ORIGINAL RESEARCH

Budget Impact of Adding Vedolizumab to a Health Plan Formulary as Another First-Line Biologic Option for Ulcerative Colitis and Crohn's Disease

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BACKGROUND: Vedolizumab is a biologic drug approved by the US Food and Drug Administration (FDA) for the treatment of adults with moderately to severely active Crohn's disease (CD) or ulcerative colitis (UC) who have had inadequate response to, lost response to, or were intolerant of immunomodulators or tumor necrosis factor (TNF) blocker therapy, or who had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroid therapy. The biologics approved by the FDA for CD and/or UC include adalimumab, infliximab, golimumab, certolizumab, and ustekinumab.

OBJECTIVE: To assess the budget impact of including vedolizumab in a health plan formulary among current options as a preferred first-line biologic therapy for UC and CD rather than only for patients who failed anti-TNF therapy.

METHODS: We developed a 3-year budget impact model for a 1-million-member health plan. Comparators included all currently approved brand-name biologic and biosimilar agents for the treatment of UC (ie, adalimumab, infliximab, and golimumab) and CD (ie, adalimumab, certolizumab, infliximab, and ustekinumab). Clinical inputs included therapy response probabilities, disease remission, and surgery risk. Given the lack of head-to-head clinical trials, we estimated indirect comparisons of treatment efficacy based on clinical trial data using the Bucher method. The drug and medical costs were obtained from published literature. The model compared hypothetical health plan costs for 2 scenarios—(1) a market mix with vedolizumab included on the formulary with currently existing first- and second-line preferred treatments, and (2) vedolizumab included only with existing preferred second-line treatments on the hypothetical formulary. These scenarios were compared in the context of 3 hypothetical health plan formulary cases.

RESULTS: Including vedolizumab in a hypothetical formulary with currently preferred first-line biologic treatment options (Scenario 1) resulted in cost-savings compared with vedolizumab as a preferred second-line biologic option (Scenario 2). The total cost-savings were from $0.13 million to $1.63 million in year 1, and from $0.38 million to $4.68 million in year 3. The per-member per-month cost-savings were from $0.01 to $0.14 in year 1 and from $0.03 to $0.39 in year 3.

CONCLUSION: Based on our model's results, including vedolizumab among the current health plan formulary biologic options as a preferred first-line treatment for UC and CD can result in substantial cost-savings compared with including vedolizumab as a preferred second-line treatment only.

KEY WORDS: adalimumab, anti-TNF biologic drug, budget impact model, certolizumab, Crohn's disease, golimumab, health plan formulary, infliximab, ulcerative colitis, vedolizumab

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Inflammatory bowel disease (IBD) is a chronic, lifelong disorder of the gastrointestinal tract associated with an unpredictable relapsing and remitting disease course.[1] Ulcerative colitis (UC) and Crohn's disease (CD) are 2 common phenotypes of IBD.[1,2] Patients with IBD often have considerable symptom burden despite appropriate treatment, and IBD frequently leads to debilitating com-

KEY POINTS

- Patients with inflammatory bowel disease often have considerable symptom burden despite available treatment.
- This budget impact model of a 1-million-member hypothetical health plan compared currently available biologic treatments for ulcerative colitis (UC) and Crohn's disease (CD).
- The model compared costs for adding vedolizumab as a first-line biologic option in a formulary's preferred biologic options as well as a second-line treatment.
- The total cost-savings of adding vedolizumab to existing preferred first-line options were up to $1.63 million in year 1 and up to $4.68 million in year 3.
- In this model, adding vedolizumab as a preferred first-line treatment reduced per-member per-month costs in this model's 3-year time frame.
- The greatest cost-savings were seen with vedolizumab as a preferred first-line biologic option in a formulary with adalimumab and infliximab as preferred first- and second-line options.
- Based on this model, adding vedolizumab as a first-line biologic option for patients with UC or CD may save health plans' costs.

plications that may require hospitalization, surgery, and/or the escalation of therapy.[3]

According to the Centers for Disease Control and Prevention (CDC), up to approximately 3.1 million Americans have IBD.[4] Medical claims data from approximately 12 million commercially insured Americans indicate that in 2009, the prevalence of UC and CD in adults was 263 and 241 per 100,000, respectively.[5] IBD has considerable economic implications because of its chronic nature, associated morbidity and disability, and the common need for patients to be hospitalized and have surgery.[6,7] As such, the impact of UC and CD on healthcare resource utilization and costs is significant, especially for patients who experience suboptimal response to treatment or loss of response to treatment.[3,8,9]

By extrapolating data from available studies, the Crohn's & Colitis Foundation of America estimated in November 2014 that the total annual direct cost for all US patients with IBD was between $11 billion and $28 billion.[6] However, this number may considerably underestimate the true economic burden of IBD in the United States, because it relied on a lower prevalence of patients with IBD (ie, 1.6 million)[6] than the CDC reported in 2015-2016 (ie, 3.1 million).[2,4]

The available pharmacologic treatments for UC or CD include conventional agents (ie, aminosalicylates, corticosteroids, and immunomodulators) and biologic therapies (ie, tumor necrosis factor [TNF]-α antagonists, including adalimumab; infliximab, brand-name and biosimilar; golimumab; certolizumab pegol [certolizumab hereafter]; and the interleukin [IL]-12/IL-23 ustekinumab); and anti-integrin monoclonal antibodies.

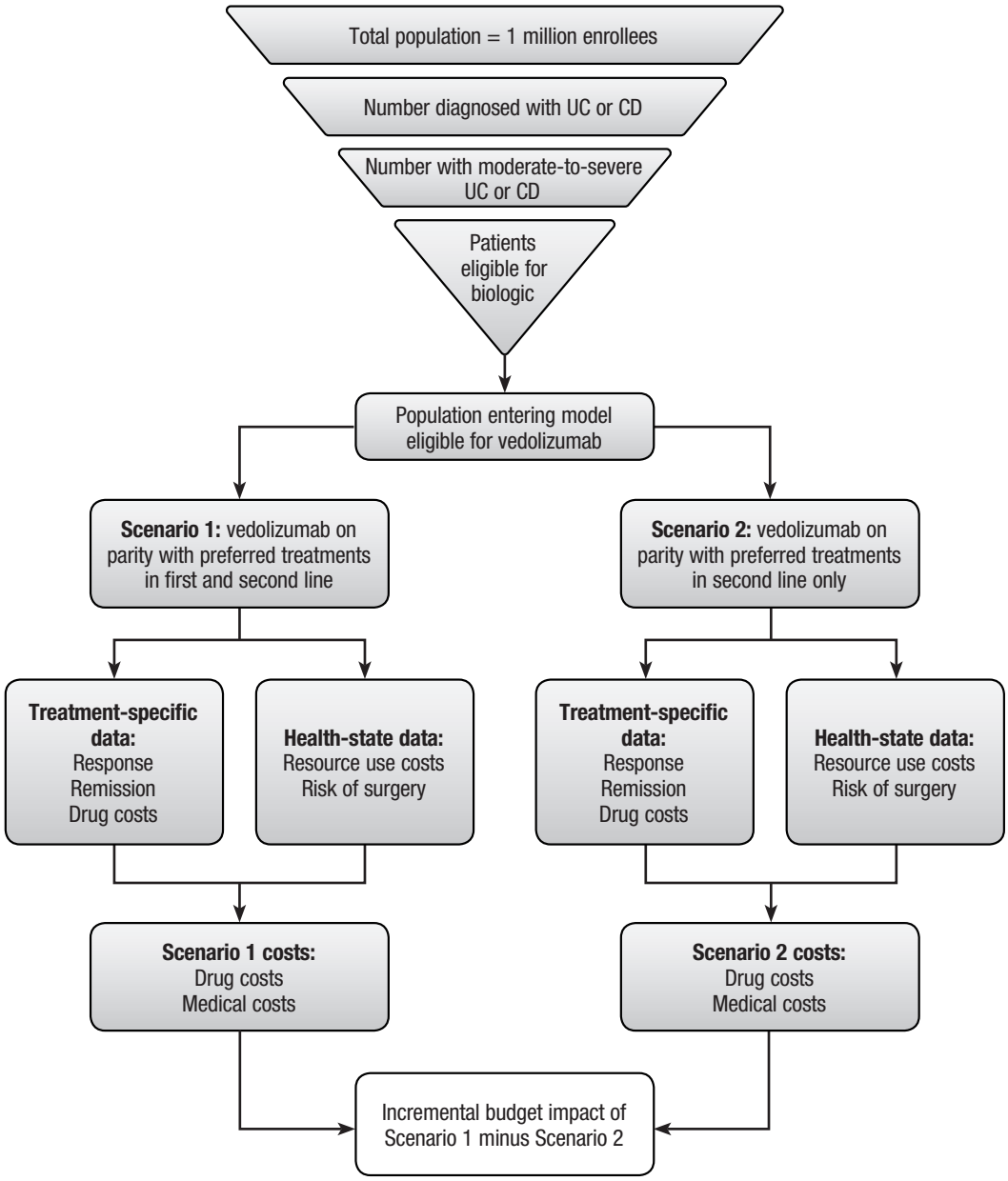
Historically, the standard approach to treatment for UC and CD has been the step-up paradigm, in which conventional agents are used first and biologics are reserved for moderate-to-severe disease in patients whose disease is refractory to or who are intolerant of conventional therapy.[10] Despite the efficacy of TNF-α antagonists compared with conventional treatments, between 20% and 40% of patients with IBD will not respond to induction therapy with TNF-α antagonists, and up to 40% will lose the response to TNF-α antagonist therapy over time.[11-13] As such, there is a need for safe options for the treatment of moderate-to-severe IBD with therapies that offer new mechanisms of action.

Vedolizumab is a humanized monoclonal antibody and an $\alpha_4\beta_7$ integrin receptor antagonist that was approved by the US Food and Drug Administration (FDA) in 2014 as a biologic therapy. Like adalimumab and infliximab, vedolizumab is indicated for the treatment of adults with moderately to severely active UC or CD who have had an inadequate response to, lost response to, or were intolerant of TNF-α antagonist or immunomodulator therapy, and for adults with IBD who had an inadequate response to, were intolerant of, or demonstrated dependence on corticosteroid therapy.[14] In clinical trials, vedolizumab has demonstrated efficacy in patients with IBD who have failed conventional therapy and are biologic naïve, as well as those who previously failed TNF-α antagonist therapy.[14-16] Therefore, vedolizumab may offer a novel biologic treatment option for patients with UC or CD as a first-line biologic option, that is, for patients who have not received biologic treatments or for patients who failed TNF-α antagonist therapy.

Furthermore, the American Gastroenterological Association care pathway for UC includes vedolizumab as one of the first-line biologic options for high-risk patients.[17] However, the latest American Gastroenterological Association guidelines do not include vedolizumab for the management of CD: these guidelines were finalized in 2013, before vedolizumab's approval.[18] These guidelines include infliximab, adalimumab, and certolizumab, but they do not provide specific recommendations regarding the line of therapy among biologics. The most frequently used biologic treatments for moderate-to-severe UC or CD are infliximab and adalimumab.[19]

The objective of this study was to develop a deci-

Figure 1 Budget Impact Model Structure



CD indicates Crohn's disease; UC, ulcerative colitis.

sion-analytic model to assess the potential budget impact of including vedolizumab on a health plan's formulary among the preferred first-line biologic treatment options for patients with UC or CD rather than including it only as a preferred second-line biologic treatment.

Methods

We developed a budget impact model to examine the incremental impact on a health plan's budget of including vedolizumab among existing, preferred first-line biologic treatments for eligible patients with UC or CD. The model was programmed using Microsoft Excel 2010 for Windows (Microsoft Corporation; Redmond, WA).

In the model, we first filtered the health plan's population to include patients who are eligible for treatment with vedolizumab (**Figure 1**). The eligible patient popu-

Table 1 Study Population Characteristics

Characteristic	Crohn's disease[22] Input	Crohn's disease[22] Cases, N	Ulcerative colitis[23] Input	Ulcerative colitis[23] Cases, N
Total members in health plan	1 million	1 million	1 million	1 million
Incidence[22,23]	0.0001	55	0.0002	160
Prevalence[5]	0.0024	2413	0.0026	2630
With moderate-to-severe disease[a]	64%	1544	57%	1499
TNF-α antagonist naïve[a]	47%	718	64%	959
TNF-α antagonist experienced[a]	—	826	—	540
Responding to biologic treatment[a]	38%	314	40%	216
TNF-α antagonist treatment failure	—	512	—	324
Patients naïve to or have failed TNF-α antagonists	—	1230	—	1283
Basic demographics[b,c]	—	—	—	—
Age, mean	36.74 yrs	—	40.36 yrs	—
Male patients	42.9%	—	57.8%	—
Weight	69.34 kg	—	76.29 kg	—

[a]Vedolizumab market share.[24]
[b]Pooled data from Crohn's disease clinical trials in the mixed-treatment comparison.[16]
[c]Pooled data from ulcerative colitis clinical trials in the mixed-treatment comparison.[25]
TNF-α indicates tumor necrosis factor alpha.

lation was divided into subpopulations by type of disease (ie, UC or CD) and experience with TNF-α antagonist therapy (naïve or treatment failure). These patients were then assigned to currently available biologic treatments based on their current market share.

Given the distribution of patients among treatments, the model estimated the proportion of patients who are responding to therapy or are in remission. The estimates of response and remission were calculated by an indirect comparison method using published estimates from phase 3 clinical trials of each treatment, following the Bucher method.[20] Direct medical costs were assigned to patients based on treatment response. Although patients could incur out-of-pocket expenses and indirect costs (eg, resulting from workdays missed), the analysis did not consider these costs, because our study's perspective is from the health plan's perspective.

Patients who did not respond to or stopped responding to treatment had an estimated annual risk for surgery. Patients were followed annually over a 3-year time horizon. The costs of therapy were undiscounted in accordance with the standard practice for budget impact analyses reported by the International Society for Pharmacoeconomics and Outcomes Research.[21]

The target patient population reflected the FDA-approved indication for vedolizumab. The model cohort's characteristics in terms of patient age, sex, and weight were based on pooled population means from the clinical trials included in the calculation of treatment efficacies (**Table 1**).[5,16,22-25] Because of the limited availability of data, we assumed that the patient demographics in these trials were similar among all subgroups.

Comparators

We estimated the budget impact of including vedolizumab among the existing preferred first-line (ie, infliximab and adalimumab) and second-line (ie, infliximab, adalimumab, golimumab [UC only], certolizumab [CD only], and ustekinumab [CD only]) biologic treatments in a hypothetical health plan formulary versus vedolizumab as a preferred second-line biologic option. To estimate this impact, we assumed that the hypothetical health plan formulary already included vedolizumab among its preferred second-line treatments. The comparators included the currently approved biologic agents for UC and CD, including vedolizumab, infliximab (brand name and biosimilar), adalimumab, and golimumab for UC, and vedolizumab, infliximab, adalimumab, certolizumab, and ustekinumab for CD.

We did not include natalizumab in the model because of low utilization.[24]

Health Plan Variation

To account for differences in health plans, we considered the following 3 hypothetical formulary cases before the introduction of vedolizumab among existing preferred first-line biologic treatments:

- Case 1: adalimumab as the existing preferred first-line biologic treatment and infliximab as the existing preferred second-line treatment
- Case 2: infliximab and adalimumab as the existing preferred first-line biologic treatments and infliximab and adalimumab as the existing preferred second-line treatments
- Case 3: infliximab as the existing preferred first-line biologic treatment and adalimumab as the existing preferred second-line treatment.

In patients with CD, ustekinumab was also considered a preferred second-line treatment in all hypothetical health plan formularies.

We initially distributed patients among available biologic treatments according to their up-to-date market share estimates, which were stratified by disease and treatment experience.[24]

For UC and CD, the changes in the distribution of biologic-naïve patients based on current market share[26] occurred by assigning new patients entering the model to a specific agent. We assigned these new patients randomly to a preferred treatment based on the health plan case and scenario. For example, if infliximab was the only preferred first-line option, then 100% of new biologic-naïve patients entering the model received infliximab as

a first-line treatment. If vedolizumab was introduced to a health plan with infliximab as an existing preferred first-line option, then 50% of new biologic-naïve patients received infliximab and 50% received vedolizumab.

For patients who were biologic naïve at baseline and subsequently failed treatment with a biologic, we did not explicitly model treatment switching. Instead, we assumed that the proportion of biologic-naïve patients relative to patients who failed biologic treatment remained constant each year. To achieve this, we assumed that 3% of anti-TNF–naïve patients annually moved to the population of patients who failed a TNF-α antagonist. These patients who newly failed a biologic were then distributed equally among the preferred second-line treatments.

We included the brand-name and the biosimilar form of infliximab in the model. As such, we made assumptions regarding the uptake of infliximab therapy. We did not allow the infliximab biosimilar to shift market share away from other treatments. Instead, we assumed that physicians who were likely to prescribe other treatments would continue to prescribe their preferred treatment, whereas a proportion of physicians who preferred infliximab would choose to prescribe the infliximab biosimilar form to new patients. We assumed that 15% of new biologic-naïve patients who began taking infliximab each year were assigned to the biosimilar. We varied this assumption in the sensitivity analysis.

Treatment Efficacy

Because there is a lack of head-to-head clinical trial data comparing modeled treatments, we used a method of indirect comparison using the available clinical trial data to estimate the treatment efficacy for assigning patients to health states given a treatment, using the Bucher method.[20] Specifically, we estimated the odds ratios relative to placebo for response and remission at the end of the maintenance period for each of the treatment comparators. We then estimated the probabilities using odds ratios and the probability of response and remission for conventional therapy (assumed to be the pooled placebo rates from the phase 3 clinical trials).[15,16,25-32]

Because clinical trials data for infliximab's biosimilar were not available at the time of this analysis, we assumed that the treatment efficacy for the infliximab biosimilar was the same as that of brand-name infliximab (ie, Remicade) for UC and CD. We varied this assumption in the sensitivity analysis. **Table 2** presents the estimated probabilities of response and remission for patients with UC or CD.[15,16,25-32]

The definitions of response and remission in the model were consistent with the definitions from the clinical trials for all treatments. For UC, we defined response as a decrease in Mayo score of ≥3 (≥30%) from baseline and remission as a Mayo score of ≤2 and no individual subscore of >1. For CD, we defined response as a reduction of ≥70 points in the Crohn's Disease Activity Index (CDAI) score from baseline and remission as a CDAI score of ≤150. These classifications of disease severity are consistent with previous models.[33,34]

Table 2 Percentage of Patients Achieving Response and Remission After 1 Year of Treatment

Disease/ current drug	Study	Patients untreated with TNF-α antagonists, %		Patients failing TNF-α antagonists, %	
		Response	Remission	Response	Remission
Ulcerative colitis					
Vedolizumab	Feagan et al, 2013[25]	65.3	45.8	37.6	28.5
Infliximab	Rutgeerts et al, 2005[26]	54.2	41.3	28.9	18.8
Adalimumab	Sandborn et al, 2012[27]	51.1	30.2	27.2	16.5
Golimumab	Sandborn et al, 2014[28]	47.2	33.2	25.2	19.2
Crohn's disease					
Vedolizumab	Sandborn et al, 2013[16]	48.1	42.0	37.9	37.9
Infliximab	Hanauer et al, 2002[29]	54.3	37.5	42.8	31.5
Adalimumab	Colombel et al, 2007[30] Sandborn et al, 2007[31]	51.7	49.0	40.6	35.2
Certolizumab	Sandborn et al, 2007[32]	47.8	31.3	37.6	25.3
Ustekinumab	Feagan et al, 2016[15]	41.2	34.3	39.3	32.8

NOTE: Response and remission rates were estimated using the Bucher method based on pooled maintenance trial data.[20]
TNF-α indicates tumor necrosis factor alpha.

For simplicity, the patients who responded to treatment were classified as being in remission or having mild disease. Nonresponders were assumed to have continuous moderate-to-severe disease. For UC, mild disease was defined as having a Mayo score of 3 to 5, and moderate-to-severe disease was defined as having a Mayo score of 6 to 12. For CD, a CDAI score of 150 to <220 and a CDAI score of 220 to 600 defined mild and moderate-to-severe diseases, respectively. Nonresponders also incurred an annual risk for surgery of 4.9% and 16.3% for UC and CD, respectively.[35]

Costs

The model included drug acquisition and administration costs associated with the available treatment options in the model (**Table 3A** and **Table 3B**).[3,36-41] The annual costs for each biologic drug in the study were estimated for standard and dose-escalation treatment regimens using wholesale acquisition costs from RED BOOK Online.[36] We assumed dose escalations (see **Supplementary Appendix** at **www.AHDBonline.com**) for all treatments based on the findings from 2 real-world analyses.[3,42]

The health-state costs were taken from previously published economic analyses and were adjusted to 2016

Table 3A Cost During Standard 1-Year Treatment

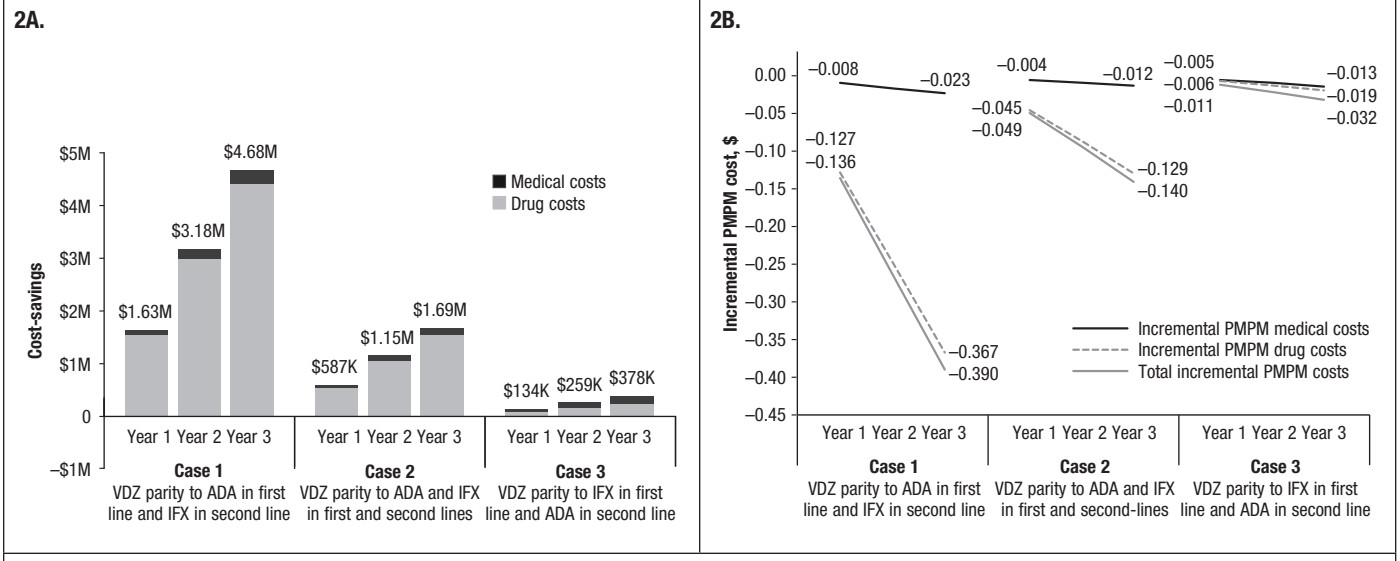
Biologic drug	Dose and frequency	Patients, %	Cost (WAC) per vial, $	Administration cost,[a] $	Weighted total annual cost,[b] $
Vedolizumab					
Standard dose	300 mg every 8 wks	94.8 (UC) 94.8 (CD)	5212.23	136.41	36,434.94 (UC) 36,434.94 (CD)
Dose escalation	300 mg every 4 wks	5.2 (UC) 5.2 (CD)	5212.23	136.41	
Infliximab (brand name)					
Standard dose	5 mg/kg every 8 wks	71.1 (UC) 69.7 (CD)	1113.27	165.05	38,382.96 (UC) 38,788.19 (CD)
Dose escalation	10 mg/kg every 8 wks	28.9 (UC) 30.3 (CD)	1113.27	165.05	
Infliximab (biosimilar)					
Standard dose	5 mg/kg every 8 wks	71.1 (UC) 69.7 (CD)	946.28	165.05	32,786.44 (UC) 33,130.90 (CD)
Dose escalation	10 mg/kg every 8 wks	28.9 (UC) 30.3 (CD)	946.28	165.05	
Adalimumab					
Standard dose	40 mg every 2 wks	86.9 (UC) 83.3 (CD)	2048.54	0.00	60,239.22 (UC) 62,156.65 (CD)
Dose escalation	40 mg every wk	13.1 (UC) 16.7 (CD)	2048.54	0.00	
Golimumab					
Standard dose	100 mg every 4 wks	86.9 (UC)	4382.87	0.00	64,441.34 (UC)
Dose escalation	200 mg every 4 wks	13.1 (UC)	4382.87	0.00	
Certolizumab					
Standard dose	400 mg every 4 wks	65.2 (CD)	3510.15	0.00	66,243.55 (CD)
Dose escalation	800 mg every 4 wks	34.8 (CD)	3510.15	0.00	
Ustekinumab					
Standard dose	90 mg every 8 wks	100 (CD)	17,680.44	136.41	115,863.08 (CD)
Dose escalation	N/A	N/A	N/A	N/A	

Table 3B Health-State Costs During Standard 1-Year Treatment

Health-state variables	Weighted total annual cost,[b] $
Ulcerative colitis[c]	
Remission	2650.63
Mild disease (applied to responders without remission)[c]	7564.30
Moderate-to-severe disease (nonresponders)[c]	18,154.32
Surgery[d]	91,767.17
Crohn's disease[c]	
Remission	3916.78
Mild disease (applied to responders without remission)[c]	11,177.61
Moderate-to-severe disease (nonresponders)[c]	26,826.26
Surgery[d]	91,767.17

[a]Administration costs for infliximab were estimated using *CPT* codes 96413 and 96415 and for vedolizumab, *CPT* code 96413.[38]
[b]Total treatment cost includes acquisition and administration costs. Acquisition costs are from RED BOOK Online.[36]
[c]Cohen et al estimated nonpharmacy costs of $17,133 for patients with moderate-to-severe UC in 2013 US dollars.[39] We converted this to 2016 US dollars using the medical Consumer Price Index.[37] For mild disease and remission, we estimated the costs assuming similar costs relative to moderate-to-severe disease, as seen in Malone et al, who presented monthly costs of $212 for remission, $605 for mild disease, and $1452 for moderate-to-severe disease in 2008 US dollars.[40] For Crohn's disease, Rubin et al estimated total annual costs of $18,736 for CD and $12,679.54 for UC.[3] This equated to CD costs being 1.48 times higher than those of UC. As such, we estimated the CD costs per health state by multiplying the UC costs by 1.48.
[d]Cohen et al presented a cost of surgery of $77,097 in 2008 US dollars.[41] We inflated this to 2016 US dollars using the medical Consumer Price Index.[37]
CD indicates Crohn's disease; *CPT*, *Current Procedural Terminology*; N/A, not applicable; UC, ulcerative colitis; WAC, wholesale acquisition cost.

Figure 2 Medical, Drug, and Total Annual and PMPM Cost-Savings of Adding Vedolizumab as a Preferred Biologic Option in 3 Hypothetical Formulary Cases During 3 Years



NOTE: Hypothetical formulary Case 1 includes adalimumab as an existing preferred first-line treatment and infliximab as an existing preferred second-line treatment. Hypothetical formulary Case 2 includes infliximab and adalimumab as existing preferred first- and second-line treatments. Hypothetical formulary Case 3 includes infliximab as an existing preferred first-line treatment and adalimumab as an existing preferred second-line treatment. Ustekinumab was included as an existing preferred second-line treatment for patients with CD in all cases.

ADA indicates adalimumab; CD, Crohn's disease; IFX, infliximab; PMPM, per-member per-month; VDZ, vedolizumab.

US dollars using the medical Consumer Price Index.[37] Because of the short time horizon and because clinical trials do not suggest a significant difference in mortality between biologic treatments, we did not consider mortality in the model.[15,16,25-32]

The model estimated the total annual and per-member per-month (PMPM) costs. The PMPM budget impact provided a way to translate the total annual cost-savings into the cost-savings each member of the health plan would have. The total annual and PMPM costs were reported for 2 scenarios of a hypothetical formulary: (1) a market mix with vedolizumab included with existing preferred first- and second-line biologic treatments, and (2) vedolizumab included only with existing preferred second-line biologic treatments. The model estimated the budget impact of including vedolizumab as a preferred first-line biologic treatment by subtracting the costs of Scenario 2 from Scenario 1.

Sensitivity Analysis

We performed a one-way sensitivity analysis (varying 1 parameter at a time while simultaneously fixing other parameters) to test the robustness of the model's assumptions and parameter estimates, given their uncertainty. The impact of all parameters was examined, excluding treatment costs. Uncertainty regarding model parameter estimates was based on their calculated or reported patient counts, standard errors, or range, depending on the parameter. Specifically, we used beta distribution to estimate the confidence interval for response or remission probabilities and the gamma distribution for health-state costs. We also estimated the impact of specifically varying the dose-escalation assumptions (see Supplementary Appendix at www.AHDBonline.com).

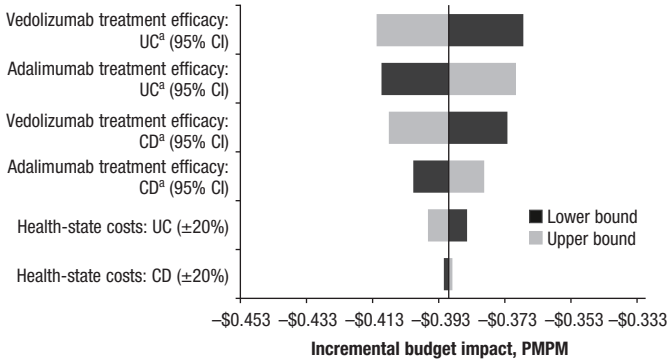
Results

Figure 2A and **Figure 2B** present the incremental total cost-savings of including vedolizumab among the existing preferred first-line biologic treatments for UC and CD for each hypothetical formulary case (see Supplementary Appendix at www.AHDBonline.com for detailed budget impact results) in a 1-million-member health plan. In all hypothetical formulary cases, including vedolizumab on parity with current options as a preferred first-line biologic treatment reduced health plan costs across all 3 years in the analysis.

The model demonstrated the most cost-savings assuming Case 1's hypothetical formulary (Figure 2A). The total annual cost-savings in Case 1 increased from $1.63 million in the first year to $4.68 million in the third year. The total annual cost-savings increased from $587,000 in the first year to $1.69 million in the third year for Case 2, and from $134,000 to $378,000 from the first year to the third year in Case 3.

The drug cost-savings differed depending on which hypothetical health plan formulary was assumed. For

Figure 3 One-Way Sensitivity Analysis: Incremental Year 3 PMPM Total Costs of Adding Vedolizumab as Preferred First-Line Biologic Option in a Hypothetical Formulary



[a]Anti-TNF treatment naïve.

CD indicates Crohn's disease; CI, confidence interval; PMPM, per member per month; TNF, tumor necrosis factor; UC, ulcerative colitis.

example, the drug cost-savings represented approximately 94% of the total budget impact in each year in Case 1. In Case 2, 91% of the total annual cost-savings resulted from savings in drug costs, whereas approximately 58% of the total cost-savings using Case 3 as a hypothetical formulary resulted from drug costs.

The PMPM cost-savings followed the same pattern as the total annual budget impact for all 3 years; in all hypothetical formulary cases, the introduction of vedolizumab as a preferred first-line treatment resulted in PMPM reduced costs during the 3 years (Figure 2B). The largest cost-savings were seen in Case 1, with total PMPM cost-savings of approximately −$0.14, −$0.27, and −$0.39 in years 1, 2, and 3, respectively.

Sensitivity Analysis Results

The results of a one-way sensitivity analysis on the total difference in year 3 PMPM budgets (representing the largest total budget impact) for the inclusion of vedolizumab among existing preferred first-line biologic options in the first hypothetical formulary case are shown in **Figure 3**. Because the 2 alternative market scenarios represent only a change in the treatment-naïve population, only varying parameters tied to this population and preferred first-line treatments affected the results.

The model was most sensitive to the estimates of vedolizumab's treatment efficacy for UC. For example, in Case 1, shifting the vedolizumab efficacy (ie, response and remission) parameter estimates to its upper bound (ie, assuming vedolizumab was more efficacious) resulted in an incremental PMPM budget savings of −$0.414, whereas varying the parameters to their lower bound (assuming vedolizumab is less efficacious) resulted in a PMPM budgetary impact of −$0.370. Other parameters to which the model was sensitive were the treatment efficacy of the preferred first-line treatment(s) on the formulary and health-state costs. Overall, the model showed robustness of results in the sensitivity analysis while varying all parameters, because none of the variations in parameter estimates resulted in a net increase in the PMPM cost.

Discussion

Our findings indicated that for each hypothetical health plan formulary we examined, including vedolizumab as a preferred first-line biologic treatment for patients with UC and CD produced cost-savings each year during a 3-year period. The majority of the cost-savings came from drug costs, with medical costs representing a smaller portion of the overall savings. Real-world dose-escalation patterns contributed to the observed differences in cost-savings across the plans. For example, approximately 30% and 15% of patients with UC and CD received an escalated dosing pattern for infliximab and adalimumab, respectively, versus approximately 5% for vedolizumab. The dose-escalation patterns for patients with UC and CD who received adalimumab led to approximately twice the annual cost of vedolizumab, whereas infliximab dose escalation resulted in an equivalent annual cost of vedolizumab. Thus, for Case 1, the introduction of vedolizumab as a preferred first-line treatment substantially saves more in treatment costs because vedolizumab reduces the use of adalimumab more in Case 1 than in the other cases.

To our knowledge, although a few studies examined the cost-effectiveness of biologic treatments in IBD, no published studies have estimated the health plan budget impact of including vedolizumab as a preferred first-line biologic treatment for UC and CD. In the cost-effectiveness assessments of vedolizumab, Wilson and colleagues developed a hybrid decision tree/Markov model to compare vedolizumab with other biologics for biologic-naïve patients with UC in the United Kingdom.[43] Erim and colleagues developed a Markov model to estimate the cost-effectiveness of vedolizumab with or without dose escalation of adalimumab in US patients with CD who failed treatment with adalimumab.[44] Both studies showed that treatment with vedolizumab was cost-effective and potentially cost-saving.

Our analysis complements these studies by considering real-world dose-escalation patterns among patients receiving biologic treatments for UC and CD. Although these studies assess different outcomes (cost-effectiveness rather than budget impact), they suggest similar benefits of vedolizumab in terms of reductions in other medical costs and the potential for overall cost-savings.

Finally, Yokomizo and colleagues estimated that the cost-effectiveness of 3 biologics (adalimumab, infliximab, and vedolizumab) was based on mucosal healing.[19] They found that vedolizumab would be cost-effective at a lower drug cost, whereas infliximab was cost-effective in the base case.[19] However, a significant limitation of the study is that it did not consider the nondrug medical costs, which is a critical component of the total IBD treatment cost. In addition, although Yokomizo and colleagues controlled for placebo response differences across the phase 3 clinical trial data, their model considered only mucosal healing as the outcome of interest,[19] whereas clinical response and remission (based on Mayo score for UC and CDAI score for CD) are typically used to assess efficacy in clinical trials. Using response and remission as the bases for effectiveness, the National Institute of Health and Care Excellence in the United Kingdom concluded that vedolizumab was cost-effective or dominant compared with infliximab and adalimumab for the treatment of UC.[45,46]

The strength of our model relies on the use of advanced methods to capture the relative efficacies among a menu of currently available treatment options (brand name and biosimilar), real-world treatment pattern input data, and a robust array of hypothetically existing preferred formularies in health plans. First, to reflect the current treatment paradigms in the care of patients with UC and CD, we modeled the most current treatment options available in potential health plans, including newly approved therapies and biosimilars. Incorporating a biosimilar in our budget impact analysis of including vedolizumab as a preferred first-line biologic treatment represents a conservative approach, because the use of any biosimilar may result in lower costs for the payer.

Second, we included indirect comparisons of treatment efficacy that were estimated based on clinical trial data using the Bucher method, which controlled for differences in placebo efficacy across trials. Failing to adjust for these differences introduces error into estimating the relative efficacies among treatments. Next, we used recent real-world dose-escalation patterns among patients with UC or CD who were receiving treatments because of the known influences of dose escalation on cost. We also considered 3 hypothetical health plan formularies to present a holistic analysis of including vedolizumab on parity with existing preferred first-line treatments.

Limitations

Decision makers should be aware of several limitations of this analysis. First, no published head-to-head clinical trials for the biologics in this study are available. This requires an indirect-comparison approach to determine the efficacy of these treatments relative to one another.

In addition, limited data are available for patients who failed previous TNF-α antagonist therapy. As such, assumptions were required about the efficacy of treatments in populations for which no published clinical trial data were available (eg, infliximab in patients who failed a previous TNF-α antagonist therapy).

We also assumed that study populations included in the indirect comparison were representative of the general populations with UC and CD. It is not clear, however, what the directional difference of changing this assumption would have on our results.

Furthermore, limited data also exist on the treatment efficacy of combination therapy and dose escalation; therefore, we did not consider combination therapy in the model. We assumed similar efficacy for dose escalation, but with increased costs.

Moreover, limited market uptake information was available on ustekinumab and the biosimilar form of infliximab because of their recent introductions to the market. Finally, because of limited data, the cost offsets of corticosteroid-free remission and mucosal healing were not considered in the model.

Conclusion

The inclusion of vedolizumab on parity with existing preferred first-line biologic treatments is expected to have a substantial cost-savings impact to a health plan. The cost-savings in this study were most pronounced in Case 1, when vedolizumab was introduced as a parity-preferred treatment alongside adalimumab as first-line treatment and alongside infliximab as second-line treatment (in addition to ustekinumab as second-line treatment for CD only), as a result of Case 1 having the largest decrease in the use of adalimumab. Based on these findings, vedolizumab may offer substantial cost-savings to a health plan as a first-line treatment option in UC or CD. ■

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