Common Drug Review
Pharmacoeconomic Review Report

November 2014

Drug	golimumab (Simponi)
Indication	Adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to, or have medical contraindications for, conventional therapies including corticosteroids, aminosalicylates, azathioprine or 6-mercaptopurine
Listing request	As per indication
Manufacturer	Janssen Inc.

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The report contains an evidence-based clinical and/or pharmacoeconomic drug review, based on published and unpublished material, including manufacturer submissions; studies identified through independent, systematic literature searches; and patient-group submissions. In accordance with *CDR Update — Issue 87*, manufacturers may request that confidential information be redacted from the CDR Clinical and Pharmacoeconomic Review Reports.

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ABBREVIATIONS

5-ASA	5-aminosalicylic acid
CDR	Common Drug Review
CMA	cost-minimization analysis
EQ-5D	EuroQol 5-Dimension Health-Related Quality of Life Questionnaire
HRQoL	health-related quality of life
ICER	incremental cost-effectiveness ratio
ICUR	incremental cost-utility ratio
ITC	indirect treatment comparison
IV	intravenous
PURSUIT	Program of Ulcerative Colitis Research Studies Utilizing an Investigational Treatment
RCT	randomized controlled trial
TNF	tumour necrosis factor
UC	ulcerative colitis

TABLE 1: SUMMARY OF THE MANUFACTURER'S ECONOMIC SUBMISSION

Drug Product	Golimumab (Simponi)
Study Question	Cost-effectiveness analysis of golimumab, infliximab, and adalimumab for treatment of patients with moderately to severely active UC who are nonresponsive to conventional therapy
Type of Economic Evaluation	Cost-utility analysis
Target Population	Adult patients with moderately to severely active UC (defined by Mayo score of 6 to 12 and endoscopic subscore ≥ 2)
Treatment	Golimumab 50 mg and 100 mg
Outcome(s)	QALYs
Comparators	• Conventional therapy (placebo) • Infliximab 5 mg/kg • Adalimumab 40 mg
Perspective	Public payer perspective
Time Horizon	10 years
Manufacturer's Results (Base Case)	Golimumab 50 mg vs. conventional therapy = $41,591 per QALY Golimumab 100 mg vs. conventional therapy = $42,271 per QALY
Key Limitations and CDR Estimate(s)	A number of limitations around justification of inputs and transparency of the manufacturer's economic model were noted that limited CDR's ability to verify and test the model. Some key limitations included: • The manufacturer stated that treatment efficacies were based on their ITC; this appears to be done only for golimumab and not the comparators as such it may be biasing results in favour of golimumab. • Underlying relationship between outcome probabilities requiring the restriction of input of values for all treatments within a specific range may bias results in favour of golimumab. • Use of a time horizon beyond RCT duration may have resulted in low ICURs for golimumab, given assumptions around the durability of the treatment effect; use of reduced time horizons led to incremental cost-utility ratios of –$104,000 per QALY. • Discrepancies found within report renders validation of model and verification of results challenging.

CDR = Common Drug Review; ICUR = incremental cost-utility ratio; ITC = indirect treatment comparison; QALY = quality-adjusted life-year; RCT = randomized controlled trial; UC = ulcerative colitis.

SUMMARY

Background

Golimumab (Simponi) is an anti-tumour necrosis factor (TNF) agent indicated for the treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response to, or have medical contraindications for, conventional therapy (including corticosteroids, aminosalicylic acid, azathioprine, or 6-mercaptopurine), for inducing and maintaining clinical response (reduction in signs and symptoms). Golimumab is available in 50 mg/0.5 mL and 100 mg/1.0 mL pre-filled syringes at a price of $1,490.41 per syringe, regardless of strength. The recommended dosing for UC is 200 mg at week 0, 100 mg at week 2, and 50 mg or 100 mg every four weeks thereafter as maintenance therapy.

Summary of Economic Analysis

The manufacturer submitted a cost-utility analysis and a cost-minimization analysis (Appendix 4). The cost-utility analysis was considered the primary analysis, as biologic therapies are not listed by the majority of public drug plans, and the results of the manufacturer's indirect treatment comparison suggest that golimumab is comparable in efficacy and safety to infliximab but less costly and that golimumab is associated with improved clinical outcomes compared with adalimumab (pending review by the CADTH's Common Drug Review [CDR] for UC) in efficacy but of similar cost. The cost-utility analysis compared golimumab with conventional therapy, which is defined by the medication regimen of the placebo cohort found in the Program of Ulcerative Colitis Research Studies Utilizing an Investigational Treatment (PURSUIT) trials[1,2] (oral corticosteroids, immunomodulators [6-mercaptopurine, azathioprine, and methotrexate], and/or oral 5-aminosalicylic acid [5-ASA] compounds), and with infliximab and adalimumab. The target population consists of those with moderately to severely active UC (defined by a Mayo score of 6 to 12 and endoscopic subscore ≥ 2) following inadequate response to conventional treatments, followed over a 10-year time horizon. The efficacy of treatments for inducing response or remission was taken from an indirect treatment comparison (ITC) conducted by the manufacturer. Quality of life was estimated using utilities based on the EuroQol Five-Dimension Quality of Life Questionnaire (EQ-5D) visual analogue scale, and using published literature for post-colectomy health states. Costs of the drugs were obtained from provincial drug formularies, while resource use for concomitant medications was based on PURSUIT trials (PURSUIT Induction and PURSUIT-Maintenance).[1,2] Cost of surgeries, relapse management, and post-surgical complications were derived from published literature.

Results of Manufacturer's Analysis

The manufacturer reports that, compared with conventional therapy, golimumab 50 mg and 100 mg are associated with an incremental cost per quality-adjusted life-year (QALY; incremental cost-utility ratio [ICUR]) of $41,591 and $42,271, respectively. Infliximab and adalimumab are associated with an ICUR of $65,982 and $68,722, respectively, compared with conventional therapy.

Interpretations and Key Limitations

The key limitations identified with the submitted economic evaluation are issues with transparency regarding the data inputs used and how they were incorporated into the model. More specifically:

- The manufacturer stated that the efficacies of treatment for inducing response or remission were taken from the ITC and randomized controlled trial data; probabilities of remaining in remission or response (i.e., the treatment effect) were calculated based on estimated probabilities of one-year maintenance from the ITC. This approach appears to have been taken only for golimumab and not for the comparators; thus, possibly biasing results in favour of golimumab.

- Review of the model revealed the underlying relationship between probabilities of outcome at induction and sustained outcome at one year. Although correlation between outcome at induction and sustained outcome after one year is expected, there is no evidence to support the assumed relationship proposed by the manufacturer, the impact of which reveals how the current model design restricts the range of values allowed for input.
- The model is based on a manufacturer-conducted ITC that is limited by small numbers of trials and patients, differences in trial design, and heterogeneity in placebo comparator arms. Therefore, there was insufficient power to make statistically significant conclusions about the efficacy and safety of the comparators compared with each other.
- The economic analysis was based on a time horizon of 10 years, based on chronicity of UC patients, despite the lack of long-term data to support extended time horizons beyond the one-year trial duration.

As these issues were not appropriately documented in the pharmacoeconomic submission, validation of the model logic was complex and challenging. Therefore, interpretation of the manufacturer's reported results should be viewed with caution.

Results of Common Drug Review Analysis

Due to the identified limitations of the submitted economic evaluation, CDR was unable to conduct reanalyses to investigate the impact of alternate values for input variables and of varying the association among outcomes. To attempt to address this uncertainty, CDR conducted additional reanalyses reducing the time horizon of the analysis from 10 years to shorter durations to align with clinical data. The results of these analyses indicate that the ICUR for golimumab compared with conventional therapy could be as high as $104,000 per QALY when the time horizon is reduced to 1.25 years (15 months).

Conclusions

The issues identified by CDR in the review of the manufacturer economic evaluation suggest that the included ITC, model data transformations, underlying relationship between probability of outcome at induction and sustained outcomes at one year, and extended time horizon of 10 years may bias the results in favour of golimumab. Given the issues identified, full examination of the manufacturer's model and reanalyses using alternative clinical inputs were not possible. CDR reanalyses varying the time horizon of the manufacturer's economic model found that the ICUR for golimumab could lie in a range of $52,000 to $104,000 per QALY, where the time horizon is reduced from the manufacturer's base case of 10 years to a range of 2.5 to 1.25 years to align with available randomized controlled trial data.

REVIEW OF THE PHARMACOECONOMIC SUBMISSION

1. INTRODUCTION

1.1 Study Question

"The objective of the current analysis is to translate observed short-term and one-year effects from the completed indirect treatment comparison (ITC), as well as observational evidence on long-term colectomy outcomes, into a robust cost-effectiveness analysis of golimumab, infliximab, and adalimumab for the treatment of patients with moderately to severely active ulcerative colitis (UC) who are nonresponsive to conventional therapy."
(Manufacturer's Pharmacoeconomic Evaluation, p. 12)

1.2 Treatment

Several treatment algorithms were applied in the economic evaluation. For the base-case analysis, a treatment algorithm was applied in which a biologic therapy was used first and followed by conventional therapy. This is based on the assumption that patients enter the economic model having already had an inadequate response to at least one immunomodulator or corticosteroid.

Further, conventional therapy followed by biologic therapy, and treatment courses with sequential biologic therapy (i.e., second biologic administered after failure of first biologic) were explored for sensitivity, both with two biologics administered before conventional therapy, and with conventional therapy administered before two biologics.

1.3 Comparators

The three considered biologic interventions were golimumab (both 50 mg and 100 mg maintenance doses), infliximab 5 mg/kg, and adalimumab 40 mg. The primary comparator in this analysis was conventional therapy, which is defined by the medication regimen of the placebo cohort found in the PURSUIT trial (oral corticosteroids, immunomodulators [6-mercaptopurine, azathioprine, and methotrexate], and/or oral 5-aminosalicylic acid [ASA] compounds). All biologic interventions were assumed to be administered concomitantly with conventional therapy. In addition to immunomodulators, concomitant corticosteroid use was allowed. Surgery was not considered a direct comparator but was included as a final option for patients who are refractory to drug therapies.

1.4 Type of Economic Evaluation

The manufacturer submitted a cost-utility analysis comparing the three anti-TNF-alpha agents in moderately to severely active UC. The analysis adopted a Canadian public payer perspective.

1.5 Population

The patient population included men or women 18 years of age or older with moderately to severely active UC (defined by a Mayo score of 6 to 12 and endoscopic subscore ≥ 2). Patients must have had a biopsy result consistent with the UC diagnosis and must have been ambulatory (i.e., not at imminent risk of colectomy). Patients must also have had an inadequate response to or failed to tolerate one or more of the following pharmacotherapies: oral 5-aminosalicylic acid (5-ASA), oral corticosteroids, the immunomodulators azathioprine or 6-mercaptopurine, or have demonstrated corticosteroid dependence (i.e., an inability to successfully taper corticosteroids without a return of the symptoms of UC). The manufacturer did not provide stratification based on disease severity to consider the impact on severely versus moderately affected patients.

2. METHODS

Please see Table 12 for a summary of the key limitations associated with the methodology used by the manufacturer.

2.1 Model Structure

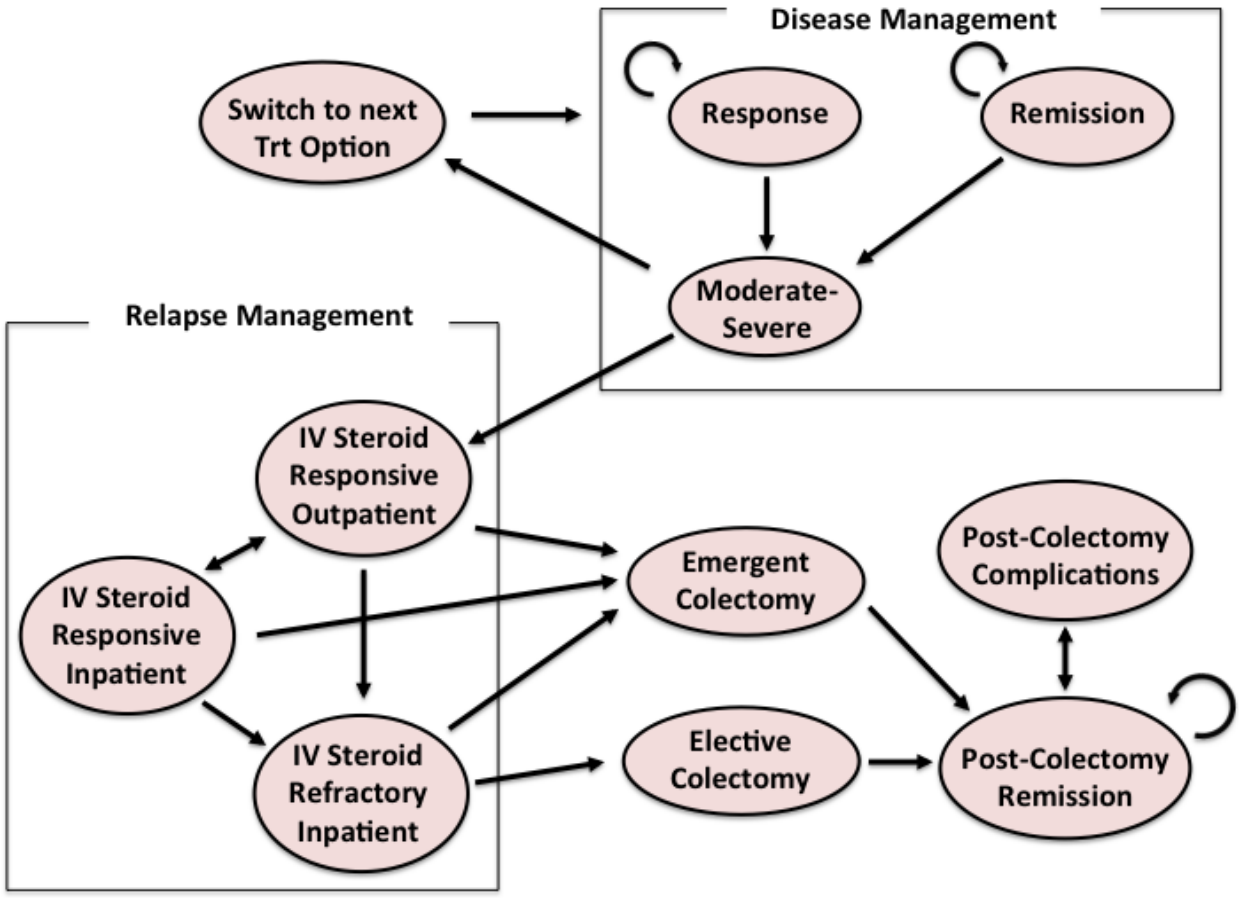
The model consisted of three separate stages representing the different categories for treatment and care that UC patients incurred as their disease and treatment responses progressed over time. In the first stage consisting of disease management, patients received pharmacotherapy (primary and secondary) depending on the arm (biologic or conventional therapy only); and the health states in this stage included "response," "remission," or "moderate/severe" (during relapse). The second stage — relapse management — commenced when patients had relapsed (lost response to both primary and secondary pharmacotherapy) and consisted of outpatient and in-patient management with intravenous steroids. At the final stage —colectomy — patients underwent surgery, and this would act as an end state (aside from the ability to go into the 'post-colectomy' complications state); the health states included colectomy remission and post-colectomy complications. These health states and treatment algorithms are summarized in Figure 1.

All health states at every stage were mutually exclusive, and patients moved between states after every three-month cycle. The moderately to severely active state was the starting state for all patients simulated in the Markov model and was clinically defined by a Mayo score of 6 to 12. The response health state was clinically defined as a Mayo score of 3 to 5, which is also commonly referred to as "mild" UC. The remission health state was clinically defined as a Mayo score of 0 to 2 and represents a state where most or all symptoms were completely suppressed. These definitions were used in accordance with all randomized controlled trials (RCTs) included in the ITC. When patients failed a pharmacotherapy (i.e., relapsed from remission or response to moderate or severe UC), they were switched to the next treatment option. When patients had failed all of the treatment options included in their pharmacotherapy treatment course, they transitioned into relapse management.

During relapse management, additional treatment options involved patient treatment in an outpatient setting, which included intravenous steroid treatment and other immunomodulators.[3] If patients became refractory to steroids, they were hospitalized. Outpatients could also be hospitalized for other factors that would result in disease exacerbations. Hospitalized patients would typically incur a delay between hospitalization and colectomy, representing their willingness to postpone colectomy. These outpatient and in-patient management settings were assumed in accordance with recent treatment guidelines[3] and confirmed in consultations with clinical experts.

Patients who were no longer able to attain remission or response in the outpatient or in-patient setting underwent colectomy (either emergent or elective; see Figure 1). Patients who have had a colectomy may experience a number of short-term and long-term complications that are both costly to treat and temporarily diminish patients' quality of life. In addition, it was assumed that post-colectomy remission is different from pre-colectomy remission.[1,4]

FIGURE 1: MODEL FIGURE



2.2 Clinical Inputs

2.2.1 Efficacy

The submitted pharmacoeconomic report indicates that efficacies of treatments for inducing response or remission were taken from the manufacturer-conducted ITC and RCT data and that probabilities of remaining in response or remission were back-calculated based on the probabilities of one-year sustained outcomes (remission/response) as obtained from the ITC. Based on the model structure proposed by the manufacturer, the agents' treatment effects are defined by the agents' impact on the transition probabilities between health states, thus affecting the duration of time spent in each health state. Response and remission rates at induction were derived from the ITC odds ratios using a common conventional therapy probability for each health state. In particular, the probability of remission and response at induction with conventional therapy was determined as the pooled probability among Active Ulcerative Colitis Trial 1 (ACT-1), Active Ulcerative Colitis Trial 2 (ACT-2), Ulcerative Colitis Long-Term Remission and maintenance with Adalimumab 1 (ULTRA-1), and Ulcerative Colitis Long-Term Remission and maintenance with Adalimumab 1 (ULTRA-2) rather than as the ITC.[5] The PURSUIT-Maintenance trial was excluded because of its randomized-withdrawal design and its implications with the placebo comparator. The manufacturer assumed a normal distribution around the corresponding log odds; the distributions were derived by logit transforming the 95% confidence intervals of the pooled proportions, and approximating the standard error from the width of the confidence interval (i.e., dividing the width by 3.92).

Finally, the probabilities of remission and response at induction with any of the considered biologics were reported to be derived from their posterior distributions in the Bayesian ITC. That is, based on the assumed normal distribution for the log odds in the placebo group, and the estimated distribution of the log odds ratios for each of the biologics versus placebo, the posterior distributions were derived for the log odds associated with each biologic.

However, upon review by CDR, there was no clear evidence of odds ratios being used from an ITC for the estimation of transition probabilities for golimumab, infliximab, and adalimumab. Estimation of probabilities appears to have been achieved by pooling the number of events per single treatment arms without proper adjustment for the comparator. This methodology appears to be crude and contradictory to what the manufacturer had indicated in the report.

2.2.2 Drug Costs

The cost of all therapies was estimated using the published price in the Saskatchewan Drug Formulary, which was chosen by the manufacturer because this database included all of the most recent price updates for infliximab, adalimumab, and golimumab, as of July 2013 (Table 2). Concomitant therapy costs per cycle were truncated at $10,000 if they exceeded this ceiling; however, no rationale was provided as to why the truncation was done. The costing source for concomitant therapies was taken from the Ontario Drug Benefit Formulary (July 2013).

TABLE 2: COSTS OF THERAPIES USED IN THE MODEL

Treatment	Dose	Unit Cost	Cost (First Cycle)	Cost (Subsequent Cycle)
Infliximab	5 mg/kg (75 kg patient) at weeks 0, 2, 6 and every 8 weeks thereafter	$968.20	$10,892	$5,446
Adalimumab	160 mg week 0, 80 mg week 2, and 40 mg every 2 weeks thereafter	$740.36	$7,404	$4,442
Golimumab	200 mg week 0, 100 mg at week 2, and every 4 weeks thereafter	$1,490.41	$7,854	$4,470

Source: Manufacturer's Pharmacoeconomic Evaluation, Table 4, page 22.

2.2.3 Administration Costs

Although golimumab (50 and 100 mg) is administered subcutaneously, the product monograph indicates that the product's two dosage forms (auto-injector and pre-filled syringes) may be self-administered by the patient after medical consultation and appropriate training. Therefore, no administration costs were included in the manufacturer's analysis for either golimumab or the other comparators, which is a conservative approach toward golimumab. Although patient self-administration is suggested for golimumab, administration costs for the initial doses as well as costs of patient training to self-inject should be considered and possibly included.

2.2.4 Event Treatment Costs

Cost of colectomy was differentiated by the type of colectomy (conventional, ileal anastomosis, and pro-colectomy with ileal anastomosis). Average cost of surgery was obtained from published Canadian studies[5,6] and estimated to be $19,269. During relapse management, patients were assumed to continue on concomitant conventional therapy. Patients would also incur cost of hospitalization; the cost of a UC-related hospital stay used in the model is the average cost of admission for a primary diagnosis of UC. The average cost per hospital stay was reported at $15,459. The manufacturer conducted a review of the literature and consulted with expert clinicians to identify information regarding the rate of early and late complications for patients with UC who have undergone colectomy (Table 3).

TABLE 3: COSTS OF TREATMENT EVENTS USED IN THE MODEL

Treatment	% Patients	Cost	Source[5]
In-patient management		$15,459	Bernstein et al. (2012)[6]
Colectomy		$19,269	Bernstein et al. (2012)[6]
Early complications			UK IBD Audit Steering Group (2007)[5]; Kim et al. (2012)[7]
• Parenteral nutrition	-	$400	Marshall et al. (2005)[8]
• Intra-abdominal sepsis	2.4% per year	$22,082	OCCI Database accessed in June 103[9]; Park et al. (2012)[4]
• Wound infection	3.5% per year	$3,937	Zoutman et al. (1998)[10]
• Small bowel obstruction	2.4% per year	$6,399	OCCI Database accessed in June 103[9]; Park et al. (2012)[4]
Late Complications			
• Pouchitis	28.2% per 5 years	$191.64	OCCI Database accessed in June 103[9]; Park et al. (2012)[4]
• Small bowel obstruction	24.7% per 5 years	$6,399	OCCI Database accessed in June 103[9]; Park et al. (2012)[4]
• Anal fistula	8.2% per 5 years	$9,795	OCCI Database accessed in June 103[9]; Park et al. (2012)[4]
Serious infections		$8,605	OCCI Database accessed in June 103[9]; Park et al. (2012)[4]

IBD = inflammatory bowel disease; OCCI = Ontario Case Costing Initiative.
Source: Manufacturer's Pharmacoeconomic Evaluation, Table 6, Page 24.

2.2.5 Utilities

The manufacturer used Mayo scores observed in the PURSUIT[1,2] trial to estimate the baseline disease severity and change in disease severity related to treatment effect. The associated health-related quality of life was estimated using utilities for these health states using EuroQol 5-Dimension Quality of Life Questionnaire **(**EQ-5D) visual analogue scale (VAS). A study by Stark et al. (2010) has validated the use of EQ-5D VAS as the most sensitive health-related quality of life measure in inflammatory bowel disease.[5,11] To remain consistent, the manufacturer obtained the utilities for the considered health states as mean average across treatment arms, meaning a remission in placebo arm is equivalent to remission in the drug arm. Utility associated with colectomy and post-colectomy health states were not available in the trial data. Therefore, utilities for post-colectomy states were obtained from the observational literature and previous cost-effectiveness analyses.[12] Finally, the manufacturer assumed adverse events and discontinuations due to adverse events were associated with a disutility of 0.10. This final assumption was not substantiated by evidence but was based on available literature (not identified) that is suggestive of the validity of this disutility estimate.

TABLE 4: UTILITIES AND DISUTILITIES

Component	Assumed Utility/Disutility	Reference
Pre-colectomy		
• Remission	0.82[a]	PURSUIT[1,2]
• Response	0.72[a]	
• Moderate-severe[b]	0.55[a]	
Post-colectomy		
• Remission	0.67[c]	Park et al. (2012)[4]
• Complication	0.49[c]	
Health event disutility		
• Serious adverse event	–0.10[d]	Guo et al. (2008)[13]
• Discontinuation due to adverse event	–0.10[d]	Currie et al. (2005)[14]
• Hospitalization during relapse management	–0.05[d]	

[a] From PURSUIT.
[b] Weighted average of the utility of having moderately active disease (0.57) and the utility of having severely active disease (0.50). It is assumed that 70% of the population has moderately active disease, and 30% has severely active disease.
[c] From observations data.
[d] From consultation with physician subject matter experts.
Note: Utilities and disutilities were derived from the EQ-5D scale.
Source: Manufacturer's Pharmacoeconomic Evaluation, Table 3, Page 21.

2.2.6 Time Horizon

The base-case time horizon for the analysis is 10 years, with a cycle length of three months. A five-year time horizon was tested by the manufacturer using sensitivity analyses. The manufacturer based the 10-year time horizon on trial data and considered it to be short relative to the chronicity of UC; the time horizon was selected to match patient severity, as patients with moderately to severely active UC have already been diagnosed with UC for more than five years. However, there is a deficiency in the literature in measuring long-term survival of patients with moderately to severely active UC.

2.2.7 Discounting

The manufacturer assumed an annual discount rate of 3% for both health and cost outcomes, although the CADTH guidelines recommend a 5% discount rate. No rationale was provided as to why 3% was selected for the base case; however, a 5% discount was applied in a sensitivity analysis.

2.2.8 Validation

There is no clear evidence indicating that the submitted model has been validated for use in modelling the cost-effectiveness of biologics in moderately to severely active UC.

3. RESULTS

The following section outlines the results of the manufacturer's base case and of the most relevant sensitivity analysis submitted in the pharmacoeconomic evaluation report for golimumab 50 mg and 100 mg.

3.1 Manufacturer's Base Case

The manufacturer's pharmacoeconomic evaluation reported the total costs and total mean utility gains per cycle over the full 10-year time horizon (Table 5). The mean total cost for patients treated with golimumab 50 mg, golimumab 100 mg, infliximab, and adalimumab over 10 years was $154,599, $154,894, $161,032, and $150,435, respectively. The mean total QALYs per cycle for golimumab 50 mg, golimumab 100 mg, infliximab, and adalimumab was 0.5733, 0.5735, 0.5708, and 0.5306, respectively. Reporting of the results provided in Table 5 is not readily available from the submitted model and is not reproducible when sensitivity analyses are conducted. The model does not provide the mean total utilities (i.e., QALYs) during the entire 10-year duration to correspond with the reported mean total costs over the same duration.

TABLE 5: TOTAL COSTS AND UTILITIES OVER THE 10-YEAR TIME HORIZON

Treatment	Mean Total Cost ($)	Mean Utility per Cycle
Conventional therapy	131,438	0.5596
Golimumab 50 mg	154,599	0.5733
Golimumab 100 mg	154,894	0.5735
Infliximab	161,032	0.5708
Adalimumab	150,435	0.5669

Source: Manufacturer's Pharmacoeconomic Evaluation, Table 7, Page 26.

The three-month cycle mean incremental cost, utility gains, and median ICURs are presented in Table 6.

TABLE 6: INCREMENTAL COSTS, INCREMENTAL QUALITY-ADJUSTED LIFE-YEARS, AND INCREMENTAL COST-UTILITY RATIOS FOR TREATMENTS VERSUS CONVENTIONAL THERAPY

Treatment	Mean Incremental Cost ($)	Mean Incremental Utilities	ICUR[a]
Golimumab 50 mg	569	0.0132	$41,591
Golimumab 100 mg	585	0.0137	$42,271
Infliximab	727	0.0108	$65,982[b]
Adalimumab	463	0.0069	$68,722[c]

ICUR = incremental cost-utility ratio.
[a] Calculated as median ICURs by manufacturer due to concern that data could become skewed.
[b] Dominance by golimumab (50 mg and 100 mg).
[c] Extended dominance by golimumab (50 mg and 100 mg) and infliximab.

3.2 Summary of the Manufacturer's Sensitivity Analyses

The manufacturer's main sensitivity analyses examined reducing the time horizon to five years, use of "real-world" data to estimate probabilities of being in response or remission health states, and sequential biologic therapy. Results show that the ICUR is sensitive; higher ICURs are shown with reduced model horizons and use of sequential biologic therapy, while ICURs are lower when using real-world data to estimate model transition probabilities.

3.2.1 One-way Sensitivity Analyses

According to the manufacturer's submitted report, reducing the time horizon to five years increased the incremental cost-effectiveness ratio (ICER) for golimumab 50 mg and 100 mg to $46,766 and $45,873 per QALY, respectively, while infliximab had an ICER of $76,869 per QALY and adalimumab had an ICER of $76,380/QALY (Table 7).

TABLE 7: INCREMENTAL COSTS, INCREMENTAL QUALITY-ADJUSTED LIFE-YEARS, AND INCREMENTAL COST-UTILITY RATIOS OVER A 5-YEAR TIME HORIZON

Treatment	Mean Incremental Cost ($)	Mean Incremental Utilities	ICUR[a]
Golimumab 50 mg	1,049	0.0224	$46,766
Golimumab 100 mg	1,083	0.0137	$45,873
Infliximab	1,420	0.0108	$76,869[b]
Adalimumab	862	0.0069	$72,380[c]

ICUR = incremental cost-utility ratio.
[a] Calculated as median ICURs by manufacturer due to concern that data could become skewed.
[b] Dominance by golimumab (50 mg and 100 mg).
[c] Extended dominance by golimumab (50 mg and 100 mg) and infliximab.

Use of real-world data (based on observational studies[3,5,15-19]) to inform pharmacotherapy remission, response, and relapse transition probabilities led to moderate increases in mean incremental costs and QALYs with golimumab and infliximab, and mild increases with adalimumab, leading to ICERs less than those in the base case (Table 8).

TABLE 8: INCREMENTAL COSTS, INCREMENTAL UTILITIES, AND INCREMENTAL COST-UTILITY RATIOS USING REAL-WORLD DATA

Treatment	Mean Incremental cost ($)	Mean Incremental Utilities	ICUR[a]
Golimumab 50 mg	616	0.0173	$34,235
Golimumab 100 mg	630	0.0187	$32,613
Infliximab	782	0.0142	$52,648[b]
Adalimumab	476	0.0092	$51,032[c]

ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.
[a] Calculated as median ICURs by manufacturer due to concern that data could become skewed.
[b] Dominance by golimumab (50 mg and 100 mg).
[c] Extended dominance by golimumab (50 mg and 100 mg) and infliximab.

Sequential biologic therapy (i.e., when a second biologic is introduced) resulted in increases in both mean incremental costs and mean incremental QALYs with golimumab 100 mg followed by adalimumab, being the most cost-effective option. The only treatment that was dominated was infliximab followed by adalimumab (Table 9).

TABLE 9: INCREMENTAL COSTS, INCREMENTAL UTILITIES, AND INCREMENTAL COST-UTILITY RATIOS USING SEQUENTIAL BIOLOGIC THERAPY

Treatment	Mean Incremental Cost ($)	Mean Incremental Utilities	ICUR[a]
Golimumab 50 mg then infliximab	991	0.0175	$56,760
Golimumab 50 mg then adalimumab	847	0.0149	$56,655
Golimumab 100 mg then infliximab	990	0.0177	$55,942
Golimumab 100 mg then adalimumab	853	0.0158	$54,463
Infliximab then golimumab 50 mg	1,078	0.0173	$62,324
Infliximab then golimumab 100 mg	1,058	0.0174	$60,794
Infliximab then adalimumab	1,010	0.0127	$80,640[b]
Adalimumab then golimumab 50 mg	810	0.0135	$60,046

[a] Calculated as median ICURs by manufacturer due to concern that data could become skewed.
[b] Dominated.

3.2.2 Probabilistic Sensitivity Analysis

A probabilistic sensitivity analysis was not necessary for this submitted model, as uncertainty associated with transition probabilities between pre-surgery health states, between surgery rates, and for treatment discontinuations and adverse events, as well as incorporated health care resource cost estimates, were incorporated through the assigned probability distributions for these parameters.

3.3 Common Drug Review Analyses

As part of the review of the manufacturer-submitted pharmacoeconomic evaluation for golimumab, CDR detected inconsistencies between the submitted economic report and the technical model, as well as inaccuracies within the economic report. To confirm the impact of these inaccuracy issues on the results, the CDR attempted to re-run the manufacturer's base-case scenario using the submitted technical file. The results of this re-run of the manufacturer's base case by CDR aligned with the results reported by the manufacturer.

There is limited literature assessing long-term sustained response and sustained remission rates for anti-TNF agents in patients with moderately to severely active UC. The manufacturer's sensitivity analysis using a reduced time horizon (five years) shows an increase in the incremental costs and incremental QALY gains. Reanalyses by CDR used reduced time horizons up to 1.25 years (15 months), as the technical model would not accept time horizons of one year (12 months) or shorter. For a 1.25 year analysis, the ICUR increases to approximately $104,000 per QALY (Table 10).

TABLE 10: RESULTS OF COMMON DRUG REVIEW REANALYSES USING ALTERNATE TIME HORIZONS

Time Horizon	Treatment Algorithm	Incremental Cost ($)	Incremental Utility (QALYs)	ICUR[a] per QALY
10 years[b]	Golimumab (50 mg)	528	0.0121	$43,680
	Golimumab (100 mg)	555	0.0131	$43,713
	Infliximab	709	0.01	$73,199
	Adalimumab	441	0.0065	$64,775
5 years[b]	Golimumab (50 mg)	997	0.0219	$45,838
	Golimumab (100 mg)	1,006	0.0234	$41,866
	Infliximab	1,409	0.017	$81,073
	Adalimumab	889	0.0119	$73,920
2.5 years	Golimumab (50 mg)	1,919	0.0366	$52,801
	Golimumab (100 mg)	1,950	0.038	$51,979
	Infliximab	2,638	0.03	$85,808
	Adalimumab	1,591	0.0192	$76,447
2 years	Golimumab (50 mg)	2,596	0.038	$71,286
	Golimumab (100 mg)	2,665	0.0429	$62,651
	Infliximab	3,532	0.0317	$112,727
	Adalimumab	2,140	0.0201	$94,777
1.5 years	Golimumab (50 mg)	3,570	0.0376	$85,162
	Golimumab (100 mg)	3,637	0.0422	$81,795
	Infliximab	4,914	0.0325	$163,781
	Adalimumab	3,114	0.0165	$183,687
1.25 years	Golimumab (50 mg)	4,231	0.0375	$104,079
	Golimumab (100 mg)	4,314	0.0418	$101,886
	Infliximab	5,998	0.035	$185,808
	Adalimumab	3,855	0.0165	$206,017

ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

[a] Calculated as median ICURs by manufacturer due to concern that data could become skewed.

[b] Reported by manufacturer.

Based on the lack of long-term efficacy and safety data for golimumab as treatment for moderately to severely active UC, a reanalysis was performed by CDR based on various price reduction scenarios to determine the cost-effectiveness of golimumab (100 mg) over a reduced time horizon of 1.25 years (15 months). Results are reported in Table 11.

TABLE 11: COMMON DRUG REVIEW ANALYSIS OF INCREMENTAL COST-UTILITY RATIOS BASED ON VARIOUS PRICE REDUCTION SCENARIOS OF GOLIMUMAB 100 MG

Scenario	ICUR per QALY
Manufacturer's base case at 1.25-year time horizon	$101,886
10% price reduction	$91,250
25% price reduction	$77,509
50% price reduction	$47,927
60% price reduction	$38,286
70% price reduction	$29,288
80% price reduction	$18,307
90% price reduction	$9,175

ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

4. DISCUSSION

The manufacturer submitted a cost-utility analysis comparing golimumab 50 mg and 100 mg with conventional therapy, infliximab, and adalimumab for the treatment of moderately to severely active UC. Treatment effects of the comparators for inducing response or remission were based on RCT trial data and a manufacturer-conducted ITC of the anti-TNF-alpha agents.

Several limitations were identified that raise the uncertainty surrounding the ICURs estimated for golimumab 50 mg and 100 mg. In detailing the methodology for estimating the transition probabilities of remission and response for the comparators used in the model, the manufacturer indicated that the response and remission rates at induction were derived from the ITC odds ratios using a common conventional therapy probability. Review by CDR has found no evidence of this approach being applied in the submission; instead, the response and remission rates appear be based on pooling of single treatment arms without proper adjustment for the comparator. When CDR applied the alternate method (pooling) to replicate the transition probabilities, the results were similar to those estimated for conventional therapy (placebo), infliximab, and adalimumab. It was unclear how the transition probabilities of remission and response at induction were obtained for golimumab 50 mg and 100 mg. Further correspondence from the manufacturer provided information on the methods used for the transition probabilities; specifically, clinical trial data were transformed using Bayesian methodology. The ITC included both PURSUIT trials (PURSUIT-SC and PURSUIT-Maintenance) as one RCT for golimumab. However, the trial design of PURSUIT-Maintenance employed a randomized-withdrawal maintenance phase, while the studies included for the other agents used parallel-group designs, leading to the conclusion that the placebo comparator groups in the clinical trials are heterogeneous. The PURSUIT induction trial (PURSUIT-SC) had a duration of six weeks compared with the maintenance trial duration of 54 weeks. Although placebo was still included in the ITC despite the issues of heterogeneity, the manufacturer excluded placebo data from PURSUIT in the economic evaluation. As discussed earlier, the trial data were transformed using Bayesian methodology; however, no Bayesian models or data were supplied to CDR, and hence any assessments by CDR to include PURSUIT trial data in estimating the transition probabilities was not feasible.

The limitations identified in the submitted ITC, as well as transition probabilities for induction and sustained outcome (response/remission) for golimumab, led CDR to consider conducting a reanalysis varying the induction probabilities for outcome for golimumab based on alternate data transformations that are not obtained from the ITC. The results of these analyses were counterintuitive and revealed that the probabilities are based on a relationship between the probability of outcome at induction and the probability of a sustained outcome at one year. Either probability cannot be varied independently from the other to produce intuitive results unless that it is varied within a very narrow margin that may not reflect alternate data sources or acceptable clinical practice. This relationship was based on the manufacturer's assumption that patients would continue on a treatment after induction only if they responded to treatment (i.e., attained clinical response or clinical remission),[5] with nonresponders switched to the next therapy.[5] If patients did respond and continued on treatment, then subsequent three-month cycle probabilities would be back-calculated using probabilities of outcome at induction and one-year probabilities of sustaining response and remission. This relationship has an impact on reanalyses using alternate probabilities: changes in the probabilities at induction are only within a specific margin that may not be informative or reflective of the reanalyses considered by CDR.

Another limitation is the discrepancies detected between the transcribed report of the economic analysis and the technical model itself. As an example, the manufacturer assumed that that probabilities of sustained remission at three months were equal to those of sustained response at the same time point (calculated based on probabilities of sustained response after one year of maintenance) and showed these probabilities in a table (Pharmacoeconomic Review Report, Table 2, Page 17). However, the inputs file associated with the technical model shows variation between the probabilities of sustained response and remission at one year. Another example pertains to the relapse management stage; the manufacturer assumed a yearly 7.5% risk of becoming refractory to steroids, translating to a 1.9% risk per three-month cycle. However, the technical model displays a three-month rate of patients becoming refractory to steroids of 98.2%, back-calculated from 30% at five years. Finally, standard error values used in deriving distributions for some of the parameters in the economic report do not match those observed in the technical model. Discovery of such inaccuracies and discrepancies increases the uncertainty surrounding the estimates produced by the technical model.

The manufacturer's sensitivity analysis reducing the model time horizon from 10 years to five years resulted in a lower ICUR for golimumab than for conventional therapy. Reanalyses by CDR further reducing the time horizon to reflect the scarcity of long-term data on the effectiveness of golimumab show higher ICURs compared with conventional therapy. It is not clear why longer time horizons improve results, given that fewer patients would likely continue to receive anti-TNF-alpha agents over time.

The key limitations associated with the manufacturer's submission are summarized in Table 12.

TABLE 12: KEY LIMITATIONS OF THE MANUFACTURER'S ECONOMIC SUBMISSION

Parameter / Assumption	Issue	Impact
Conducting of ITC	Placebo comparator arms in RCTs included in the ITC were heterogeneous.	Uncertain: inclusion of placebo arms from PURSUIT trials in ITC may have overestimated the treatment effects of golimumab. The ICUR for golimumab may have been higher than reported.
Transition probabilities from ITC ORs	Uncertain: no evidence to support use of ITC OR data to obtain transition probabilities.	Uncertain: CDR unable to reliably estimate cost-effectiveness due to uncertainty.
Linking of probabilities of induction and sustained remission/response	The probabilities were highly related, thus any modification could be done only within a very narrow margin.	Uncertain: the margin for modification is too narrow for CDR to conduct a reanalysis using alternate probabilities.
10-year model time horizon	No long-term data on the effectiveness of golimumab beyond 1-year trial data.	Model is unable to report results of 1-year time horizon. ICUR is expected to increase significantly if using 1-year time horizon.

CDR = Common Drug Review; ICUR = incremental cost-utility ratio; ITC = indirect treatment comparison; OR = odds ratio; RCT = randomized controlled trial.

4.1 Patient Input

The patient input highlighted the avoidance of lengthy infusion treatments and reduced need for regular health care appointments, as golimumab can be administered by self-injection at home once every four weeks. Patients were also concerned about the cost of the drug. The submitted economic evaluation did not incorporate administration costs for any of the comparators included.

5. CONCLUSIONS

CDR identified a number of limitations with the manufacturer's analysis, which raise the uncertainty surrounding the reported ICURs and are suggestive of bias in favour of golimumab (leading to low ICURs for golimumab compared with conventional therapy). Given the issues identified, full examination of the manufacturer's model and reanalyses using alternative clinical inputs were not possible. CDR reanalyses varying the time horizon of the manufacturer's economic model found that the ICUR for golimumab could lie in a range of $52,000 to $104,000 per QALY, where the time horizon is reduced from the manufacturer's base case of 10 years to a range of 2.5 to 1.25 years to align with available RCT data.

APPENDIX 1: COST COMPARISON TABLE FOR BIOLOGIC AGENTS FOR ULCERATIVE COLITIS

Clinical experts have deemed the comparators presented in Table 13 to be appropriate. Comparators may be recommended (appropriate) practice rather than actual practice. Comparators are not restricted to drugs, but may be devices or procedures. Costs are manufacturer list prices, unless otherwise specified.

TABLE 13: COST COMPARISON TABLE FOR BIOLOGIC AGENTS FOR ULCERATIVE COLITIS

Drug/ Comparator	Strength	Dosage Form	Price ($)	Recommended Dose	Average Annual Drug Cost ($)
Golimumab (Simponi)	**50 mg/0.5 mL 100 mg/1.0 mL**	**Pre-filled syringe or auto-injector**	**1,490.41[a]**	**200 mg week 0, 100 mg week 2, and 50 or 100 mg every 4 weeks thereafter**	**Year 1: 22,356 Thereafter: 19,375**
Infliximab (Remicade)	100 mg/10 mL	Vial for IV infusion	968.20	5 mg/kg at weeks 0, 2, and 6, and every 8 weeks thereafter[b]	Year 1: 29,046 Thereafter: 23,600
Other treatments used but not indicated for UC in Canada					
Adalimumab (Humira)	40 mg/0.8 mL	Pre-filled syringe or auto-injector	740.36	160 mg week 0, 80 mg week 2, and 40 mg every 2 weeks thereafter[c]	Year 1: 22,210 Thereafter: 19,249

IV = intravenous; UC = ulcerative colitis.
[a] Manufacturer-submitted price. All prices are from the Ontario Drug Benefit Formulary (accessed September 2013) unless otherwise indicated and do not include dispensing fees.
[b] Assumes 75 kg patient and no wastage of partially used vials.
[c] Dosing for adalimumab is based on the US product monograph for Humira.[20]
Note: For details of other comparators with a different mechanism of action, see Appendix 2.

APPENDIX 2: ADDITIONAL COMPARATORS COST TABLE

TABLE 14: OTHER TREATMENTS FOR ULCERATIVE COLITIS

Drug / comparator	Strength	Dosage form	Price ($)	Recommended use	Average daily drug cost ($)	Average annual cost ($)
Aminosalicylic acid						
5-ASA (Asacol, Asacol 800)	400 mg	Tablet	0.3951	Active: 0.8 to 3 g daily in divided doses Maintenance: 1.6 g daily in divided doses	0.79–4.74 1.58	288–1,731 577
	800 mg	Ent. tab	1.0565	4.8 g daily in divided doses	4.23	1,542
5-ASA (Mesasal)	500mg	Ent. tab	0.6368	Active: 1.5 to 3 g tabs daily in divided doses Maintenance: 1.5 g daily in divided doses	1.91–3.82 1.91	698–1,395 697
5-ASA (Pentasa)	500 mg	Delayed-release tablet	0.5569	2 to 4 g daily in divided doses	2.23–4.46	813–1,626
	1 g 1 g/100 mL 4 g/100 mL	Suppository Enema Enema	1.6000 3.7000 4.4600	Suppository: 1 g daily Enema: 1 to 4 g daily	1.60 3.70–4.46	584 1,350–1,628
5-ASA (Salofalk)	500 mg	Ent. tab	0.5536	3 to 4 g daily in divided doses	3.32–4.43	1,212–1,617
	500 mg 1 000 mg	Suppository Suppository	1.2236 1.7977	Suppository: 1 to 1.5 g daily	1.80 – 3.67	656–1,340
	2 g/100 mL 4 g/100 mL	Rectal suspension	3.8000[a] 6.6950	Active: 4 g nightly Maintenance: 2 g nightly or 4 g every 2 nights	6.70 3.35–3.80	2,444 1,222–1,387
Olsalazine (Dipentum)	250 mg	Capsule	0.5125	Active: 1 to 3 g daily in divided doses Maintenance: 1 g daily in divided doses	2.05–6.15 2.05	748–2,245 748
Sulfasalazine (Salazopyrin and generic)	500 mg 500 mg	Tablet Ent. tab	0.1804 0.2816	Active: 1 to 2 g 3 to 4 times daily	1.08–4.51	395–1,645

Drug / comparator	Strength	Dosage form	Price ($)	Recommended use	Average daily drug cost ($)	Average annual cost ($)
				Maintenance: 1 g 2 to 3 times daily	0.72–1.69	263–617
Immunosuppressants						
6-mercaptopurine (Purinethol)	50 mg	Tablet	4.7684	50 to 100 mg daily	4.77–9.54	1,741–3,481
Azathioprine (Imuran)	50 mg	Tablet	0.2405	2.5 mg/kg daily	0.84	307
Cyclosporine IV (Sandimmune)	50 mg/mL	Ampuls (1 mL)	4.7930[a]	2 to 4 mg/kg IV daily	14.38–28.76	NA
Corticosteroids						
Betamethasone (Betnesol)	5 mg/ 100 mL	Enema	9.9471	5 mg nightly	9.95	3,631
Budesonide (Entocort)	0.02 mg/mL	Enema	8.3400[a]	2 mg nightly	8.34	3,044
Hydrocortisone (Hycort/Cortenema) (Cortifoam)	100 mg/ 60 mL 15 g/pk (14 doses)	Enema Rectal aerosol	5.4357 87.18	60 mL nightly or every other night One dose nightly or every other night	2.72–5.44 3.11–6.23	992–1,984 1,136–2,273
Hydrocortisone (Solu-cortef)	100 mg 250 mg	Vial	3.3700[b] 6.3600[b]	300 to 400 mg IV daily	8.05–11.42	NA
Methylprednisone (generic)	40 mg/mL 80 mg/mL 100 g/5mL	Injectable suspension	3.2250 6.4500 11.4500	40 mg to 60 mg IV daily	3.23–4.84	NA
Prednisone (generic)	1 mg 5 mg 50 mg	Tablet	0.1066 0.0220 0.1735	40 mg to 60 mg daily to induce remission; then lower dose	0.18–0.22	64–79 or lower

Ampuls = ampoule; ASA = aminosalicylic acid;Ent = enteric-coated; IV = intravenous; NA = not applicable; pk = pack.
All prices are from the Ontario Drug Benefit Formulary (September 2013) unless otherwise indicated.
[a] McKesson Canada wholesale price (September 2013).
[b] Saskatchewan Formulary (September 2013).

APPENDIX 3: ADDITIONAL INFORMATION

TABLE 15: SUBMISSION QUALITY

	Yes/ Good	Somewhat/ Average	No/ Poor
Are the methods and analysis clear and transparent?			X
Comments	The Common Drug Review identified inaccuracies in data reporting / use between the manufacturer's economic report and technical model.		
Was the material included (content) sufficient?		X	
Comments	Additional information on data transformations were provided but could not be validated.		
Was the submission well organized and was information easy to locate?		X	
Comments	None		

TABLE 16: AUTHOR INFORMATION

Authors	Affiliations
Kristian Thorlund Eric Druyts Edward Mills	MacReviews Health Consulting

	Yes	No	Uncertain
Authors signed a letter indicating agreement with entire document	X		
Authors had independent control over the methods and right to publish analysis	X		

APPENDIX 4: SUMMARY OF COST-MINIMIZATION ANALYSIS

The manufacturer submitted a cost-minimization analysis (CMA) comparing golimumab with infliximab and adalimumab in ulcerative colitis (UC) patients. The perspective of the CMA was that of a public drug plan and the time horizon was five years. A 5% discount rate was applied for costs beyond the first year in the base-case scenario. Only drug costs were considered. No wastage of infliximab was assumed. The manufacturer's decision to submit a CMA was based on an assumption of "essential equivalence" as reported in an unpublished indirect treatment comparison (ITC) submitted by the manufacturer.[5]

Based on the manufacturer's cost calculations over a five-year period, use of golimumab would result in savings of approximately $22,812 over five years compared with infliximab and $183 compared with adalimumab (assuming adalimumab is approved in Canada for the treatment of UC, treatment is recommended at the doses specified in the US product monograph,[20] and the price remains at the current level).

Key Limitations

Adalimumab Costing: The cost for the initial year for a UC patient receiving adalimumab was overestimated in the manufacturer's CMA. Assuming the dosing from the adalimumab clinical trial[21] and the approved product monograph for the US,[20] a total of 30 units would be used the first year (four in week 0, 2 in week 2, with 24 remaining 2-week periods), rather than the 31 units used in the manufacturer's analysis. Using the correct number of units in the calculation yields a lower cost of $24,020 in the first year (Table 17), rather than $24,819, as in the manufacturer's submission. The five-year discounted cost of adalimumab would be $94,336. Therefore, based on the correct number of doses for adalimumab, golimumab would be $157 more expensive than adalimumab in the first year, and $616 more expensive over five years (Table 17).

TABLE 17: COMMON DRUG REVIEW-CALCULATED COSTS FOR GOLIMUMAB, INFLIXIMAB, AND ADALIMUMAB

Costs	Golimumab	Infliximab	Adalimumab
Treatment initiation year (year 1)			
Total	$24,177	$31,402	$24,020
Maintenance years (years 2 to 5)			
Total Undiscounted Discounted	 $83,829 $70,775	 $102,080 $86,345	 $83,285 $70,316
Overall 5-year total			
Undiscounted **Discounted**	**$108,006** **$94,952**	**$133,481** **$117,764**	**$107,305** **$94,336**
Incremental 5-year total discounted savings (cost)			
	..	**$22,812**	**($616)**

Parentheses () indicate cost savings.

Relative Costs Sensitive to Body Weight: Unlike golimumab and adalimumab, infliximab is dosed by body weight. The average patient weight of 75 kg that was used by the manufacturer in the CMA is reasonable, based on the mean baseline body weights of patients in the clinical trials included in the indirect comparison. However, while a 75 kg UC patient requires 3.75 vials per dose of infliximab, UC patients who weigh 60 kg require three vials per dose. The discounted cost of infliximab for 41 kg to

60 kg patients (i.e., patients who would require three vials per dose assuming wastage; see next paragraph) is $94,096 over five years (undiscounted cost $106,817) compared with $94,952 for golimumab (undiscounted cost $108,006). Thus, golimumab will be more expensive than infliximab in UC patients who weigh 60 kg or less and will not produce any cost savings in such patients. Note that approximately 25% of patients in the golimumab studies submitted by the manufacturer,[22-24] all of whom were at least 18 years of age, weighed 60 kg or less, although this assumption may be conservative, as the mean weights of patients in trials of other biologics were higher than found in the golimumab studies.

Wastage of Infliximab: At 5 mg/kg, a 75 kg UC patient would need 3.75 vials of infliximab per infusion. The manufacturer assumed no wastage of partially used vials, which is a conservative assumption. However, as infliximab contains no preservatives, amounts not used within three hours must be discarded.[25] A Common Drug Review (CDR) reanalysis of the manufacturer's base case that accounted for wastage of infliximab indicated that the relative costs associated with golimumab and infliximab depend on body weight; specifically, the incremental five-year cost of golimumab is at least $22,812 lower than that of infliximab in patients who weigh more than 60 kg, but golimumab costs $856 more than infliximab in patients who weigh less 60 kg. This is considered to be a "worst case scenario" for infliximab, as it is likely that physicians in practice would prescribe doses that would minimize such wastage.

Assumption of Equivalence: The manufacturer assumed that golimumab is "essentially equivalent" to infliximab and adalimumab for treating UC patients, based on an indirect comparison of these agents (see Appendix 8 of the Clinical Report). CDR reviewers noted that the indirect comparison was overall well conducted and reported, but as there were few included studies and heterogeneity in study design, data from head-to-head trials are required to substantiate the clinical equivalence of treatments.

Summary of Findings

Based on the manufacturer's calculations, use of golimumab ($1,490.41 per syringe) would result in discounted savings of $22,812 over five years compared with infliximab ($968.20 per vial). Based on CDR reanalysis of the manufacturer's base case to include weigh-based dosing and account for potential wastage of excess infliximab, the incremental five-year cost of golimumab is at least $22,812 lower than that of infliximab in patients who weigh more than 60 kg, but golimumab costs $856 more than infliximab in patients who weigh less 60 kg.

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