalysis considered a dose of 3 mg/kg at Weeks 0, 2, and 6, then 3 mg/kg every eight weeks thereafter. Depending on response, however, the dose can be increased up to 10 mg/kg and/or treatment can be given as often as every four weeks. The choice of dose in the reanalysis was based on the available evidence of equivalent efficacy and safety compared with IV golimumab, as shown in the submitted indirect treatment comparison.[1] Using higher or more frequent doses of IV infliximab would incur additional costs.

[b] The reanalysis considered doses of 4 mg/kg every four weeks. However, the approved product monograph allows a higher dose of 8 mg/kg every four weeks depending on response. The choice of dose in the reanalysis was based on the available evidence of equivalent efficacy and safety compared with IV golimumab, as shown in the submitted indirect treatment comparison.[1] Using a higher dose of IV tocilizumab would incur additional costs.

FIGURE 1: INCREMENTAL THREE-YEAR TREATMENT COSTS FOR IV GOLIMUMAB RELATIVE TO OTHER BDMARDS, BY BODY WEIGHT



bDMARD = biologic disease-modifying antirheumatic drug; IV = intravenous; SC = subcutaneous

Note: Values were obtained from Table 2 and represent the difference in treatment cost over three years for each comparator versus IV golimumab. Positive values indicate cost savings associated with IV golimumab.

5. CONCLUSIONS

IV golimumab is available at a price of $826.86 per vial. When administered at the recommended dose of 2 mg/kg at Weeks 0 through 4, then every eight weeks thereafter, the cost of treatment with IV golimumab is $23,152 in the first year and $21,498 annually thereafter (based on an average patient weight of 75 kg to 80 kg). When only drug costs are considered, whether IV golimumab is cost saving or more costly relative to its comparators depends on body weight. For patients who weigh between 70 kg and 75 kg, IV golimumab is $4,489 to $13,122 less costly over three years compared with SC golimumab, IV infliximab, IV abatacept, SC adalimumab, IV etanercept, or SC certolizumab. However, in patients who weigh between 75 kg and 90 kg, IV golimumab is more costly than all other treatment options, and it is frequently the most costly treatment option in patients who weigh more than 90 kg. The price of IV golimumab would need to be reduced by 18% (to $679.70) to equal the average cost of other bDMARDs, and by 52% (to $395.10) to equal the cost of the lowest-priced bDMARD (low-dose tocilizumab).

APPENDIX 1: PRICE REDUCTION ANALYSIS

CADTH Common Drug Rewview (CDR) reviewers calculated the price reduction that would be required to produce a three-year cost of IV golimumab that would be equivalent to (a) the average cost of other biologic disease-modifying antirheumatic drugs (bDMARDs), and (b) the lowest-priced bDMARD currently reimbursed by public plans in Canada, based on a body weight of between 75 kg and 90 kg.

As shown in Table 3, the price of intravenous (IV) golimumab would need to be reduced by 18% to equal the average price of other bDMARDs, which would result in a cost consequence ranging from incremental costs of $23,468 to savings of $8,248 over three years. The price of IV golimumab would need to be reduced by 52% to equal the cost of the lowest-priced bDMARD (low-dose tocilizumab), which would result in cost savings of $0 to $31,717 over three years.

TABLE 3: CADTH COMMON DRUG REVIEW ANALYSIS OF PRICE REDUCTION SCENARIOS FOR IV GOLIMUMAB

Scenario	Current Price ($)	Reduction Needed (%)	Reduced Price ($)	Savings[a] ($) (min. to max.)
Price reduction needed to equal average cost of alternatives[b]	826.86	17.79	679.73	–23,468.84 to 8,247.93
Price reduction needed to equal cheapest alternative (IV tocilizumab 4 mg/kg)		52.22	395.06	0 to 31,716.77
Price reduction needed to equal SC certolizumab		18.36	675.05	–23,083.47 to 8,633.30
Price reduction needed to equal SC golimumab		17.16	685.01	–23,904.14 to 7,7812.63
Price reduction needed to equal IV abatacept		12.64	722.33	–26,980.90 to 4,735.87
Price reduction needed to equal SC adalimumab		12.61	722.63	–27,005.91 to 4,710.86
Price reduction needed to equal IV etanercept		8.30	758.23	–29,940.71 to 1,776.06
Price reduction needed to equal the most expensive alternative (IV infliximab)		5.69	779.77	–31,716.77 to 0

CDR = CADTH Common Drug Review; IV = intravenous; min = minimum; max = maximum; SC = subcutaneous.
Note: Prices were based on an average patient weight of > 75 kg to ≤ 80 kg.
[a] Savings per patient over three years (including the initiation year).
[b] Alternatives included in the average price were IV tocilizumab, SC adalimumab, IV etanercept, and SC certolizumab, IV abatacept, IV infliximab, and SC golimumab.

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