

## Budget Impact Analysis of Tofacitinib for treatment of Rheumatoid Arthritis

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### Abstract

**Objective:** Tofacitinib is a novel oral biologic that has been approved for treating adults with Rheumatoid arthritis (RA) having inadequate response to or are intolerant of methotrexate (MTX). The objective of this study was to conduct a budget impact model (BIM) analysis for estimating direct annual drug costs for individuals with RA before and after the introduction tofacitinib as a formulary option.

**Research Design and Methods:** The BIM was developed using a US healthcare payer's perspective with a one-year time frame. The tumor necrosis factor inhibitors (anti-TNFs) adalimumab, etanercept, infliximab, golimumab and certolizumab were considered as comparators. The BIM tested two base-case scenarios: "Base-case scenario 1: Incident anti-TNF users"; "Base-case scenario 2: Prevalent anti-TNF users". Both the scenarios were evaluated under the following two conditions: (1) assuming monotherapy except for infliximab and golimumab and (2) assuming combination therapy with MTX. One way sensitivity analyses were conducted to test the uncertainty in model parameters.

**Main Outcome Measures:** Per member per month cost.

**Results:** Under scenario 1, the decrease in total annual budget for the revised formulary was expected to be \$449,769 or \$0.04 per member per month (PMPM). With combination therapy, the over-all budget decrease was \$43,482 or \$0.004 PMPM. For scenario 2, the total annual budget savings with the revised formulary was expected to be \$1,536,712 or \$ 0.13 PMPM and \$ 148,564 or \$ 0.012 PMPM for mono and combination therapy, respectively. One-way sensitivity analysis revealed that results were sensitive to adherence rates of anti-TNFs and tofacitinib.

**Conclusion:** Given the easier route of administration and minimal impact on budget of health plans, tofacitinib can be considered as a viable treatment option for individuals with RA.

**Keywords:** Rheumatoid arthritis; Budget impact; Tofacitinib; Anti TNF drugs

### Introduction

Rheumatoid arthritis (RA) is an inflammatory autoimmune disease that affects an estimated 1% of the global population [1] and approximately 1.5 million adults in the United States (US) [2]. In addition to negatively impacting patient's quality of life, RA has substantial socioeconomic impact. Compared to patients without RA, individuals with RA have 3 times higher gender- and age-adjusted direct healthcare costs, twice the hospitalization rates, and 10 times the work disability rates [3]. Also, 66% of direct costs in individuals with RA can be attributed to prescription drug costs alone [4].

In the past, very few treatment options such as non-steroidal anti-inflammatory drugs and conventional non-biologic disease modifying anti-rheumatic drugs (DMARDs), for example methotrexate (MTX) and sulfasalazine were available for RA therapy [5]. The introduction of biologics such as tumor necrosis factor inhibitors (anti-TNFs) represented a paradigm shift in the available treatments for patients with RA [3]. The superiority of biologics in reducing joint damage caused by RA has been well established [6] and clinical studies have shown that these agents are effective at slowing disease progression and inducing disease remission [7]. However, annual medication costs with biologic agents continue to be high and range from \$15,000 to \$20,000 per patient per year [8].

Tofacitinib is a novel oral drug that has been approved by the US Food and Drug Administration as a targeted immunomodulator and disease-modifying therapy in RA [9]. Tofacitinib is a small-molecule,

oral selective inhibitor of Janus kinase (JAK) 1 and JAK3 and, to a lesser extent, JAK2. JAKs mediate signal-transduction activity by the surface receptors for multiple cytokines, IL- 2, 4, 6, 7, 9, 15, and 21 [10]. It has been approved for treating adults with moderate to severe active RA who have had an inadequate response to or who are intolerant of MTX [11]. Given the chronic nature of RA, the economic costs associated with the disease and the high costs of biologics, it is imperative for managed care to incorporate the value of biologics in their healthcare decision making [12]. Thus, evaluating the economic impact of adding tofacitinib can be valuable for optimal resource allocation, especially for reimbursements in a managed care settings. This study aims to develop a budget impact model (BIM) of biologic agents approved for treatment of RA and estimate the direct annual drug costs before and after the introduction tofacitinib in the formulary.

### Patients and Methods

The BIM was developed using a US healthcare payer's perspective

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with a one-year time frame. Based on the American College of Rheumatology treatment algorithm, MTX is utilized as a first line agent for treatment of individuals with RA and for those patients failing to achieve treatment goals with MTX, biologic agents can then be used as an add-on or as monotherapy [13]. Several biologic agents such as anti-TNFs (adalimumab, etanercept, infliximab, certolizumab and golimumab), anti-interleukin receptor inhibitor (tocilizumab), T cell co-stimulation blocker (abatacept) and immune system B-cell depletion agent (rituximab) have been shown to be effective in the treatment of RA [13,14]. In the treatment algorithm, abatacept, rituximab and tocilizumab are usually recommended after anti-TNFs have been tried in patients [15]. As per FDA recommendations, tofacitinib can be introduced into the RA treatment regimen when individuals have either failed or are intolerant to MTX treatment. Therefore, it was assumed that for individuals who are either intolerant to MTX or have failed MTX monotherapy, treatment with anti-TNFs is the next option. Thus, anti-TNFs such as adalimumab, etanercept, infliximab, certolizumab and golimumab were considered as direct comparators for tofacitinib in the BIM.

Using a hypothetical cohort of 1 million health-plan enrollees with a 0.5% RA prevalence [16] among whom 12% were incident users [17] (had failed MTX treatment and started using anti-TNF in the current year) and 41% were prevalent anti-TNF users [17] (used anti-TNF in the previous year), the BIM tested two base-case scenarios: "Base-case scenario 1: Incident users" and "Base-case scenario 2: Prevalent users". As anti-TNFs (except infliximab and golimumab) can be prescribed both as monotherapy and in combination with MTX, both scenarios were evaluated assuming the following two conditions (1) monotherapy except for infliximab and golimumab and (2) combination therapy with MTX. For combination therapy with MTX, the average dose of MTX was considered as 15 mg/week [18].

All drug costs were based on 2013 Average Wholesale Price (AWP) derived from the Red Book. Costs for both initial and maintenance doses and drug administration (infliximab IV infusion [19]) were considered in the study. Based on the average co-pay reported in the

literature [20], the mean cost-sharing for anti-TNF agents was assumed to be \$128. All costs were adjusted for inflation and expressed as 2013 US dollars. Table 1 provides the monthly costs for all the drugs used in the BIM. Market share data on the comparators were derived from Medicare and Medicaid market share data for top 5 inflammatory conditions [21]. In 2011, adalimumab (45.2%, 49.3%), etanercept (44.8%, 38.4%), infliximab (3.4%, 4.3%), golimumab (3.3%, 2.9%) and Certolizumab (1.5%, 2.6%) together accounted for 98.2% and 97.5% of Medicaid and Medicare market shares for inflammatory conditions, respectively. The BIM used an average of Medicare and Medicaid market share and added a constant factor of 0.43 to make the total market share as 100%. As market share for tofacitinib was not available, it was assumed that upon introduction, tofacitinib will have a 10% market share, matched by a 2% reduction in the share of the remaining 5 anti-TNF comparators. Another assumption in the BIM was that adherence rates for base-case scenarios were set at 100%.

On-way sensitivity analyses were conducted to examine how changes in key model parameters affected results of the modeled base-case scenarios. For sensitivity analysis the adherence rates for tofacitinib, golimumab and Certolizumab were varied at 80%, as real world adherence data for these drugs were unavailable. For adalimumab, etanercept, infliximab the respective adherence rates were varied at 51% [22], 41% [22] and 81% [23].

## Results

In the hypothetical cohort of 1 million health plan enrollees, 5,000 individuals were estimated to have RA based on the disease prevalence data. Among anti-TNF users, incident and prevalent cases were estimated at 600 (12%) and 2,050 (41%), respectively. Under "Base-case scenario 1", for anti-TNF naive individuals with RA on monotherapy, the total RA medication costs were estimated at \$25,876,421 or \$2.16 per member per month (PMPM) and \$25,426,652 or \$2.12 PMPM before and after the addition of tofacitinib to the formulary. Thus, the decrease in total annual budget with the revised formulary was expected to be \$449,769 or \$0.04 PMPM. With combination therapy, the over-

Medications	Strength	Form	Dose	Time Frame for dose	Package Size	Monthly Use Unit: Package	AWP Package Price (\$) <sup>a</sup>	Total Year Cost (\$) <sup>a</sup>
Methotrexate <sup>b</sup>	2.5 mg	TAB	15 mg	Weekly	36 ea	0.67	145.80	1,166.40
Tofacitinib	5 mg	TAB	5 mg	Twice Daily	60 s each	1	2,466	29,592
Etanercept	50 mg/ml	SOL	50 mg	Once Weekly	0.98 ml 4 s each	1	2,653	31,836.00
Adalimumab	40 mg/0.8 ml	SOL	40 mg	Once Weekly	2 s each	2	2,627.50	63,060.00
Adalimumab+MTX	40 mg/0.8 ml	SOL	40 mg	Once Every Other Week	2 s each	1	2,627.50	31,535.52
Infliximab Initial Dose <sup>c</sup>	100 mg	IV	3 mg/kg	At week 0, 2 and 6	each	NA	974	6,576.32
Infliximab Maintenance Dose	100 mg	IV	3 mg/kg	Every 8 weeks	each	NA	974	10,960.54
Infliximab administration Cost <sup>e</sup>								1,896.00
Total Infliximab Cost								19,428.00
Total Infliximab+MTX								20,594.40
Certolizumab Initial Dose	200 mg/ml	SOL	400 mg	At week 0, 2 and 4	2 s each	3	2,664.00	5,328.00
Certolizumab Maintenance Dose	200 mg/ml	SOL	400 mg	Every 4 weeks	2 s each	1	2,664.00	29,304.00
Total Certolizumab Cost								34,152.00
Golimumab +MTX <sup>d</sup>	50 mg/0.5 ml	SOL	50 mg	Once Every Month	0.5 ml	1	2,846.33	35,318.40

Note: <sup>a</sup>All costs expressed in 2013 US Dollars; <sup>b</sup>A weekly dose of 15 mg was assumed; <sup>c</sup>Based on an individual weighing 75 Kg; each year an incident Infliximab user will undergo 8 (3 initial + 5 maintenance) infusions and prevalent users will undergo 5 maintenance doses. Infliximab dose is 3 mg/Kg. Therefore an average individual weighing 75 Kg will require 3\*75=225 mg of the drug. Cost of 100 mg of the drug was \$974.27. Therefore 225 mg of the drug would cost \$974.27\*(225/100) = \$2192.11. The 3 initial doses will thus cost \$6576.32 and the 5 maintenance doses will cost \$10,960.55. <sup>d</sup>IV Administration cost per visit is \$224. <sup>e</sup>Golimumab total cost 34, 318.00 + MTX cost 1,166.40.

Tab: Tablet, SOL: Solution, IV: Intravenous

**Table 1:** Estimating the monthly costs for individuals with RA undergoing treatment.

all budget decrease was \$43,482 or \$0.004 PMPM. Under “Base-case scenario 2”, the total RA treatment costs before and after addition of tofacitinib to the formulary were estimated at \$88,411,107 or \$7.37 PMPM and \$86,874,394 or \$7.24 PMPM, respectively (assuming monotherapy) and \$63,478,622 or \$5.29 PMPM and \$63,330,058 or \$5.28 PMPM, respectively (assuming combination therapy). Overall, the total annual budget savings with the revised formulary was expected to be \$1,536,712 or \$0.13 PMPM and \$148,564 or \$0.012 PMPM for monotherapy and combination therapy, respectively. Tables 2 and 3 present the monotherapy condition for “Basecase scenarios 1 and 2”. Results for combination therapy are not presented in tabular form.

One way sensitivity analysis was conducted to test the uncertainties in model parameters. Under base-case scenario 1 and assuming monotherapy, if drug costs were varied by ± 20% of the base-case estimate, the PMPM savings varied from \$0.03 to \$0.05 and if the market share of tofacitinib was varied from 5%-15%, the decrease in PMPM costs varied from \$0.02-\$0.06. Assuming combination therapy,

the PMPM savings in drug costs and market share ranged from \$0.003-\$0.044 and \$0.002-\$0.005. However, if adherence rates for tofacitinib, adalimumab, etanercept, infliximab, golimumab and certolizumab were reduced to 80%, 51%, 41%, 81%, 80% and 80%, respectively, then PMPM cost increased by \$0.001 (monotherapy) and \$0.02 (combination therapy). Similarly, under base-case scenario 2, the respective PMPM savings for monotherapy and combination therapy ranged from \$0.10-\$0.15 and \$0.01-\$0.02 after varying drug costs, \$0.06-\$0.20 and \$0.006-\$0.02 by varying market share; and PMPM costs increased by \$0.002 and \$0.07 by varying the adherence rates.

### Discussion

Treatment costs in rheumatoid arthritis are an area of significant interest for all payers. The therapeutic category of biologic agents used to treat RA including anti-TNF agents, often approximates one-third of all specialty pharmacy spending and is the largest category of specialty drug spending [21]. Budget impact models are an important tool for

Time frame	12 months									
	Total Members	Total Member months	Target Population	Tofacitinib	Etanercept	Adalimumab	Infliximab+MTX	Certolizumab	Golimumab+MTX	TOTAL
Total Members	1,000,000	1,000,000	1,000,000	1,000,000	1,000,000	1,000,000	1,000,000	1,000,000	1,000,000	
Total Member months	12,000,000	12,000,000	12,000,000	12,000,000	12,000,000	12,000,000	12,000,000	12,000,000	12,000,000	
Target Population	600	600	600	600	600	600	600	600	600	
Average Yearly Costs (\$)	29,592.00	31,836.00	63,060.00	20,594.40	34,632.00	35,318.40	215,032.80			
Adherence Rates	100%	100%	100%	100%	100%	100%	100%			
Average Yearly Co-pay (\$)	1536	1536	1536	1536	1536	1536				
Adjusted Average Yearly Costs (\$)	28,056.00	30,300.00	61,524.00	19,058.40	33,096.00	33,782.40				
Current Market Share	0.00%	47.68%	42.03%	4.28%	3.53%	2.48%	100%			
Current Total RX Cost (\$)	0	8,668,224.00	15,515,122.32	489,419.71	700,973.28	502,682.11	25,876,421			
Current PMPM (\$)	0	0.722352	1.29292686	0.040784976	0.05841444	0.041890176	2.16			
New Market Share	10.00%	45.68%	40.03%	2.28%	1.53%	0.48%	100%			
New Total RX Cost (\$)	1,683,360.00	8,304,624.00	14,776,834.32	260,718.91	303,821.28	97,293.31	25,426,652			
New Cost for PMPM (\$)	0.14028	0.692052	1.23140286	0.021726576	0.02531844	0.008107776	2.12			
<b>NET BUDGET IMPACT PMPM (\$)</b>	<b>-0.04</b>									

Note: Based on hypothetical cohort of 1 million health-plan enrollees with a 0.5% RA prevalence of whom 12% were incident anti-TNF users (had failed MTX treatment and have started using anti-TNF in the current year). Results presented in the table are derived assuming monotherapy with anti-TNFs except for infliximab and golimumab. PMPM: Per member per month

Table 2: Base-Case Scenario 1 - Budget impact model for Tofacitinib for incident anti-TNF users.

Time frame	12 months									
	Total Members	Total Member months	Target Population	Tofacitinib	Etanercept	Adalimumab	Infliximab+MTX	Certolizumab	Golimumab+MTX	TOTAL
Total Members	1,000,000	1,000,000	1,000,000	1,000,000	1,000,000	1,000,000	1,000,000	1,000,000	1,000,000	
Total Member months	12,000,000	12,000,000	12,000,000	12,000,000	12,000,000	12,000,000	12,000,000	12,000,000	12,000,000	
Target Population	2050	2050	2050	2050	2050	2050	2050	2050	2050	
Average Yearly Costs (\$)	29,592.00	31,836.00	63,060.00	20,594.40	34,632.00	35,318.40	215,032.80			
Adherence Rates	100%	100%	100%	100%	100%	100%	100%			
Average Yearly Co-pay (\$)	1536	1536	1536	1536	1536	1536				
Adjusted Average Yearly Costs (\$)	28,056.00	30,300.00	61,524.00	19,058.40	33,096.00	33,782.40				
Current Market Share	0.00%	47.68%	42.03%	4.28%	3.53%	2.48%	100%			
Current Total RX Cost (\$)	0.00	29,616,432.00	53,010,001.26	1,672,184.02	2,394,992.04	1,717,497.22	88,411,107			
Current PMPM (\$)	0	2.468036	4.417500105	0.139348668	0.19958267	0.143124768	7.37			
New Market Share	10.00%	45.68%	40.03%	2.28%	1.53%	0.48%	100%			
New Total RX Cost (\$)	5,751,480.00	28,374,132.00	50,487,517.26	890,789.62	1,038,056.04	332,418.82	86,874,394			
New Cost for PMPM (\$)	0.47929	2.364511	4.207293105	0.074232468	0.08650467	0.027701568	7.24			
<b>NET BUDGET IMPACT PMPM (\$)</b>	<b>-0.13</b>									

Note: Based on hypothetical cohort of 1 million health-plan enrollees with a 0.5% RA prevalence among whom 41% were prevalent anti-TNF users (were anti-TNF users in the previous year). Results presented in the table are derived assuming monotherapy with anti-TNFs except for infliximab and golimumab. PMPM: Per member per month.

Table 3: Base-Case Scenario 2 - Budget impact model for Tofacitinib for prevalent anti-TNF users.

making formulary decisions and allow health plan managers to evaluate the potential economic impact resulting from the introduction of new pharmaceutical agents on medical and pharmacy budgets beyond just forecasting utilization. This study addresses the important issue of the formulary impact of tofacitinib for a vulnerable population who have failed desired response to widely accepted first line agent MTX.

The results of BIM indicate that shifting of formulary share to 10% in favor of tofacitinib will actually lead to a decrease in the managed care's formulary budget. However, caution has to be exercised since results were sensitive to adherence rates since different adherence rates for tofacitinib and comparators increased the formulary budget under both base-case scenarios. In a recent literature review Salt et al., commented that adherence to DMARDs in individuals with RA vary from 30% to 107%. Thus, studies using real world data needs to be conducted to truly understand the impact of medication adherence to tofacitinib on formulary budget [24].

With its oral route of administration, tofacitinib offers an advantage over the existing biologics which can only be administered parentally. Furthermore, not every biologic works for every RA patient [25] and the combination of anti-TNFs with MTX have been reported to work for only 30% of patients [26,27]. Thus, new treatment options are needed for patients who do not respond to anti-TNF monotherapy or combination therapy. While tofacitinib is easy to administer, there is not sufficient evidence to understand its impact on the progression of structural damage in RA. With no real world evidence on long-term efficacy or safety issues, providers may have to tread caution in prescribing tofacitinib [28]. Based on published studies, tofacitinib does appear to have comparable safety, efficacy and adverse event profile compared to other biologic such as adalimumab [9]. Given its minimal impact on health plans budget, providers and third party payers may want to consider tofacitinib as a viable treatment option for RA.

The results should be interpreted in light of model assumptions and limitations. The market share data of anti-TNF agents are based on 2010-2011 data which might have changed as of 2012-2013. Drug prices were based on AWP which are often considered as inflated [29]. Also, due to unavailability of data, model could not include any drug discount information. The study perspective was that of a health plan which does not include costs due to productivity loss and disability, [30,31] which are considered high among individuals with RA. The costs related to adverse events were not considered in this study. After failing methotrexate therapy patients with RA may opt to try out conventional DMARDs instead of biologics or may try non anti-TNF biologics such as rituximab, abatacept and tocilizumab; these scenarios were not examined in this study. Based on the study using data from Consortium Of Rheumatology Researchers Of North America Registry, the rates of prevalent anti-TNF use was estimated at 40% and new anti-TNF use at 12%; however studies based in other setting may report different estimates.

## Conclusion

The BIM results indicate that introduction of tofacitinib will have no significant impact on formulary budget under the assumption that plan members with RA are adherent to their respective drug regimen. As new agents for treatment of RA (e.g. fostamatinib) are expected to be launched in near future, the model framework presented in the study may be useful in estimating the initial impact of these drugs on the formulary budget and thus, aid in decision making.

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