

CADTH Health Technology Review

# Initiation of Biologic Disease-Modifying Antirheumatic Drugs for Rheumatoid Arthritis: A Budget Impact Analysis

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## Abbreviations

<b>bDMARD</b>	biologic disease-modifying antirheumatic drug
<b>BIA</b>	budget impact analysis
<b>csDMARD</b>	conventional synthetic disease-modifying antirheumatic drug
<b>RA</b>	rheumatoid arthritis

## Key Messages

- There is variation across Canadian jurisdictions in time to the initiation of biologic disease-modifying antirheumatic drug (bDMARD) therapy among adults with rheumatoid arthritis.
- From a pan-Canadian perspective, harmonizing time to bDMARD initiation across jurisdictions may result in savings to publicly funded drug plans in some jurisdictions but increased drug expenditures in others.
- The extent of savings or increased costs is dependent on jurisdiction, the number of new bDMARD users, and whether patients receive a biosimilar or originator bDMARD.

## Executive Summary

Biologic disease-modifying antirheumatic drugs (bDMARDs) may improve outcomes for patients with rheumatoid arthritis (RA) but represent high costs to public drug plans.<sup>1</sup> Reimbursement criteria for bDMARDs vary across Canadian jurisdictions, which may contribute to differences in the timing of initiating bDMARD therapy for patients with similar disease status. In a concurrent CADTH study of the utilization of bDMARDs for the treatment of RA across public drug plans in Canada, the longest mean time to a first bDMARD was observed in Alberta, Ontario, and British Columbia, with shorter times observed in Saskatchewan, Manitoba, and the Atlantic provinces. This budget impact analysis (BIA) examined the potential budgetary impact to Canadian provincial public drug plans of harmonizing the duration of conventional synthetic disease-modifying antirheumatic drug (csDMARD) use before initiating bDMARD therapy across jurisdictions.

An applied, policy-oriented BIA was developed to facilitate the consideration of alternative scenarios representing harmonized time to the initiation of bDMARD therapy from the perspective of the Canadian publicly funded drug plans. Three scenarios were considered: a reference scenario and 2 harmonization scenarios. The reference scenario reflects the status quo and was informed by the findings of the CADTH Utilization Study,<sup>2</sup> which assessed the jurisdiction-specific duration of csDMARD use before the initiation of bDMARD therapy for RA across public drug plans in Canada. Notably, an approximately 4-month difference in csDMARD use before the initiation of bDMARD therapy was found between patients in the Atlantic provinces, Manitoba, and Saskatchewan and those in Ontario, Alberta, and British Columbia. The reference scenario was compared with 2 harmonization scenarios, which considered alternative durations of csDMARD use before the initiation of bDMARD therapy, such that time to a first bDMARD was harmonized across jurisdictions (i.e., mean duration of csDMARD use before bDMARD therapy was aligned within approximately 1 month across jurisdictions). The first harmonization scenario considers the impact of increasing the mean time to the initiation of bDMARD therapy by 4 months for patients in the Atlantic provinces, Manitoba, and Saskatchewan, while the second scenario considers the impact of reducing the mean time to the initiation of bDMARD therapy by 4 months for Ontario, Alberta, and British Columbia. In both harmonization scenarios, time to the initiation of bDMARD therapy was assumed to be unchanged for the remaining jurisdictions. The BIA considers a cohort of patients who are newly diagnosed with RA in 2018. Patients are assumed to initiate treatment with a csDMARD at the time of diagnosis and to continue csDMARD treatment until initiating bDMARD therapy, the timing of which is varied between the reference and harmonization scenarios. The cumulative time on csDMARD and bDMARD therapy was analyzed over the

subsequent 3-year period to explore the impact to the public drug plans of initiating bDMARDs at various time points after diagnosis.

From a pan-Canadian perspective, CADTH estimated that increasing the time to the initiation of bDMARD therapy by 4 months in the Atlantic provinces, Manitoba, and Saskatchewan would result in a savings of \$9,555,958 over a 3-year period. Conversely, decreasing the time to the initiation of bDMARD therapy by 4 months in Ontario, Alberta, and British Columbia would result in an incremental cost to the drug plans of \$41,725,061 over 3 years. The projected impact of these changes varied by jurisdiction based on the number of new users. The findings were robust to most assumptions. However, when all new users were assumed to start on a biosimilar bDMARD (instead of an originator, if available), the impact of harmonizing the time to the initiation of bDMARD therapy was reduced by approximately 25% in both harmonization scenarios.

Key limitations include assuming that the market share of each bDMARD would remain unchanged over a 3-year analysis period, which does not account for the introduction of new bDMARDs, including new biosimilars. The introduction of new biosimilars may result in lower overall costs and reduce the differential between the reference and harmonization scenarios. Additionally, time to the initiation of bDMARD therapy was based on observed data for patients aged 67 years and older and was assumed to apply to all new adult users. The number of new bDMARD users with RA may be overestimated owing to the use of claims-based methodology in the Utilization Study, which may have captured patients receiving bDMARDs for the treatment of other rheumatic disease (e.g., ankylosing spondylitis, psoriatic arthritis). Individual results for the Atlantic provinces (i.e., Nova Scotia, New Brunswick, Prince Edward Island, Newfoundland and Labrador) are unavailable owing to low patient numbers in the concurrent Utilization Study. Finally, this analysis does not consider the health impacts of initiating bDMARD treatment at different times.

Harmonizing time to the initiation of bDMARD therapy across Canadian jurisdictions will have a budgetary impact on the public drug plans. From a pan-Canadian perspective, increasing time to the initiation of bDMARD therapy may result in savings to publicly funded drug plans, while decreasing time to bDMARD initiation may result in increased drug expenditures. The extent of savings or costs is dependent on jurisdiction, the number of new bDMARD users, and whether patients receive a biosimilar or originator bDMARD.

## Budget Impact Analysis

### Background

Rheumatoid arthritis (RA) is a chronic, systemic, autoimmune disease<sup>3,4</sup> that affects physical function and health-related quality of life.<sup>5</sup> Approximately 1.25% of Canadians are estimated to have RA, with a higher prevalence among women.<sup>6</sup> The goal of treatment is remission and, if not possible, to reduce disease activity, control symptoms, prevent disability, and improve quality of life.<sup>7</sup> First-line treatment of RA typically consists of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs; also called traditional disease-modifying antirheumatic drugs), including methotrexate, sulfasalazine, hydroxychloroquine, and leflunomide.<sup>7</sup> For those with an inadequate response to csDMARDs (i.e., moderate to high disease activity despite treatment with at least 2 csDMARDs), biologic DMARDs (bDMARDs)



may be considered.<sup>7</sup> The introduction of bDMARDs has resulted in increased public drug program spending and public health care payers have implemented criteria for their use in the treatment of RA.<sup>8</sup> However, such strategies have been applied differently across provinces and territories,<sup>8</sup> resulting in variation in public coverage for bDMARDs. A recent CADTH Environmental Scan of the coverage criteria for bDMARDs across Canadian public drug plans found that the reimbursement criteria are largely comparable across jurisdictions in the drugs covered but differ in the number of lines of prior therapy with csDMARDs required before accessing a bDMARD.<sup>8</sup> As noted in the CADTH study of the utilization of csDMARDs and bDMARDs for the treatment of RA across public drug plans in Canada (hereafter referred to as the “Utilization Study”),<sup>2</sup> the time to the initiation of bDMARD therapy among new users aged 67 years and older in Canada varies across jurisdictions, with the longest time to bDMARD initiation observed in Alberta, Ontario, and British Columbia, and shorter time to a first bDMARD in Saskatchewan, Manitoba, and the Atlantic provinces.

As part of the CADTH Technology Review of the harmonization of public coverage policies for biologic drugs for the treatment of RA, a budget impact analysis (BIA) was undertaken to explore the potential budgetary impact to Canadian public drug plans of harmonizing time to the initiation of bDMARD therapy across jurisdictions.

## Decision Problem

The objective of this BIA was to address the following question:

- What is the budget impact of harmonizing time to the initiation of bDMARD therapy across publicly funded drug plans in Canada compared to current jurisdiction-specific time to bDMARD?

Specifically, an applied BIA was constructed to facilitate the consideration of the financial impact of harmonizing time to bDMARD initiation for the treatment RA in adults. The BIA was conducted from the perspective of Canadian publicly funded provincial drug plans, excluding Quebec, over a 3-year time horizon. Owing to the drug plan perspective, only costs covered by the public drug plans were captured (i.e., drug costs). Time to bDMARD initiation was jurisdiction-specific (Table 2), as found in the accompanying Utilization Study.<sup>2</sup>

Two scenarios were considered, termed “harmonization scenarios.” In both, the duration of csDMARD use before the initiation of bDMARD therapy among bDMARD-naïve patients was aligned so that mean time to a first bDMARD was within the same time frame (i.e., approximately within a 1-month range) in all jurisdictions. Other variables (e.g., prescribing behaviour, wait times) were assumed to be unaffected by the harmonization scenarios.

**Harmonization Scenario 1:** Time to the initiation of bDMARD therapy was assumed to be increased by 4 months, compared to the jurisdiction-specific current time to bDMARD initiation, for the Atlantic provinces, Manitoba, Saskatchewan.

**Harmonization Scenario 2:** Time to the initiation of bDMARD therapy was assumed to be decreased by 4 months, compared to the jurisdiction-specific current time to bDMARD initiation, for Alberta, British Columbia, and Ontario.

## Study Design and Methods

A BIA was conducted using an Excel-based tool developed for this project. This tool has the flexibility to conduct various scenario analyses and to report the estimates of budget impact

disaggregated by jurisdiction. The ISPOR – International Society for Pharmacoeconomics and Outcomes Research – principles of good practice for BIAs were followed for the design and conduct of the BIA.<sup>9</sup>

## Patient Population

The population considered within this analysis consists of bDMARD-naive RA patients. Specifically, the population included patients taking a bDMARD for the first time following the use of at least 1 csDMARD (termed “new users”) as defined in the Utilization Study.<sup>2</sup> It was assumed that harmonizing the time to the initiation of bDMARD therapy would not change the current eligibility for bDMARD therapy as defined by the public drug programs and would thus not affect the number of people eligible for bDMARD therapy. No stratification of the target population was incorporated into the analysis.

A closed cohort was considered over the 3-year time horizon such that no new users were added after the first year and mortality was assumed to be negligible. The starting year for the cohort was 2018, consistent with the most recent year of utilization data available.<sup>2</sup> Thus, in the CADTH base case, the results reflect the impact of harmonizing time to bDMARD initiation for a cohort of newly diagnosed patients initiating csDMARD treatment in 2018; the impact of initiating bDMARDs at different times on the overall cost of treatment over the subsequent 3 years was assessed. In a scenario analyses, alternative starting years were considered.

The population for the BIA (i.e., new bDMARD users) was defined based on data from a CADTH Utilization Study.<sup>2</sup> Because the Non-Insured Health Benefits program, federal public drug plans, and Quebec were not captured in the Utilization Study, these programs are similarly not reflected in the BIA. In the Utilization Study, Nova Scotia, New Brunswick, Prince Edward Island, and Newfoundland and Labrador are grouped as “the Atlantic provinces” because of low patient numbers; this convention was similarly adopted in the BIA.

## Harmonization Scenarios

Three scenarios were considered in the BIA: a reference scenario that reflects the 2018 utilization of bDMARDs and jurisdiction-specific mean time to bDMARD initiation for adults with RA; and 2 new harmonization scenarios in which the time to a first bDMARD is harmonized across jurisdictions. Time to bDMARD initiation was conceptualized as the duration of time between the initiation of a csDMARD to the initiation of a first bDMARD. The harmonization scenarios were defined based on data from the Utilization Study,<sup>2</sup> which found an approximately 4-month difference in the mean duration of csDMARD use before bDMARD initiation between patients in the Atlantic provinces, Manitoba, and Saskatchewan and those in Ontario, Alberta, and British Columbia.

### *Reference Scenario*

The reference scenario reflects the mean jurisdiction-specific time to the initiation of bDMARD therapy based on the concurrent Utilization Study.<sup>2</sup> The study focused on the 67 years and older age group to capture a homogenous patient population across public drug plans. Patients aged 65 years and younger were assumed to potentially transition between multiple sources of coverage (e.g., public, private, out of pocket), which would impact the observed time to a bDMARD. In contrast, all patients aged 67 years and older are assumed to be eligible for public coverage. The jurisdiction-specific duration of csDMARD use before the initiation of bDMARD therapy observed among patients aged 67 years and older was assumed to be consistent across all adult new users in that jurisdiction.

### **Harmonization Scenarios**

The harmonization scenarios were informed by the CADTH Utilization Study.<sup>2</sup> Based on the findings of the Utilization Study, jurisdictions were grouped as having either a longer or shorter time to the initiation of bDMARD therapy. Group 1 comprised jurisdictions with a shorter mean time to bDMARD initiation (the Atlantic provinces, Manitoba, and Saskatchewan), whereas Group 2 comprised jurisdictions with a longer mean time to bDMARD initiation (Ontario, Alberta, British Columbia).

In Harmonization Scenario 1, the jurisdiction-specific mean time to bDMARD initiation (Table 2) was increased by 4 months for each jurisdiction in Group 1 (i.e., patients were assumed to remain on csDMARDs for an additional 4 months before initiating a bDMARD). Time to bDMARD initiation was assumed to be unchanged for the remaining jurisdictions.

In Harmonization Scenario 2, the jurisdiction-specific mean time to bDMARD initiation (Table 2) was decreased by 4 months for each jurisdiction in Group 2. The time to bDMARD initiation was assumed to be unchanged for the remaining jurisdictions.

### **Time Horizon**

The time horizon of the analysis was 3 years (2018 to 2020). Based on data availability, 2018 was adopted as the starting year of the cohort, as this is the most recent year with available utilization data.<sup>2</sup> No discounting was applied to the analysis.

### **Perspective**

The perspective of this analysis was Canadian publicly funded drug plans, excluding Quebec and federal drug plans. Therefore, only costs covered by public drug plans were captured (i.e., broader health care system costs; costs to individuals and private payers were not incorporated).

### **Analytic Framework Description**

An applied, policy-oriented economic BIA model was created to facilitate the consideration of alternative scenarios reflecting the timing of initiating bDMARD therapy. For consistency between the Utilization Study<sup>2</sup> and the BIA, the starting year of the analysis was assumed to be 2018 and the number of new users and market share between bDMARDs was assumed to be static (i.e., no forecasting of market changes was undertaken). The model schematic is shown in Figure 1.

The Reference and Harmonization Scenarios were used to estimate the incremental changes (costs or savings) resulting from the adoption of each alternative time to bDMARD initiation. For each jurisdiction, the total cost of bDMARD treatment per patient over the 3-year analysis horizon was estimated for the Reference Scenario and for each harmonization scenario. The total cost for each scenario was calculated by summing the annual cost associated with each bDMARD by the total duration of bDMARD use across all new users during the analysis period.

The budget impact is represented by the incremental costs (or savings) between scenarios over the 3-year analysis horizon. The incremental budget impact was determined separately for each alternative harmonization scenario compared to the Reference Scenario.

## Model Inputs

### Population Inputs

The number of new bDMARD users (Table 1) and the duration of csDMARD use before bDMARD initiation (Table 2) across jurisdictions was obtained from the Utilization Study.<sup>2</sup> New bDMARD users (aged<sup>3</sup> 18 years) were defined as individuals who had at least 1 RA biologic drug claim and no claims for any RA biologic drug in the 365 days before their first claim for an RA biologic drug (first prescription). The duration of csDMARD use before a first bDMARD was based on data pertaining to new users aged 67 years and older,<sup>2</sup> and was assumed to be consistent for all adult RA patients.

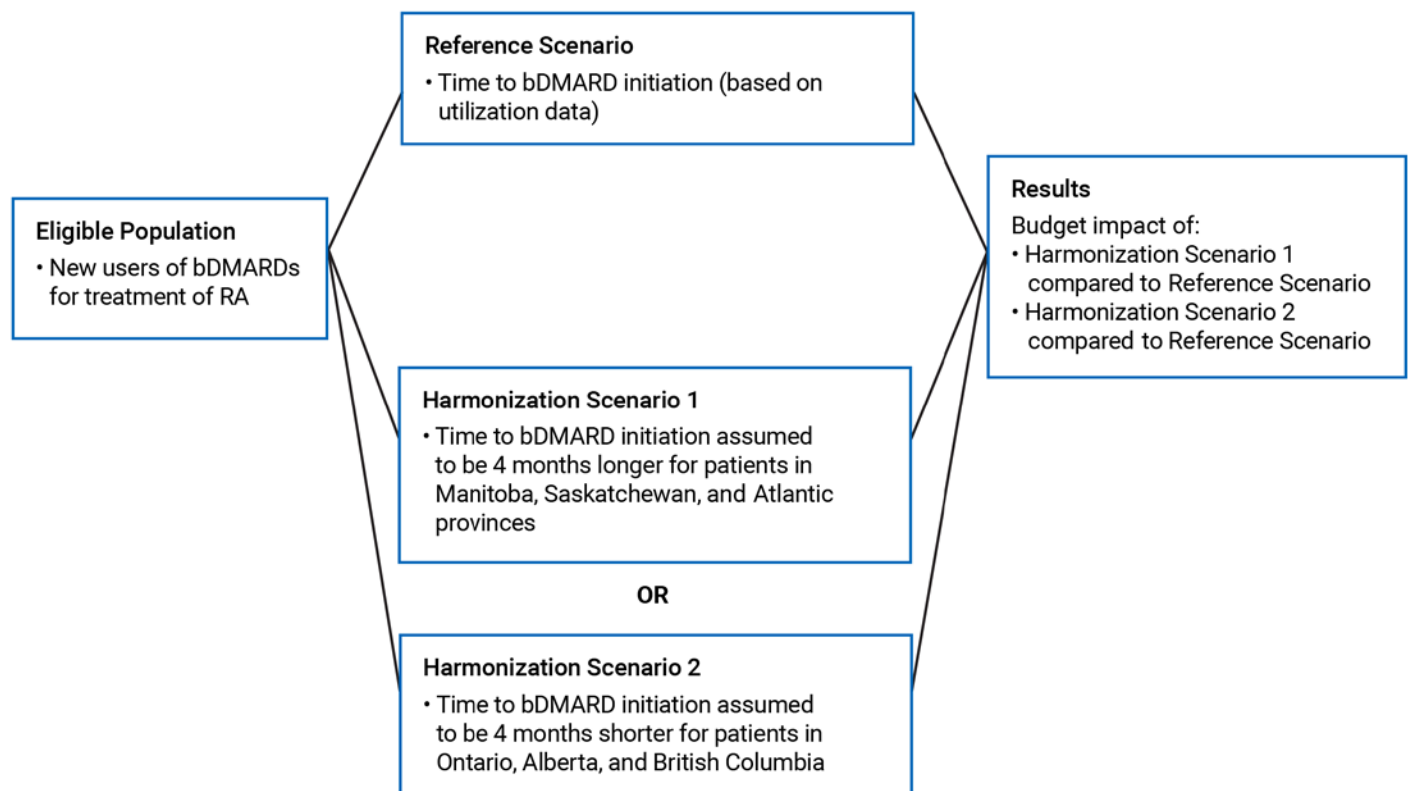
### Market Share

The market share attributed to each bDMARD was based on the number of unique users of each bDMARD from the Utilization Study<sup>2</sup> (Table 1) and was assumed to be constant for the 3-year analysis horizon.

### Cost Inputs

The BIA incorporated drug acquisition costs for bDMARDs. Where possible, publicly available, jurisdiction-specific prices for bDMARDs were used to estimate the cost of each treatment approach; where this was not available, prices from Ontario were used as a proxy in the base case. For bDMARDs with initial loading or initiation dosing, separate costs for the first and subsequent years of treatment were included in the model. Drug administration, markup,

**Figure 1: Analytic Framework**



bDMARD = biologic disease-modifying antirheumatic drug; RA = rheumatoid arthritis.

and dispensing fees were not included in the analysis and drug prices were assumed to be constant over the analysis horizon.

The recommended dosage and administration schedule for each bDMARD for the treatment of RA was obtained from the Health Canada–approved product monograph (Table 9); these were used in the calculation of the number of units used per patient for each bDMARD. For bDMARDs with multiple biosimilars (e.g., infliximab), the most expensive was included in the cost calculation in the base case.

The cost of csDMARDs was not included in the analysis because it was assumed that csDMARD usage would not be affected by the harmonization of the time to bDMARD initiation (i.e., csDMARD usage would be similar between the reference and harmonization scenarios). The clinical expert consulted by CADTH for this BIA indicated that, for patients initiating a first bDMARD, the bDMARD would be added to a background of csDMARDs and that the number and dosage of csDMARDs would remain constant for at least the first 3 to 4 months of

**Table 1: Number of New bDMARD Users, by Jurisdiction**

bDMARD	Number of new users ( <sup>a</sup> 18 years), 2018					
	Atlantic Provinces	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia
Abatacept (originator)	23	90	NR <sup>a</sup>	14	50	96
Adalimumab (originator)	278	1,374	189	148	564	645
Certolizumab (originator)	36	112	NR <sup>a</sup>	24	49	89
Etanercept (originator)	57	225	16	10	77	77
Etanercept (biosimilars)	27	395	49	47	49	190
Golimumab (originator)	118	238	38	79	142	132
Infliximab (originator)	112	482	6	NR <sup>a</sup>	240	53
Infliximab (biosimilars)	7	179	30	NR <sup>a</sup>	59	86
Rituximab (originator)	29	272	53	60	50	266
Tocilizumab (originator)	16	117	18	12	52	63

bDMARD = biologic disease-modifying antirheumatic drug; NR = not reported because of suppressed cell counts.

<sup>a</sup>Suppressed cells were assumed to include 5 patients in the base case.

Source: CADTH Utilization Study.<sup>2</sup>

**Table 2: Duration of csDMARD Use Prior to bDMARD Initiation, by Jurisdiction**

Scenario	Duration of csDMARD use, <sup>a</sup> mean days					
	Atlantic Provinces	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia
Reference scenario <sup>a</sup>	664	748	668	681	792	749
Harmonization Scenario 1	<b>786</b>	748	<b>790</b>	<b>803</b>	792	749
Harmonization Scenario 2	664	<b>626</b>	668	681	<b>670</b>	<b>627</b>

bDMARD = biologic disease-modifying antirheumatic drug; csDMARD = conventional synthetic disease-modifying antirheumatic drug.

<sup>a</sup>Based on the average time to initiate biologic therapy for publicly insured rheumatoid arthritis new users ≥ 67 years old, 2015 to 2018.<sup>2</sup>

treatment. Any differences in the number or dosages of csDMARDs between scenarios were deemed unlikely to drive the conclusions of the analysis owing to the low price of csDMARDs relative to bDMARDs.

### Analyses

Table 4 summarizes the key assumptions made in the base-case analysis of the BIA. Some base-case assumptions were tested in scenario and sensitivity analyses using a range of different assumptions. The scenarios explored and the inputs used for sensitivity analyses are presented in Table 5.

### Uncertainty and Scenario Analyses

Sensitivity and scenario analyses were conducted to explore the impact of parameter uncertainty and assumptions made in the base case on the BIA results. These included adopting an alternative patient weight – assuming that new users would preferentially start on a biosimilar form – using price data from an alternative jurisdiction as a proxy for those without publicly available drug prices and adopting 2021 as the starting year of the cohort. Details of the analyses are available in Table 5.

**Table 3: Annual Cost of bDMARD Treatment**

bDMARD	Average Annual Cost (\$) Per Patient <sup>a,b,c,d</sup>					
	Atlantic Provinces <sup>e</sup>	Ontario	Manitoba <sup>e</sup>	Saskatchewan	Alberta	British Columbia
Abatacept (originator)	SC: 19,437 IV: 22,515	SC: 19,437 IV: 22,515	SC: 19,437 IV: 22,515	SC: 19,437 IV: 22,515	SC: 19,437 IV: 22,515	SC: 20,409 IV: 23,641
Adalimumab (originator)	20,422	20,422	20,422	20,422	20,422	21,443
Certolizumab (originator)	19,935	19,935	19,935	19,935	19,935	20,932
Etanercept (originator)	21,111	21,111	21,111	21,111	20,880	19,890
Etanercept (biosimilar)	12,532	12,532	12,532	12,532	12,532	13,535
Golimumab (originator)	SC: 18,662 IV: 21,108	SC: 18,662 IV: 21,108	SC: 18,662 IV: 21,108	SC: 18,666 IV: 21,108	SC: 18,19 IV: 21,108	SC: 40,013 IV: 21,108
Infliximab (originator)	23,701	23,701	23,701	23,448	23,701	23,701
Infliximab (biosimilar)	12,600	12,600	12,600	15,600	12,600	13,230
Rituximab (originator)	19,292	19,292	19,292	19,292	19,292	20,257
Tocilizumab (originator)	SC: 9,332 IV: 11,882	SC: 9,332 IV: 11,882	SC: 9,332 IV: 11,882	SC: 9,332 IV: 11,882	SC: 9,332 IV: 11,882	SC: 9,798 IV: 12,476

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

<sup>a</sup>First year of treatment. Subsequent year costs were incorporated for bDMARDs with alternative initiation and maintenance dosing.

<sup>b</sup>For biosimilars with multiple available products, the most expensive within each jurisdiction was included in the base case.

<sup>c</sup>Dosages, administration schedules, and prices used in the determination of annual costs are available in Appendix 1.

<sup>d</sup>Ontario costs were used as proxy costs for the Atlantic provinces and Manitoba, as bDMARD prices were not publicly available for these jurisdictions.

**Table 4: Key Base-Case Assumptions**

Parameter	Assumption	Scenario analysis
<b>Analysis starting year</b>	2018. <sup>a</sup>	2021: Additional assumptions about jurisdiction-specific population growth and market share were required (described in the following section).
<b>bDMARD market share</b>	Assumed to remain constant for the 3-year analysis horizon.	New users were assumed to preferentially start on a biosimilar bDMARD (i.e., new users of infliximab were assumed to all receive the biosimilar form). Scenarios with a starting year of 2021 also incorporated new bDMARDs introduced since 2018.
<b>Patient cohort</b>	The number of users in the cohort was assumed to be constant over the 3-year model horizon (i.e., no new users were added to the cohort, and mortality was assumed to be negligible).	None.
<b>Number of new users</b>	For each cell with data suppressed owing to low patient counts (i.e., $\leq 5$ ), it was assumed that there were 5 patients per cell.	Suppressed cells were assumed to have a zero count.
<b>bDMARD dosage</b>	bDMARD dosage was assumed to not change based on clinical response. This is a simplifying assumption, as bDMARD dosage may be increased or stepped down depending on the treatment response. The clinical expert consulted by CADTH indicated that any dosage changes would not occur for at least the first 3 to 4 months after initiating a bDMARD.	None.
<b>bDMARD administration form</b>	All new users of abatacept, golimumab, and tocilizumab were assumed to receive the subcutaneous form in the base case.	All new users of abatacept, golimumab, and tocilizumab were assumed to receive the IV form.
<b>bDMARD cost</b>	Publicly available, jurisdiction-specific drug prices were used, where available. Prices for Ontario were used as a proxy for jurisdictions where public drug prices were unavailable.	Publicly available drug prices for British Columbia were used as a proxy for jurisdictions where public drug prices were unavailable.
<b>csDMARD usage</b>	The number and dosage of background csDMARDs was assumed to not change with the addition of bDMARDs, or to be affected by the harmonization scenarios.	None.
<b>Duration of csDMARD use</b>	The duration of csDMARD use before the initiation of the first bDMARD for patients aged 67 years and older was assumed to be consistent across all age groups.	None.

Parameter	Assumption	Scenario analysis
<b>Patient weight</b>	Patient weight was assumed to be 75 kg (for bDMARDs with weight-based dosing).	Higher and lower patient weights were assumed in scenario analyses.
<b>Health impacts</b>	Changes to health outcomes because of different durations of csDMARD use before bDMARD initiation were not modelled (i.e., changes to the timing of bDMARD initiation were assumed to have no effect on health outcomes or health care system costs).	None.

bDMARD = biologic disease-modifying antirheumatic drug; csDMARD = conventional synthetic disease-modifying antirheumatic drug.

<sup>2</sup>2018 reflects the most recent data available from the CADTH Utilization Study<sup>2</sup> regarding the number of new users by jurisdiction.



## Results

The pan-Canadian results of the BIA are presented here. Full disaggregated results are presented in Appendix 1.

### CADTH Base Case

#### *Harmonization Scenario 1*

From a pan-Canadian perspective (excluding Quebec), CADTH estimated that increasing the time to the initiation of bDMARD therapy by 4 months in each of the Atlantic provinces, Manitoba, and Saskatchewan would result in a savings of \$9,555,958 over 3 years (Table 6). The projected savings were greatest in the Atlantic provinces (Table 10) because of highest number of new users (i.e., compared to the number of new users in Manitoba and Saskatchewan).

**Table 5: Scenario Analyses**

Parameter	CADTH base case	CADTH scenarios
1. Patient weight	75 kg	50 kg
2. Patient weight	75 kg	100 kg
3. bDMARD administration form (abatacept, golimumab, tocilizumab)	All new users assumed to receive the subcutaneous form	All new users assumed to receive the IV form
4. Province used as proxy for bDMARD prices (for those without publicly available prices)	Ontario	British Columbia
5. bDMARD biosimilar price (for those with multiple biosimilar forms)	Most expensive	Least expensive
6. Suppressed cell counts	Assumed to represent 5 new users	Assumed to represent 1 new user
7. Cohort starting year	2018	2021 <sup>a</sup>
8. Cohort starting year	2018	2021, with all new bDMARD users assumed to start on a biosimilar <sup>a</sup>
9. Cohort starting year	2018	2021, with new bDMARDs introduced since 2018 incorporated <sup>a,b</sup>
10. Duration of csDMARD use	Jurisdiction and harmonization scenario-specific: Assumed to increase by 4 months in Harmonization Scenario 1 and to decrease by 4 months in Harmonization Scenario 2, depending on jurisdiction (Figure 1)	Time to bDMARD initiation was harmonized across jurisdictions by assuming that jurisdiction-specific current time was concurrently increased by 2 months in the Atlantic provinces, Manitoba, and Saskatchewan, and decreased by 2 months in Alberta, British Columbia, and Ontario (Harmonization Scenario 3)

bDMARD = biologic disease-modifying antirheumatic drug.

<sup>a</sup>The number of new users was increased by jurisdiction-specific population growth rates; all other parameters were held constant unless otherwise stated.

<sup>b</sup>10% of new users were assumed to start on sarilumab, with market share taken from tocilizumab, on the basis of clinical expert opinion. All new users for adalimumab, etanercept, infliximab, and rituximab were assumed to start on the biosimilar form.

### Harmonization Scenario 2

From a pan-Canadian perspective (excluding Quebec), CADTH estimated that decreasing the time to the initiation of bDMARD therapy by 4 months in each of Ontario, Alberta, and British Columbia would result in an incremental cost of \$41,725,061 over 3 years (Table 7). By jurisdiction, the projected costs were greatest in Ontario (Table 11) because of the highest number of new users (i.e., compared to the number in Manitoba and Saskatchewan).

### Scenario and Sensitivity Analyses

The pan-Canadian results of key scenario analyses are presented in Table 8 (jurisdiction-specific results are presented in Table 12 and Table 13). Of these, from a pan-Canadian perspective, none had a large effect on the expected impact of harmonizing time to bDMARD initiation among new users, with the exception of including new bDMARDs introduced since 2018 (i.e., biosimilars for adalimumab and rituximab, sarilumab originator) and assuming that all new users would receive a biosimilar form (Scenario 9). From a pan-Canadian perspective, the Harmonization Scenario 1 assumption that all new users would initiate on a biosimilar form (where available) resulted in an approximately 25% reduction in savings, while in Harmonization Scenario 2, this assumption resulted in approximately 24% lower costs.

In scenario analyses, CADTH explored the impact of a third harmonization scenario in which the duration of time to bDMARD initiation was harmonized across jurisdictions by increasing or decreasing the current mean time to a first bDMARD by 2 months, depending on the jurisdiction (i.e., changes in time to bDMARD initiation were implemented for all public plans). Specifically, time to the initiation of bDMARD therapy was assumed to be concurrently increased by 2 months in the Atlantic provinces, Manitoba, and Saskatchewan, and decreased by 2 months in Alberta, British Columbia, and Ontario. Compared to the reference scenario, this harmonization scenario resulted in higher overall costs to the drug plans from a pan-Canadian perspective because of the increased time on bDMARDs in Alberta, British Columbia, and Ontario (\$16 million over 3 years). Jurisdiction-specific results for this scenario are presented in Table 12.

**Table 6: Pan-Canadian Budget Impact Analysis Results – Harmonization Scenario 1**

Scenario	Three-year total costs (\$)
Reference Scenario	151,922,685
Harmonization Scenario	142,366,726
Impact	-9,555,958

Note: Harmonization Scenario 1 – Time to the initiation of biologic disease-modifying antirheumatic drug therapy was increased by 4 months for the Atlantic provinces, Manitoba, and Saskatchewan.

**Table 7: Pan-Canadian Budget Impact Analysis Results – Harmonization Scenario 2**

Scenario	Three-year total costs (\$)
Reference Scenario	151,922,685
Harmonization Scenario	193,647,746
Impact	41,725,061

Note: Harmonization Scenario 2 – Time to the initiation of biologic disease-modifying antirheumatic drug therapy was assumed to be decreased by 4 months for Alberta, British Columbia, and Ontario.

**Table 8: Key Scenario Analysis Results**

Analysis	Scenario	Harmonization Scenario 1 <sup>a</sup> (\$)	Harmonization Scenario 2 <sup>b</sup> (\$)
Base case	Reference Scenario	151,922,685	151,922,685
	Harmonization Scenario	142,366,726	193,647,746
	<b>Impact</b>	<b>-9,555,958</b>	<b>41,725,061</b>
Scenario 1: Lower patient weight (50 kg)	Reference Scenario	143,720,725	143,720,725
	Harmonization Scenario	134,523,616	183,178,719
	<b>Impact</b>	<b>-9,197,109</b>	<b>39,457,994</b>
Scenario 2: Higher patient weight (100 kg)	Reference Scenario	154,448,408	154,448,408
	Harmonization Scenario	144,749,350	196,904,986
	<b>Impact</b>	<b>-9,699,057</b>	<b>42,456,578</b>
Scenario 3: All users assumed to receive IV forms of abatacept, golimumab, and tocilizumab	Reference Scenario	152,391,754	152,391,754
	Harmonization Scenario	142,819,055	192,766,937
	<b>Impact</b>	<b>-9,572,700</b>	<b>40,375,182</b>
Scenario 4: British Columbia drug prices adopted as proxy for Atlantic and Manitoba drug prices	Reference Scenario	156,609,782	156,609,782
	Harmonization Scenario	145,728,151	198,334,843
	<b>Impact</b>	<b>-10,881,631</b>	<b>41,725,061</b>
Scenario 5: Least expensive bDMARD price incorporated	Reference Scenario	151,634,893	151,634,893
	Harmonization Scenario	142,093,761	193,284,146
	<b>Impact</b>	<b>-9,541,131</b>	<b>41,649,253</b>
Scenario 6: Suppressed cell counts assumed to represent 1 new user	Reference Scenario	151,565,711	151,565,711
	Harmonization Scenario	142,109,897	193,290,772
	<b>Impact</b>	<b>-9,455,814</b>	<b>41,725,061</b>

Analysis	Scenario	Harmonization Scenario 1 <sup>a</sup> (\$)	Harmonization Scenario 2 <sup>b</sup> (\$)
Scenario 7: Cohort starting year assumed to be 2021 <sup>c</sup>	Reference Scenario	157,642,026	157,642,026
	Harmonization Scenario	147,857,893	201,101,733
	<b>Impact</b>	<b>-9,784,133</b>	<b>43,459,707</b>
Scenario 8: Cohort starting year assumed to be 2021 <sup>c</sup> and all new users assumed to start on a biosimilar (if available)	Reference Scenario	144,067,076	144,067,076
	Harmonization Scenario	134,960,383	183,760,572
	<b>Impact</b>	<b>-9,106,693</b>	<b>39,693,497</b>
Scenario 9: Cohort starting year assumed to be 2021, <sup>c</sup> all new users assumed to start on a biosimilar, and bDMARDs introduced since 2018 incorporated <sup>d</sup>	Reference Scenario	114,667,490	114,667,490
	Harmonization Scenario	107,487,961	146,208,669
	<b>Impact</b>	<b>-7,179,528</b>	<b>31,541,180</b>
Scenario 10: Harmonization Scenario 3 (time to bDMARD initiation is adjusted by 2 months across jurisdictions) <sup>e</sup>	Reference Scenario	151,922,685	
	Harmonization Scenario	168,193,140	
	<b>Impact</b>	<b>16,270,455</b>	

bDMARD = biologic disease-modifying antirheumatic drug.

Note: Negative values denote cost savings.

<sup>a</sup>Harmonization Scenario 1 – Time to a first bDMARD was increased by 4 months for the Atlantic provinces, Manitoba, and Saskatchewan.

<sup>b</sup>Harmonization Scenario 2 – Time to a first bDMARD was assumed to be decreased by 4 months for Alberta, British Columbia, and Ontario.

<sup>c</sup>The number of new users was increased by jurisdiction-specific population growth rates; all other parameters were held constant unless otherwise stated.

<sup>d</sup>Market share for sarilumab was estimated based on input provided by the clinical expert consulted by CADTH for this review.

<sup>e</sup>Time to bDMARD initiation was harmonized across jurisdictions by assuming that jurisdiction-specific current time was concurrently increased by 2 months in the Atlantic provinces, Manitoba, and Saskatchewan, and decreased by 2 months in Alberta, British Columbia, and Ontario.

## Summary of Findings

In this BIA, CADTH explored the costs to Canadian public drug plans associated with harmonizing the duration of time on csDMARDs before the initiation of bDMARD therapy among new users across jurisdictions. As found in the CADTH Utilization Study<sup>2</sup> of bDMARDs for the treatment of RA across public drug plans in Canada, the duration of csDMARD use before the initiation of a first bDMARD varies across jurisdictions. Notably, the Utilization Study found a divergence between British Columbia, Alberta, and Ontario compared to Manitoba, Saskatchewan, and the Atlantic provinces, with an approximately 4-month difference in time to bDMARD initiation among patients in the former and latter jurisdictions. Thus, in this BIA, CADTH explored the budgetary impact to the public drug plans of harmonizing the time to bDMARD initiation such that patients in all jurisdictions would have a similar duration of csDMARD use before initiating a first bDMARD.

Two harmonization scenarios were considered based on the findings of the Utilization Study, such that mean time to the initiation of bDMARD therapy would be similar (i.e., within 1 month) across jurisdictions.<sup>2</sup> In the first scenario, jurisdiction-specific time to bDMARD initiation was assumed to be increased by 4 months, compared to current time to bDMARD initiation, for the Atlantic provinces, Manitoba, and Saskatchewan. In the second scenario, jurisdiction-specific time to bDMARD initiation was assumed to be decreased by 4 months, compared to current usage patterns, for Alberta, British Columbia, and Ontario. The total mean duration of csDMARD use before bDMARD initiation in the reference and harmonization scenarios by jurisdiction are provided in Table 2. As noted in the Utilization Study, the differences in duration of csDMARD use before initiating bDMARD therapy observed in the reference scenario may be owing in part to differences in coverage criteria in the number of lines of therapy that are required to be trialled before accessing publicly reimbursed bDMARD therapy. Both harmonization scenarios assumed that all variables other than time to a first bDMARD are constant between the reference and harmonization scenarios (e.g., no changes to prescribing behaviour, wait times).

In the first Harmonization Scenario, increasing time to the initiation of bDMARD therapy by 4 months for the Atlantic provinces, Manitoba, and Saskatchewan was associated with expected savings of \$9,555,958 to the drug plans over the 3-year analysis period compared to the reference scenario. The projected savings were greatest in the Atlantic provinces because of the highest number of new users. In the second Harmonization Scenario, reducing time to bDMARD initiation by 4 months in each of Ontario, Alberta, and British Columbia was associated with increased costs of \$41,725,061 to the drug plans over the 3-year analysis period, relative to the reference scenario. The projected savings were greatest in Ontario because of the highest number of new users.

Several scenario and sensitivity analyses were conducted to explore the uncertainty associated with these findings. These included adopting alternative patient weight, assuming that new users would preferentially start on biosimilar bDMARDs, using proxy price data from an alternative jurisdiction for those without publicly available drug prices, and adopting 2021 as the starting year of the cohort. The findings were robust to all scenarios considered, except when 2021 was adopted as the starting year and new biosimilar and originator bDMARDs introduced since 2018 were incorporated in the analysis (assuming all new users started on a biosimilar form, if available). This reduced the savings associated with Harmonization Scenario 1 by approximately 25% and reduced the costs associated with Harmonization Scenario 2 by approximately 24%. New bDMARDs introduced since 2018 were biosimilars for adalimumab and rituximab, as well as the originator sarilumab; however, the impact of

this scenario analysis was largely driven by the introduction of adalimumab biosimilars, as adalimumab represented 40% of the market share.

Several key assumptions were incorporated in the BIA and potential limitations associated with these should be acknowledged. First, the starting year of the cohort in the base case was assumed to be 2018, which reflects the most recent year for which bDMARD utilization data were available from the CADTH Utilization Study.<sup>2</sup> The market share of each bDMARD was assumed to remain unchanged over a 3-year analysis period (i.e., no forecasting was undertaken), which was a simplifying assumption. If new patients were preferentially started on biosimilar formulations, this would result in lower overall costs and reduce the differential between the reference and harmonization scenarios.

Second, time to the initiation of bDMARD therapy among new adult users in the BIA was assumed to be equivalent to the observed trends among patients aged 67 years and older in the Utilization Study.<sup>2</sup> The cohort of patients aged 67 years and older was assumed to reflect patients eligible for public drug plans; in contrast, patients aged younger than 65 years may have public or private insurance and some patients may transition between these. The time to bDMARD initiation among new users aged 18 to 65 years who are eligible for public drug plan coverage is unknown. Additionally, individual results for the Atlantic provinces (i.e., Nova Scotia, New Brunswick, Prince Edward Island, Newfoundland and Labrador) are unavailable because of low patient numbers in the concurrent Utilization Study.

Third, because the starting year of the cohort was assumed to be 2018, bDMARDs approved since 2018 are not reflected in the base case. This includes biosimilars for adalimumab and rituximab, and the originator sarilumab. In scenario analyses, incorporating these new bDMARDs and assuming that new users would preferentially start on a biosimilar reduced the savings associated with Harmonization Scenario 1 and reduced the costs associated with Harmonization Scenario 2. Newer bDMARDs not currently reimbursed on public formularies (e.g., Remsima, a subcutaneous form of infliximab) are not included in this analysis.

Fourth, the cost of csDMARDs was not incorporated in the BIA. This was a simplifying assumption that is not expected to have an important effect on the budgetary impact of harmonizing time to bDMARD initiation. As indicated by the clinical expert consulted by CADTH for this BIA, bDMARDs are expected to be added to patients' existing csDMARD regimen and their usage is not likely to be affected by altering time to the addition of a bDMARD. Further, the cost of csDMARDs is low compared to bDMARDs and changes to csDMARD regimens would not be expected to have an important budgetary impact.

Fifth, the health implications (including on health care system costs) of altering the duration of time that a patient spends on csDMARDs before initiating a first bDMARD was not considered in the budget impact analysis.

Finally, it should be noted that the data from the CADTH Utilization Study (i.e., new users, time to a first bDMARD) may include patients receiving bDMARDs for the treatment of other rheumatic disease (e.g., ankylosing spondylitis, psoriatic arthritis) owing to the use of claims-based methodology.<sup>2</sup> CADTH further notes that, while the focus of this BIA was on estimating the budgetary impact of aligning time to the initiation of bDMARD therapy across jurisdictions, time to bDMARD initiation may be influenced by many factors (e.g., reimbursement criteria, prescribing behaviour, rural versus urban location, wait times); analyzing the impact of such particular factors was beyond the scope of this analysis.

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## Appendix 1: Budget Impact Analysis Tables

**Table 9: Cost Table for bDMARDs for the Treatment of Rheumatoid Arthritis**

bDMARD	Recommended dosage	Strength/ concentration	Price (\$) <sup>a,b,c</sup>			
			Ontario <sup>d</sup>	Saskatchewan	Alberta	British Columbia
Abatacept (originator)	SC: 125 mg weekly; IV: 750 mg <sup>e</sup> at week 0, 2, 4, then every 4 weeks	SC: 125 mg/mL	373.7881	373.7900	373.7875	392.4775
		IV: 250 mg	500.3411	500.3400	500.3400	525.3582
Adalimumab (originator)	40 mg SC every 2 weeks	40 mg/0.2 mL	392.7250	392.7250	392.7250	NA
		40 mg/0.8 mL	785.4500	785.4500	785.4500	824.7225
Adalimumab (biosimilar) <sup>f</sup>	40 mg SC every 2 weeks	20 mg/0.4 mL	235.6400	NA <sup>g</sup>	235.6400	247.422
		40 mg/0.8 mL	471.2700		471.2700	494.8335
Certolizumab (originator)	400 mg SC at week 0, 2, 4, followed by 200 mg every 2 weeks	200 mg/mL	664.5100	664.5100	664.5100	697.7355
Etanercept (originator)	50 mg SC weekly	25 mg/vial	202.9300	202.9300	200.7100	764.9800
		50 mg/mL	405.9850	405.9900	401.5400	382.4940
Etanercept (biosimilar)	50 mg SC weekly	50 mg/mL	241.0000	241.0000	241.0000	260.2800
Golimumab (originator)	SC: 50 mg every 4 weeks; IV 2 mg/kg at 0, 4 weeks, then every 8 weeks	SC: 100 mg/mL	1,555.1700	1,555.5000	1,516.0000	3,334.4430
		IV: 50 mg/4 mL	NA	NA	879.500	NA
Infliximab (originator)	3 mg/kg IV at 0, 2, 6 weeks, then every 8 weeks	100 mg/vial	987.5600	977.0000	987.5600	987.5600
Infliximab (biosimilar)	3 mg/kg IV at 0, 2, 6 weeks, then every 8 weeks	100 mg/vial (Inflectra)	525.0000	650.0000	525.0000	551.2500
Rituximab (originator)	One course is 2 IV infusions (1,000 mg; week 0, week 2); 2 courses per year	100 mg/10 mL	482.3080	482.3050	NA	506.4230
		500 mg/50 mL	2,411.5400	2,411.5250	NA	NA



bDMARD	Recommended dosage	Strength/ concentration	Price (\$) <sup>a,b,c</sup>			
			Ontario <sup>d</sup>	Saskatchewan	Alberta	British Columbia
Rituximab (biosimilar) <sup>f</sup>	One course is 2 IV infusions (1,000 mg; week 0, week 2); 2 courses per year	100 mg/10 mL	297.0000	297.0000	297.0000	320.7600
		500 mg/50 mL	1,485.0000	1,485.0000	1,485.0000	1,603.8000
Sarilumab (originator) <sup>f</sup>	200 mg SC every 2 weeks	150 mg/1.14 mL 200 mg/1.14 mL	737.5800	737.5800	737.5800	NA <sup>h</sup>
Tocilizumab (originator)	SC: patients < 100 kg: 162 mg every other week; patients ≥ 100 kg: 162 mg weekly. IV: 4 mg/kg every 4 weeks	SC: 162 mg/0.9 mL	358.9050	358.9050	358.9050	376.8503
		IV: 80 mg/4 mL and	182.8000	182.8000	182.8000	191.9100
		200 mg/10 mL	457.0000	457.0000	457.0000	479.8500

IV = intravenous; NA = not applicable; SC = subcutaneous.

<sup>a</sup>For biosimilars with multiple available products, the most expensive within each jurisdiction was included in the base case.

<sup>b</sup>A patient weight of 75 kg was assumed in the base case for biologic disease-modifying antirheumatic drugs with weight-based dosages.

<sup>c</sup>Source: Ontario Drug Benefit Formulary,<sup>10</sup> Ontario Exceptional Access Program,<sup>11</sup> Saskatchewan Drug Plan,<sup>12</sup> Alberta Blue Cross, and British Columbia PharmaCare.<sup>13</sup>

<sup>d</sup>Ontario costs were used as proxy costs for the Atlantic provinces and Manitoba in the base case, as bDMARD prices were not publicly available for these jurisdictions.

<sup>e</sup>Dosage for patient with a body weight of 60 kg to 100 kg (for patients < 60 kg, 500 mg; for patients > 100 kg, 1,000 mg).

<sup>f</sup>Introduced after the base case cohort starting year (2018); this bDMARD was therefore not included in the CADTH base case.

<sup>g</sup>Not currently covered by the public drug plan. In scenario analyses, the Ontario price was used as a proxy.

<sup>h</sup>Reimbursed by the public payer per day of use. In scenario analyses where sarilumab is included, the Ontario price per unit was used as a proxy.

**Table 10: Pan-Canadian Budget Impact Analysis Results by Jurisdiction – Harmonization Scenario 1**

Scenario	Atlantic Provinces	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Pan-Canadian impact
Reference Scenario	\$16,496,280	\$62,937,265	\$8,676,717	\$8,509,143	\$21,710,751	\$33,592,529	\$151,922,685
Harmonization Scenario <sup>a</sup>	\$11,895,957	\$62,937,265	\$6,213,669	\$6,016,555	\$21,710,751	\$33,592,529	\$142,366,726
Budget Impact	-\$4,600,323	\$0	-\$2,463,047	-\$2,492,588	\$0	\$0	-\$9,555,958

Note: Negative values denote cost savings.

<sup>a</sup>Time to the initiation of biologic disease-modifying antirheumatic drug therapy was increased by 4 months for the Atlantic provinces, Manitoba, and Saskatchewan.

**Table 11: Pan-Canadian Budget Impact Analysis Results by Jurisdiction – Harmonization 2**

Scenario	Atlantic Provinces	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Pan-Canadian impact
Reference Scenario	\$16,496,280	\$62,937,265	\$8,676,717	\$8,509,143	\$21,710,751	\$33,592,529	\$151,922,685
Harmonization Scenario <sup>a</sup>	\$16,496,280	\$84,436,745	\$8,676,717	\$8,509,143	\$30,276,695	\$45,252,167	\$193,647,746
Budget Impact	\$0	\$21,499,480	\$0	\$0	\$8,565,944	\$11,659,637	\$41,725,061

<sup>a</sup>Time to the initiation of biologic disease-modifying antirheumatic drug therapy was assumed to be decreased by 4 months for Alberta, British Columbia, and Ontario.

**Table 12: Pan-Canadian Budget Impact Analysis Scenario Results by Jurisdiction – Harmonization Scenario 1**

Scenario <sup>a</sup>	Atlantic Provinces	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Pan-Canadian impact
<b>Base case</b>							
Reference Scenario	\$16,496,280	\$62,937,265	\$8,676,717	\$8,509,143	\$21,710,751	\$33,592,529	\$151,922,685
Harmonization Scenario	\$11,895,957	\$62,937,265	\$6,213,669	\$6,016,555	\$21,710,751	\$33,592,529	\$142,366,726
<b>Budget Impact</b>	<b>-\$4,600,323</b>	<b>\$0</b>	<b>-\$2,463,047</b>	<b>-\$2,492,588</b>	<b>\$0</b>	<b>\$0</b>	<b>-\$9,555,958</b>
<b>Scenario 1: Lower patient weight (50 kg)</b>							
Reference Scenario	\$15,437,374	\$58,602,302	\$8,477,541	\$8,436,418	\$19,931,008	\$32,836,083	\$143,720,725
Harmonization Scenario	\$11,121,171	\$58,602,302	\$6,068,619	\$5,964,434	\$19,931,008	\$32,836,083	\$134,523,616
<b>Budget Impact</b>	<b>-\$4,316,203</b>	<b>\$0</b>	<b>-\$2,408,922</b>	<b>-\$2,471,984</b>	<b>\$0</b>	<b>\$0</b>	<b>-\$9,197,109</b>
<b>Scenario 2: Higher patient weight (100 kg)</b>							
Reference Scenario	\$16,672,582	\$63,975,212	\$8,873,216	\$8,636,154	\$22,113,567	\$34,177,678	\$154,448,408
Harmonization Scenario	\$12,022,485	\$63,975,212	\$6,354,173	\$6,106,236	\$22,113,567	\$34,177,678	\$144,749,350
<b>Budget Impact</b>	<b>-\$4,650,097</b>	<b>\$0</b>	<b>-\$2,519,043</b>	<b>-\$2,529,918</b>	<b>\$0</b>	<b>\$0</b>	<b>-\$9,699,057</b>
<b>Scenario 3: All users assumed to receive IV forms of abatacept, golimumab, and tocilizumab</b>							
Reference Scenario	\$16,843,804	\$64,037,774	\$8,798,489	\$8,738,322	\$22,292,357	\$31,681,009	\$152,391,754
Harmonization Scenario	\$12,235,135	\$64,037,774	\$6,342,696	\$6,230,084	\$22,292,357	\$31,681,009	\$142,819,055
<b>Budget Impact</b>	<b>-\$4,608,668</b>	<b>\$0</b>	<b>-\$2,455,793</b>	<b>-\$2,508,238</b>	<b>\$0</b>	<b>\$0</b>	<b>-\$9,572,700</b>
<b>Scenario 4: British Columbia drug prices adopted as proxy for Atlantic and Manitoba drug prices</b>							
Reference Scenario	\$19,871,095	\$62,937,265	\$9,988,999	\$8,509,143	\$21,710,751	\$33,592,529	\$156,609,782
Harmonization Scenario	\$14,318,685	\$62,937,265	\$7,152,365	\$6,016,555	\$21,710,751	\$33,592,529	\$145,728,151

Scenario <sup>a</sup>	Atlantic Provinces	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Pan-Canadian impact
<b>Budget Impact</b>	-\$5,552,409	\$0	-\$2,836,634	-\$2,492,588	\$0	\$0	-\$10,881,631
<b>Scenario 5: Least expensive bDMARD price incorporated</b>							
Reference Scenario	\$16,490,053	\$62,806,572	\$8,650,252	\$8,488,090	\$21,673,136	\$33,526,789	\$151,634,893
Harmonization Scenario	\$11,891,401	\$62,806,572	\$6,194,396	\$6,001,467	\$21,673,136	\$33,526,789	\$142,093,761
<b>Budget Impact</b>	-\$4,598,653	\$0	-\$2,455,856	-\$2,486,623	\$0	\$0	-\$9,541,131
<b>Scenario 6: Suppressed cell counts assumed to represent 1 new user</b>							
Reference Scenario	\$16,496,280	\$62,937,265	\$8,494,282	\$8,334,604	\$21,710,751	\$33,592,529	\$151,565,711
Harmonization Scenario	\$11,895,957	\$62,937,265	\$6,081,931	\$5,891,465	\$21,710,751	\$33,592,529	\$142,109,897
<b>Budget Impact</b>	-\$4,600,323	\$0	-\$2,412,351	-\$2,443,139	\$0	\$0	-\$9,455,814
<b>Scenario 7: Cohort starting year assumed to be 2021<sup>b</sup></b>							
Reference Scenario	\$16,900,335	\$65,630,492	\$8,908,608	\$8,678,701	\$22,635,422	\$34,888,467	\$157,642,026
Harmonization Scenario	\$12,187,333	\$65,630,492	\$6,379,734	\$6,136,445	\$22,635,422	\$34,888,467	\$147,857,893
<b>Budget Impact</b>	-\$4,713,002	\$0	-\$2,528,874	-\$2,542,257	\$0	\$0	-\$9,784,133
<b>Scenario 8: Cohort starting year assumed to be 2021<sup>b</sup> and all new users assumed to start on a biosimilar (if available)</b>							
Reference Scenario	\$14,831,277	\$58,421,044	\$8,656,589	\$8,530,157	\$19,767,883	\$33,860,125	\$144,067,076
Harmonization Scenario	\$10,681,801	\$58,421,044	\$6,198,462	\$6,031,067	\$19,767,883	\$33,860,125	\$134,960,383
<b>Budget Impact</b>	-\$4,149,476	\$0	-\$2,458,126	-\$2,499,090	\$0	\$0	-\$9,106,693
<b>Scenario 9: Cohort starting year assumed to be 2021,<sup>b</sup> all new users assumed to start on a biosimilar, and bDMARDs introduced since 2018 incorporated</b>							
Reference Scenario	\$12,012,552	\$46,443,732	\$6,525,873	\$6,746,629	\$15,897,870	\$27,040,833	\$114,667,490
Harmonization Scenario	\$8,658,859	\$46,443,732	\$4,674,926	\$4,771,741	\$15,897,870	\$27,040,833	\$107,487,961

Scenario <sup>a</sup>	Atlantic Provinces	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Pan-Canadian impact
<b>Budget Impact</b>	-\$3,353,693	\$0	-\$1,850,947	-\$1,974,888	\$0	\$0	-\$7,179,528
<b>Scenario 10: Harmonization scenario 3 (time to a first bDMARD is adjusted by 2 months across jurisdictions)<sup>c</sup></b>							
Reference Scenario	\$16,496,280	\$62,937,265	\$8,676,717	\$8,509,143	\$21,710,751	\$33,592,529	\$151,922,685
Harmonization Scenario	\$14,229,567	\$73,736,508	\$7,451,596	\$7,268,769	\$26,070,098	\$39,436,602	\$168,193,140
<b>Budget Impact</b>	-\$2,266,713	\$10,799,243	-\$1,225,121	-\$1,240,374	\$4,359,347	\$5,844,072	\$16,270,455

Note: Negative values denote cost savings.

bDMARD = biologic disease-modifying antirheumatic drug.

<sup>a</sup>Harmonization Scenario 1: Time to bDMARD initiation was increased by 4 months for the Atlantic provinces, Manitoba, and Saskatchewan.

<sup>b</sup>The number of new users was increased by jurisdiction-specific population growth rates; all other parameters were held constant unless otherwise stated.

<sup>c</sup>Time to bDMARD initiation was harmonized across jurisdictions by assuming that jurisdiction-specific current time was concurrently increased by 2 months in the Atlantic provinces, Manitoba, and Saskatchewan and decreased by 2 months in Alberta, British Columbia, and Ontario.

**Table 13: Pan-Canadian Budget Impact Analysis Scenario Results by Jurisdiction – Harmonization Scenario 2**

Scenario <sup>a</sup>	Atlantic Provinces	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Pan-Canadian impact
<b>Base case</b>							
Reference Scenario	\$16,496,280	\$62,937,265	\$8,676,717	\$8,509,143	\$21,710,751	\$33,592,529	\$151,922,685
Harmonization Scenario	\$16,496,280	\$84,436,745	\$8,676,717	\$8,509,143	\$30,276,695	\$45,252,167	\$193,647,746
<b>Budget Impact</b>	<b>\$0</b>	<b>\$21,499,480</b>	<b>\$0</b>	<b>\$0</b>	<b>\$8,565,944</b>	<b>\$11,659,637</b>	<b>\$41,725,061</b>
<b>Scenario 1: Lower patient weight (50 kg)</b>							
Reference Scenario	\$15,437,374	\$58,602,302	\$8,477,541	\$8,436,418	\$19,931,008	\$32,836,083	\$143,720,725
Harmonization Scenario	\$15,437,374	\$78,743,577	\$8,477,541	\$8,436,418	\$27,826,053	\$44,257,757	\$183,178,719
<b>Budget Impact</b>	<b>\$0</b>	<b>\$20,141,275</b>	<b>\$0</b>	<b>\$0</b>	<b>\$7,895,045</b>	<b>\$11,421,674</b>	<b>\$39,457,994</b>
<b>Scenario 2: Higher patient weight (100 kg)</b>							
Reference Scenario	\$16,672,582	\$63,975,212	\$8,873,216	\$8,636,154	\$22,113,567	\$34,177,678	\$154,448,408
Harmonization Scenario	\$16,672,582	\$85,838,662	\$8,873,216	\$8,636,154	\$30,841,275	\$46,043,098	\$196,904,986
<b>Budget Impact</b>	<b>\$0</b>	<b>\$21,863,450</b>	<b>\$0</b>	<b>\$0</b>	<b>\$8,727,708</b>	<b>\$11,865,420</b>	<b>\$42,456,578</b>
<b>Scenario 3: All users assumed to receive IV forms of abatacept, golimumab, and tocilizumab</b>							
Reference Scenario	\$16,843,804	\$64,037,774	\$8,798,489	\$8,738,322	\$22,292,357	\$31,681,009	\$152,391,754
Harmonization Scenario	\$16,843,804	\$85,249,836	\$8,798,489	\$8,738,322	\$30,883,445	\$42,253,041	\$192,766,937
<b>Budget Impact</b>	<b>\$0</b>	<b>\$21,212,062</b>	<b>\$0</b>	<b>\$0</b>	<b>\$8,591,088</b>	<b>\$10,572,032</b>	<b>\$40,375,182</b>
<b>Scenario 4: British Columbia drug prices adopted as proxy for Atlantic and Manitoba drug prices</b>							
Reference Scenario	\$19,871,095	\$62,937,265	\$9,988,999	\$8,509,143	\$21,710,751	\$33,592,529	\$156,609,782
Harmonization Scenario	\$19,871,095	\$84,436,745	\$9,988,999	\$8,509,143	\$30,276,695	\$45,252,167	\$198,334,843

Scenario <sup>a</sup>	Atlantic Provinces	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Pan-Canadian impact
<b>Budget Impact</b>	\$0	\$21,499,480	\$0	\$0	\$8,565,944	\$11,659,637	\$41,725,061
<b>Scenario 5: Least expensive bDMARD price incorporated</b>							
Reference Scenario	\$16,490,053	\$62,806,572	\$8,650,252	\$8,488,090	\$21,673,136	\$33,526,789	\$151,634,893
Harmonization Scenario	\$16,490,053	\$84,265,104	\$8,650,252	\$8,488,090	\$30,224,900	\$45,165,746	\$193,284,146
<b>Budget Impact</b>	\$0	\$21,458,532	\$0	\$0	\$8,551,764	\$11,638,957	\$41,649,253
<b>Scenario 6: Suppressed cell counts assumed to represent 1 new user</b>							
Reference Scenario	\$16,496,280	\$62,937,265	\$8,494,282	\$8,334,604	\$21,710,751	\$33,592,529	\$151,565,711
Harmonization Scenario	\$16,496,280	\$84,436,745	\$8,494,282	\$8,334,604	\$30,276,695	\$45,252,167	\$193,290,772
<b>Budget Impact</b>	\$0	\$21,499,480	\$0	\$0	\$8,565,944	\$11,659,637	\$41,725,061
<b>Scenario 7: Cohort starting year assumed to be 2021<sup>b</sup></b>							
Reference Scenario	\$16,900,335	\$65,630,492	\$8,908,608	\$8,678,701	\$22,635,422	\$34,888,467	\$157,642,026
Harmonization Scenario	\$16,900,335	\$88,049,984	\$8,908,608	\$8,678,701	\$31,566,194	\$46,997,912	\$201,101,733
<b>Budget Impact</b>	\$0	\$22,419,491	\$0	\$0	\$8,930,771	\$12,109,445	\$43,459,707
<b>Scenario 8: Cohort starting year assumed to be 2021<sup>b</sup> and all new users assumed to start on a biosimilar (if available)</b>							
Reference Scenario	\$14,831,277	\$58,421,044	\$8,656,589	\$8,530,157	\$19,767,883	\$33,860,125	\$144,067,076
Harmonization Scenario	\$14,831,277	\$78,510,406	\$8,656,589	\$8,530,157	\$27,603,927	\$45,628,216	\$183,760,572
<b>Budget Impact</b>	\$0	\$20,089,362	\$0	\$0	\$7,836,044	\$11,768,091	\$39,693,497
<b>Scenario 9: Cohort starting year assumed to be 2021,<sup>b</sup> all new users assumed to start on a biosimilar, and bDMARDs introduced since 2018 incorporated</b>							
Reference Scenario	\$12,012,552	\$46,443,732	\$6,525,873	\$6,746,629	\$15,897,870	\$27,040,833	\$114,667,490
Harmonization Scenario	\$12,012,552	\$62,333,096	\$6,525,873	\$6,746,629	\$22,179,779	\$36,410,740	\$146,208,669



Scenario <sup>a</sup>	Atlantic Provinces	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Pan-Canadian impact
<b>Budget Impact</b>	<b>\$0</b>	<b>\$15,889,364</b>	<b>\$0</b>	<b>\$0</b>	<b>\$6,281,908</b>	<b>\$9,369,907</b>	<b>\$31,541,180</b>

bDMARD = biologic disease-modifying antirheumatic drug.

<sup>a</sup>Harmonization Scenario 2: Time to bDMARD initiation was assumed to be decreased by 4 months for Alberta, British Columbia, and Ontario.

<sup>b</sup>The number of new users was increased by jurisdiction-specific population growth rates; all other parameters were held constant unless otherwise stated.