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Trends in Public Drug Plan Expenditures for Patients With Crohn Disease and Ulcerative Colitis Initiating Targeted Immune Modulator Therapy

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Abbreviations

CD	Crohn disease
CIHI	Canadian Institute for Health Information
DAD	Discharge Abstract Database
IBD	inflammatory bowel disease
ICD-10-CA	*International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Canada*
NPDUIS	National Prescription Drug Utilization Information System
pCPA	pan-Canadian Pharmaceutical Alliance
TIM	targeted immune modulator
UC	ulcerative colitis

Key Messages

- The objective of this analysis was to examine the changes in drug expenditures with the initiation of targeted immune modulator (TIM) treatment in patients diagnosed with Crohn disease (CD) and ulcerative colitis (UC).
- Patient cohorts for CD and UC were identified from hospitalizations in Canada. Expenditure data for TIMs with a Health Canada–approved indication for the treatment of CD or UC were extracted from all provincial drug plans (except Quebec) and Yukon from 2016 to 2021, and a descriptive analysis was performed to assess the expenditure patterns.
- Annual expenditures on TIMs for patients with CD increased each year from 2016 to 2019 before decreasing in 2020 and 2021, whereas expenditures on TIMs in UC increased each year, generally by a greater percentage than was observed in CD (peak percentage growth of 92.5% for UC versus 15.9% for CD in 2018).
- Expenditures associated with TIM initiation among patients with CD and UC were driven by infliximab and adalimumab, with the 2 drugs accounting for nearly all expenditures in both indications in 2016 and most expenditures in 2021.
- In both CD and UC, vedolizumab expenditures increased over time, as did the proportions of TIM expenditures on ustekinumab in CD and tofacitinib in UC, albeit to a lesser extent than vedolizumab.

Background

CD and UC, the 2 predominant types of inflammatory bowel disease (IBD), involve chronic inflammation of the gastrointestinal tract.[1,2] CD most commonly affects the small intestine, with the inflammation often spreading to the deep layers of the bowel; UC causes inflammation and ulcers in the mucosa of the large intestine.[3,4] Both types of IBD cause diarrhea, abdominal pain, rectal bleeding, nausea, vomiting, reduced appetite, and weight loss.[5,6] Patients with CD may also develop mouth sores, pain or drainage near or around the anus due to fistula formation, and extraintestinal manifestations (e.g., inflammation in other organs and systems, kidney stones, anemia), whereas patients with UC commonly experience severe, frequent, and bloody diarrhea, as well as tenesmus and urgency (feeling of the need to defecate immediately).[3-5] The prevalence of CD and UC in Canada is among the highest in the world,[7-11] and is expected to increase from 259 per 100,000 persons in 2008 to 487 per 100,000 persons in 2030 for CD and from 210 per 100,000 persons to 408 per 100,000 persons during the same time period for UC.[12] In a recently published 2023 report on the impact of IBD in Canada, the prevalence of IBD was estimated to be approximately 322,600 people (0.8% of the population), with a projected growth to 470,000 people in Canada (1.1% of the population) by 2035.[13] IBD is associated with a substantial burden to patients, caregivers, and the health care system; in 2023, it was estimated that IBD resulted in $5.38 billion in combined direct and indirect costs in Canada.[13]

Approximately 1 in 5 adults with CD and 1 in 8 adults with UC are hospitalized each year based on data from Ontario, with more hospitalized patients with CD than with UC undergoing a surgical procedure during their initial hospitalization.[14] The frequency and costs of hospitalizations for IBD have decreased over the past 2 decades, possibly because of increased use of biologic therapies (with associated improvements in disease control) and advances in management strategies.[14] As such, there has been a shift away from hospitalization costs and toward drug costs as the main driver of the economic impact of IBD.[14]

Treatment approaches for CD and UC are determined by the site and extent of disease, risk factors for poor prognosis, and the severity of inflammation and symptoms.[15-20] Patients with moderately to severely active CD or UC who have either not responded to or lost response to a corticosteroid and/or conventional immunosuppressant are often recommended a TIM, such as a biologic or small molecule drug.[15-20] TIMs currently marketed in Canada for the treatment of moderately to severely active CD and UC are listed in Table 1. Most of the available TIMs are listed on public provincial drug plans across Canada with limited use, special authorization, or exception drug status coverage.[21]

Table 1: Marketed Targeted Immune Modulators for Moderately to Severely Active CD or UC

Drug	Year approved for CD	Year approved for UC	Biosimilar or generic available	Funded by at least 1 public drug plan
Tumour necrosis factor-alpha inhibitor				
Adalimumab	2007	2013	Yes	Yes
Golimumab	—	2013	No	Yes
Infliximab	1998	2006	Yes	Yes
Anti-integrin antibody				
Vedolizumab	2016	2015	No	Yes
Interleukin-23 inhibitor				
Mirikizumab	—	2023	No	No
Risankizumab	2022	—	No	Yes
Interleukin-12/23 inhibitor				
Ustekinumab	2016	2020	Yes	Yes
Janus kinase inhibitor				
Tofacitinib	—	2018	Yes	Yes
Upadacitinib	2023	2022	No	No
Sphingosine-1-phosphate receptor modulator				
Ozanimod	—	2022	No	Yes

Note: Dash indicates that it is not indicated.

Purpose of This Report

The objective of this analysis was to examine the expenditures for TIM treatment initiation in patients diagnosed with CD and UC in Canada from 2016 to 2021.

Policy Issues

There are several TIMs currently marketed for the treatment of CD and UC in Canada, as well as emerging agents that will expand the therapeutic options for these conditions. Public health administrative claims databases provide a valuable source of real-world data to assess trends in therapy. Given the evolving landscape for TIMs used to treat CD and UC and the potential impact on public drug spending, we conducted an analysis using public claims data to estimate the expenditure patterns of these therapies to help inform public drug plan formulary management and funding considerations.

Research Question

1. What was the expenditure distribution for each of the publicly funded TIMs initiated in patients with CD and UC in Canada from 2016 to 2021, including:
   a) annual expenditures for initial TIMs for CD and UC
   b) changes in expenditures for each of the approved TIMs initiated among patients with CD and UC in Canada from year to year?

Methods

Data Sources and Time Frame

Data from the Canadian Institute for Health Information (CIHI), including the Discharge Abstract Database (DAD)[22] and the National Prescription Drug Utilization Information System (NPDUIS),[23] from January 1, 2016, until December 31, 2021, were used to conduct this analysis.

Discharge Abstract Database

The DAD contains clinical, demographic, and administrative information relating to hospital acute care admissions from Yukon and all provinces in Canada except Quebec.[22] Medical conditions experienced by the patient during each hospital admission are captured in the DAD using the *International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Canada* (*ICD-10-CA*) classification codes. Patients with a diagnosis of CD or UC were identified from the DAD based on a definition of 2 hospitalizations for either CD (*ICD-10-CA* code K50.X) or UC (*ICD-10-CA* code K51.X) from January 1, 2016, until December 31, 2021. Patients who had diagnostic codes for both UC and CD in the DAD during the study period were excluded from the analysis.

National Prescription Drug Utilization Information System Database

The NPDUIS database was used to determine expenditures for a patient's first TIM dispensed for the treatment of CD and/or UC between January 1, 2016, until December 31, 2021 The NPDUIS database contains information on medication use and expenditures for Yukon and provincial drug plans, with the exception of Quebec.[23] For the purpose of this analysis, data for the calendar year 2021 were not available for New Brunswick and were only available up until September for Alberta.

Patients identified from the DAD with UC or CD were then selected if they had at least 1 claim for a conventional UC or CD treatment, including corticosteroids, anti-inflammatory agents, and immunosuppressive therapies (Appendix 2). Conventional therapies were first identified because patients are generally required to be intolerant or refractory to conventional therapies to meet the funding criteria for TIMs. Following the selection of patients with at least 1 conventional therapy claim, the first index dispensation of a relevant TIM (adalimumab, golimumab, infliximab, tofacitinib, ustekinumab, or vedolizumab, or any available biosimilars) was then identified (Appendix 2), along with its associated expenditure for the analysis period of January 1, 2016, until December 31, 2021. All medications were identified based on Drug Identification Numbers (DINs) assigned by Health Canada and by the WHO Anatomical Therapeutic Chemical (ATC) classification codes (Appendix 2).

Exclusion

Claims for drugs administered outside of public drug plans are not submitted to NPDUIS; therefore, expenditures for such claims were not included.[23] The NPDUIS database does not include information regarding prescriptions that were written but never dispensed; prescriptions that were dispensed but for which the associated drug costs were not submitted to, or not accepted by, the public drug program; or diagnoses or conditions for which prescriptions were written.[23] In addition, ozanimod (Zeposia), upadacitinib (Rinvoq), risankizumab (Skyrizi), and mirikizumab (Omvoh) were not available during the time frame of this analysis; therefore, these agents were not included. A timeline detailing the conclusion dates of pan-Canadian Pharmaceutical Alliance (pCPA) negotiations for the molecules of interest is presented in Appendix 3. These dates serve as indicative markers for the subsequent potential listings on public provincial plans.

Data Analysis

The total public drug plan expenditures for the first index TIM dispensed among patients with either CD or UC in each year from 2016 to 2021 were aggregated from province-level data and presented at the national level. Expenditures were calculated based on the total dollar amount of a prescription accepted by the drug plan as eligible toward a deductible or for reimbursement, which includes the drug cost as well as the associated professional fees and markup, if applicable. Total annual expenditures were calculated and reported based on diagnosis (UC or CD) for all TIMs as well as for each TIM from 2016 to 2021. Finally, the proportion of TIMs expenditures for either CD or UC was calculated.

Findings

Expenditures of TIMs Initiated in Patients With Crohn Disease and Ulcerative Colitis

The cumulative expenditures of initial TIM therapy for patients with CD was $272,959,998 from 2016 to 2021. During this time period, the annual expenditures of initial TIM therapy increased by 17.2% from $39,315,956 in 2016 to $46,063,174 in 2021. The largest total expenditure for TIMs in patients with CD was in 2019 ($49,273,431). The total expenditures for initial TIMs in patients with CD are listed in Table 2.

From 2016 to 2021, the cumulative expenditures of initial TIM therapy for patients with UC was $70,386,523. Similar to patients with CD, the annual expenditures for initial TIM therapy increased over time, from $5,834,016 in 2016 to $15,326,161 in 2021. The largest year-over-year increase in expenditures was observed in 2018 ($6,928,190 in 2017 to $13,334,468 in 2018). The total expenditures for initial TIMs by year in patients with UC are listed in Table 2.

Most of the expenditures on initial TIMs from 2016 to 2021 was for CD (79.4% versus 20.6% for UC) (Table 3). However, the proportion of expenditures for UC increased over time (87.1% for CD and 12.9% for UC in 2016; 75.0% for CD and 25.0% for UC in 2021); the ratio of expenditures for CD relative to UC decreased each year from 6.74 in 2016 to 3.01 in 2021.

Table 2: Year-Over-Year Change in Public Expenditures for Initial TIMs in Patients With CD or UC

TIM	2016	2017	2018	2019	2020	2021	Total
CD	$39,315,956	$41,062,347	$47,571,427	$49,273,431	$48,673,662	$46,063,174	$271,959,998
Year-over-year change	—	4.4%	15.9%	3.6%	−1.2%	−5.4%	—
UC	$5,834,016	$6,928,190	$13,334,468	$14,287,271	$14,675,706	$15,326,872	$70,386,523
Year-over-year change	—	18.8%	92.5%	7.1%	2.7%	4.4%	—

CD = Crohn disease; TIM = targeted immune modulator; UC = ulcerative colitis.

Table 3: Proportion and Ratio of Public Expenditures for TIMs for CD or UC by Year

TIM	2016	2017	2018	2019	2020	2021	6-year total
CD	87.1%	85.6%	78.1%	77.5%	76.8%	75.0%	79.4%
UC	12.9%	14.4%	21.9%	22.5%	23.2%	25.0%	20.6%
Ratio (CD:UC)	6.74	5.93	3.57	3.45	3.32	3.01	3.85

CD = Crohn disease; TIM = targeted immune modulator; UC = ulcerative colitis.

Individual TIM Distribution

In patients with CD, infliximab (54.9%; $149,271,728) accounted for more than half of total expenditures associated with public claims for initial TIMs from 2016 to 2021, followed by adalimumab (32.5%;

$88,344,086), vedolizumab (9.4%; $25,543,536), ustekinumab (2.9%; $7,917,427), golimumab (0.3%; $717,514), and tofacitinib (0.06%; $165,707) (Table 4). Adalimumab and infliximab accounted for the majority of public expenditures for initial TIMs in each year included in the study period, contributing to 99.7% of costs in 2016 (adalimumab: 35.6% [$13,997,887]; infliximab: 64.1% [$25,210,289]) and 76.3% of costs in 2021 (adalimumab: 30.3% [$13,947,719]; infliximab: 46.0% [$21,190,430]) (Figure 1; Table 5). The proportion of expenditures for vedolizumab claims increased from 0% in 2016 ($0) to 17.1% ($7,865,743) in 2021. The proportion of expenditures attributable to ustekinumab also increased throughout the study period from 0.1% ($34,339) in 2016 to 6.4% ($2,927,401) in 2021. Expenditures associated with golimumab (0.2% in 2016 and 2021; peak of 0.4% in 2018) and tofacitinib (0% in 2016 to a peak of 0.06% in 2021) remained low throughout the study period.

In UC, infliximab (60.2%; $42,398,002) accounted for the majority of total expenditures associated with public claims for initial TIMs among patients from 2016 to 2021, followed by vedolizumab (23.3%; $16,392,608), adalimumab (13.4%; 9,393,357), golimumab (1.6%; $1,145,849), tofacitinib (1.4%; $960,962), and ustekinumab (0.1%; $95,745) (Table 4). Infliximab accounted for most of the public expenditures on initial TIMs in 2016 (94.1%; $5,491,676) (Figure 1; Table 5). Although the proportion of expenditures attributable to infliximab decreased from 2016 to 2021 (94.1% to 48.8%), infliximab still accounted for more expenditures than any other TIM in UC. The proportions of public TIM expenditures in UC for vedolizumab (0% [$0] in 2016; 28.2% in 2021 [$4,326,161]; peak of 30% [$4,410,340] in 2020), adalimumab (4.9% [$285,756] in 2016; 15.8% [$2,419,075] in 2021), and tofacitinib (0% [$0] in 2016; 5.6% [$853,825] in 2021) increased throughout the study period. The proportions of annual public expenditures for golimumab (0.6% [$37,752] in 2016; 1.5% [$225,928] in 2021; peak of 2.0% [$261,310] in 2018) and ustekinumab (0.3% [$18,832] in 2016; 0.2% [$27,161] in 2021) were low throughout the study period.

Year-over-year changes in public expenditures for TIMs among patients with CD, UC, and IBD overall by molecule are presented in Table 5. The greatest year-over-year percent increases in expenditures for adalimumab, golimumab, and infliximab were observed in 2017 and 2018 in CD and UC, followed by subsequent year-over-year decreases or reduced rates of growth for these molecules between 2019 and 2021. Year-over-year percent increases for tofacitinib were greatest in 2018 for CD (in which it is not indicated) and in 2021 for UC. The greatest year-over-year percent increases in expenditures for ustekinumab were observed in 2018 for CD and IBD overall, and in 2020 for UC. Similarly, the greatest increase in expenditures for vedolizumab across CD, UC, and IBD overall was observed in 2018, followed by decreasing rates of growth in each subsequent year of the analysis.

Table 4: Proportion of Public Expenditures for Each Initial TIM for CD or UC Over the Full Study Period (2016 to 2021)

Drugs	CD	UC
Adalimumab		
Expenditures	$88,344,086	$9,393,357
Proportion of total	32.5%	13.4%
Golimumab		
Expenditures	$717,514	$1,145,849
Proportion of total	0.3%	1.6%
Infliximab		
Expenditures	$149,271,728	$42,398,002
Proportion of total	54.9%	60.2%
Tofacitinib		
Expenditures	$165,707	$960,962
Proportion of total	0.1%	1.4%
Ustekinumab		
Expenditures	$7,917,427	$95,745
Proportion of total	2.9%	0.1%
Vedolizumab		
Expenditures	$25,543,536	$16,392,608
Proportion of total	9.4%	23.3%

CD = Crohn disease; TIM = targeted immune modulator; UC = ulcerative colitis.

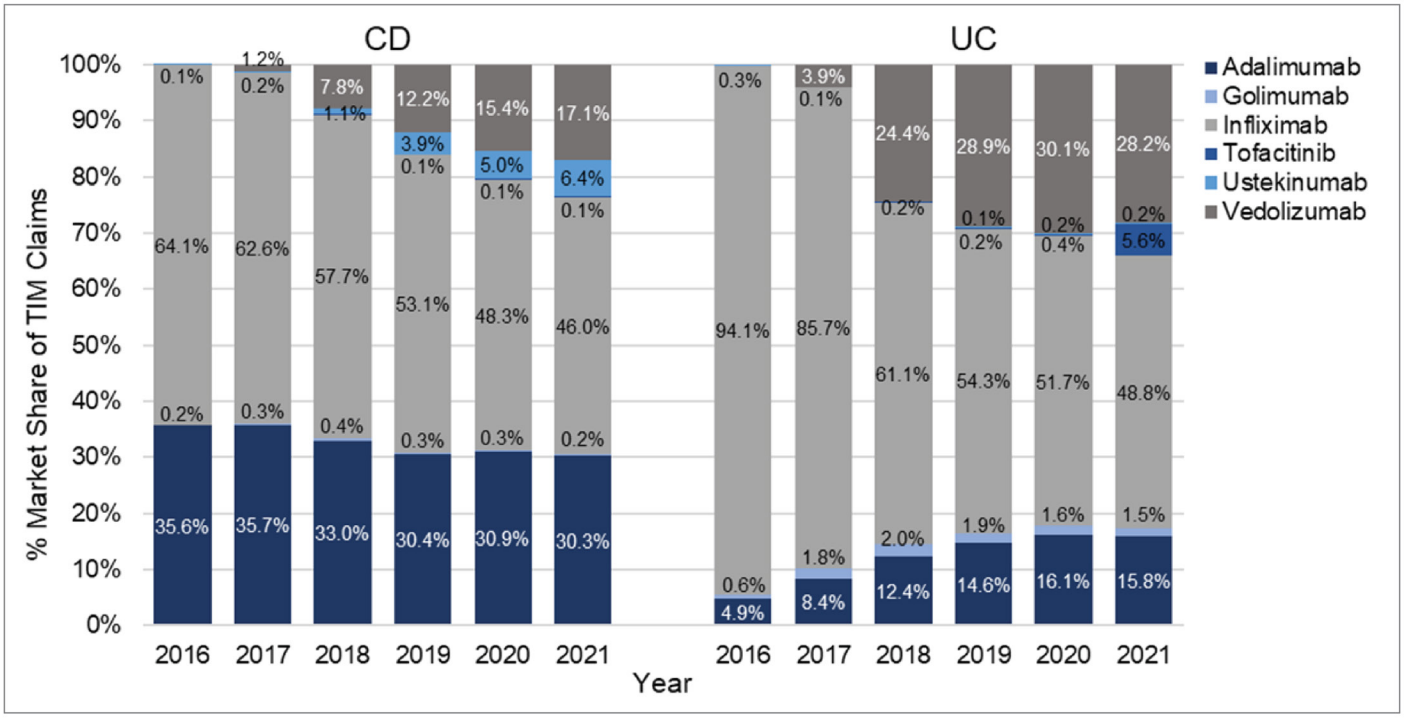
Table 5: Public Expenditures and Year-Over-Year Changes for Initial TIMs for CD or UC

Public expenditures and year-over-year changes	2016	2017	2018	2019	2020	2021
Adalimumab						
CD expenditures	$13,997,887	$14,659,009	$15,677,266	$15,001,714	$15,060,491	$13,947,719
CD year-over-year change	—	4.7%	6.9%	−4.3%	0.4%	−7.4%
UC expenditures	$285,756	$584,331	$1,653,264	$2,087,934	$2,362,997	$2,419,075
UC year-over-year change	—	104.5%	182.9%	26.3%	13.2%	2.4%
Golimumab						
CD expenditures	$73,441	$107,667	$193,131	$135,799	$127,570	$79,905
CD year-over-year change	—	46.6%	79.4%	−29.7%	−6.1%	−37.4%
UC expenditures	$37,752	$126,141	$261,310	$265,296	$229,422	$225,928

Public expenditures and year-over-year changes	2016	2017	2018	2019	2020	2021
UC year-over-year change	—	234.1%	107.2%	1.5%	−13.5%	−1.5%
Infliximab						
CD expenditures	$25,210,289	$25,723,149	$27,457,502	$26,180,771	$23,509,588	$21,190,430
CD year-over-year change	—	2.0%	6.7%	−4.6%	−10.2%	−9.9%
UC expenditures	$5,491,676	$5,934,639	$8,146,072	$7,760,748	$7,590,146	$7,474,722
UC year-over-year change	—	8.1%	37.3%	−4.7%	−2.2%	−1.5%
Tofacitinib						
CD expenditures	$0	$4,585	$18,361	$29,342	$61,442	$51,977
CD year-over-year change	—	—	300.4%	59.8%	109.4%	−15.4%
UC expenditures	$0	$0	$22,823	$24,793	$59,521	$853,825
UC year-over-year change	—	—	—	8.6%	140.1%	1,334.5%
Ustekinumab						
CD expenditures	$34,339	$72,640	$524,140	$1,920,500	$2,438,407	$2,927,401
CD year-over-year change	—	111.5%	621.6%	266.4%	27.0%	20.1%
UC expenditures	$18,832	$9,502	$0	$16,970	$23,280	$27,161
UC year-over-year change	—	−49.5%	−100%	—	37.2%	16.7%
Vedolizumab						
CD expenditures	$0	$495,296	$3,701,027	$6,005,305	$7,476,164	$7,865,743
CD year-over-year change	—	—	647.2%	62.3%	24.5%	5.2%
UC expenditures	$0	$273,577	$3,251,001	$4,131,530	$4,410,340	$4,326,161
UC year-over-year change	—	—	1,088.3%	27.1%	6.7%	−1.9%

CD = Crohn disease; TIM = targeted immune modulator; UC = ulcerative colitis.

Figure 1: Proportion of Public Expenditures for Initial TIM for CD or UC per Year



CD = Crohn disease; TIM = targeted immune modulator; UC = ulcerative colitis.

Discussion

This study sought to determine the expenditures for initial TIMs among patients with CD and UC in Canada by assessing expenditures associated with public drug claims from the NPDUIS database. Patients with CD or UC initiating a TIM were identified by linking claims from the NPDUIS database to a patient cohort from the DAD using *ICD-10-CA* coding for CD and UC, which was necessary because several of the TIMs of interest are approved for other indications. Because only 1 in 5 patients with CD and 1 in 8 patients with UC are hospitalized each year,[14] most patients with IBD are treated in an ambulatory setting, and these patients were not included in this analysis. In addition, patients with IBD who require hospitalization are likely to have more severe and potentially more complicated disease than patients managed in other settings; as such, the expenditures should be interpreted as initial TIM costs among patients with a history of hospitalization for CD or UC. These points should be considered when interpreting the findings of this analysis.

Annual expenditures on initial TIMs for patients with CD increased each year from 2016 to 2019 before decreasing in 2020 and 2021, whereas expenditures on initial TIMs in UC increased in each year of the analysis, generally by a greater percentage than was observed in CD (peak percentage growth of 92.5% for UC versus 15.9% for CD in 2018). This was reflected in the ratio of TIM expenditures attributable to CD relative to UC, which decreased each year from 6.74 in 2016 to 3.01 in 2021. Nonetheless, initial

TIM expenditures remained substantially higher in CD than in UC, which may be due in part to the higher prevalence of CD than UC in Canada[12] and a greater proportion of patients with CD are hospitalized than those with UC.[14]

Expenditures associated with TIMs among patients with CD and UC were largely driven by infliximab and adalimumab, with the 2 agents accounting for nearly all expenditures in both indications in 2016 and most expenditures in 2021. These findings are in line with previous real-world treatment pattern data collected during an overlapping time period, which showed that physicians largely preferred infliximab and adalimumab as first-line biologic therapy for moderate to severe CD and UC.[24] In this report, the proportion of expenditures attributable to infliximab decreased over time for both types of IBD, particularly in patients with UC. Adalimumab accounted for a greater proportion of expenditures in CD than in UC, with a small year-over-year decline in CD and more than a 3-fold increase in percentage growth in UC throughout the study period. The increase in adalimumab expenditures among patients with UC appeared to align with the conclusion of pCPA negotiations for the branded product (Humira) in 2017, whereas pCPA negotiations for Humira were not conducted in CD.[21] The findings may also be partially explained by the timelines for biosimilar introduction in Canada because pCPA negotiations were concluded for the first infliximab and adalimumab biosimilars in 2016 and 2021, respectively.[21] However, this is challenging to discern from the present findings because policies related to nonmedical switching from originator biologics to biosimilars vary in terms of process and timing from province to province.[25]

In both CD and UC, vedolizumab expenditures increased over time after pCPA negotiations were concluded and the product was subsequently added to public drug plans as an IV formulation in 2017.[21,26] By 2021, it accounted for a greater percentage of TIM expenditures compared to 2016, especially in UC. A subcutaneous formulation of vedolizumab was also added to provincial plans in August 2021;[21] however, the effect of this addition was not fully captured in this analysis because the study period ended in December 2021. Notably, results of the phase IIIb VARSITY trial showing vedolizumab was more efficacious than adalimumab in UC were published in 2019,[16] leading several international organizations to recommend consideration of vedolizumab over adalimumab in updated treatment guidelines for moderate to severe UC.[16,17] These findings and changes in clinical practice guidelines may have potentially contributed to the increased uptake of vedolizumab in UC compared with CD.

The proportions of TIM expenditures on ustekinumab in CD and tofacitinib in UC also increased over time, albeit to a lesser extent than vedolizumab. For tofacitinib, the increase in expenditures in 2021 occurred after the conclusion of its pCPA negotiations in July 2020.[21] However, although ustekinumab received positive reimbursement recommendations from CADTH for CD in 2017 and UC in 2020,[27,28] pCPA negotiations were concluded without agreement for both indications, and ustekinumab was not listed as a benefit by public drug plans for either CD or UC at the time of conducting this analysis and writing this report.[21] Golimumab expenditures were also low in both CD (in which it is not indicated) and UC throughout the study period, with little change from year to year aside from a slight increase in UC expenditures after pCPA negotiations were concluded in August 2016.[21]

Limitations

There are several notable limitations of the current analyses:

- In all jurisdictions captured by the NPDUIS database, people covered by provincial workers' compensation boards or federal drug programs are not eligible for provincial public coverage. In Ontario, individuals who have coverage through the First Nations and Inuit Health Branch (FNIHB) have their drug claims first covered by the Ontario Drug Benefit, with remaining costs covered by FNIHB. In several provinces, including Alberta, Nova Scotia, and Prince Edward Island, claims dispensed through certain plans are not included in the NPDUIS database (refer to Appendix 1 for full details).
- The NPDUIS database does not capture public claims from all age groups in all jurisdictions. For example, the Ontario dataset only includes the Ministry of Community and Social Services and the Ontario Ministry of Health and Long-Term Care Drug Benefit Program, meaning that a sizable proportion of adult patients aged between 25 and 65 years would not have been captured in this province.
- The annual costs reported in the NPDUIS database are not adjusted for inflation; therefore, year-over-year changes in expenditures should be interpreted with this limitation in mind.
- As with any analysis of prescription claims data, there is uncertainty regarding the actual use of the prescriptions claimed and expensed in the current analysis. Therefore, any interpretations of the findings presented herein should be limited to the context of expenditures associated with initial TIM claims for CD and UC as opposed to actual use of these drugs and whether they were taken as prescribed.
- Because the claims data for TIMs from the NPDUIS database were linked to patients with diagnoses of CD or UC identified using *ICD-10-CA* codes in the DAD, it is possible that some patients with relevant diagnoses and claims for TIMs were not captured in the analysis. In addition, because patients with CD and UC were defined as having 2 hospitalizations with relevant *ICD-10-CA* codes, the results only reflect patients hospitalized for CD or CD. Many patients with IBD are diagnosed and treated in community gastroenterology clinics without being hospitalized; therefore, the results of this analysis must be interpreted within the context of patients hospitalized at least twice for CD or UC with a relevant initial TIM claim through public insurance.
- This analysis did not assess expenditures for different dosage strengths of TIMs. Although this was outside the scope of the research question for this analysis, understanding the expenditures associated with different dosage strengths of TIMs in CD and UC may be valuable to inform policy decisions and is a worthwhile consideration for future studies, especially considering the regular use of dose escalation of biologic therapies in clinical practice.[29-32]
- Although ozanimod (Zeposia) and risankizumab (Skyrizi) are currently funded by some public drug plans, they were not publicly funded during the analysis time frame. As such, expenditures associated with ozanimod and risankizumab for CD and UC are not included in this analysis.

- Finally, the COVID-19 pandemic may have affected hospitalizations for CD and UC, which would result in an underestimation of the public drug plan expenditures for initial TIMs in 2020 and 2021.

Conclusions and Implications for Decision- or Policy-Making

Overall, public expenditures on TIMs among patients with CD and UC increased from 2016 to 2021. Although TIM expenditures were considerably higher for CD than for UC throughout the study period, the percentage increase was higher for UC than for CD, which is notable because the prevalence and proportion of patients hospitalized are greater in CD than in UC.[14] In addition, there are a greater number of TIMs currently available for UC than for CD in Canada, and the changes in expenditure patterns for individual TIMs during the study period were more pronounced in UC than in CD. The most prominent trends in UC were a greater percentage decrease in infliximab expenditure and greater percentage increases in vedolizumab and adalimumab expenditures between 2016 and 2021, although infliximab continued to account for the greatest proportion of public TIM expenditures among patients with either CD or UC. It will be important for jurisdictions to monitor the trends reported herein, especially considering several new TIMs (ozanimod, upadacitinib, risankizumab, and mirikizumab) have been approved by Health Canada since the end of the study period, and the introduction of these new therapies may result in further changes in expenditure patterns. In addition, there have been several recent changes in exclusivity status for the TIMs included in this analysis: patents expired for ustekinumab and golimumab in 2021, and data protection expired for tofacitinib and vedolizumab in 2022 and July 2023, respectively. Although it is unclear whether these developments may affect expenditure patterns with the expected introduction of additional biosimilars and generics into the market over the next several years, the situation is worth monitoring. Overall, the findings of this analysis may help inform jurisdictions in formulary management and funding considerations for initial TIMs indicated for patients with CD and UC.

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Appendix 1: List of Public Plans and Programs Included in Analysis

Note that this appendix has not been copy-edited.

Table 6: List of Public Plans and Programs Included in Analysis[23]

Jurisdiction	Plan/Program Description
Alberta[a]	Non-Group Seniors Palliative Care
British Columbia	Permanent Residents of Licensed Residential Care Facilities Recipients of B.C. Income Assistance Cystic Fibrosis Children in the At Home Program No-Charge Psychiatric Medication Program Fair PharmaCare BC Palliative Care Drug Plan Smoking Cessation
Manitoba	Employment and Income Assistance Personal Home Care/ Nursing Homes Palliative Care Pharmacare
New Brunswick	New Brunswick Prescription Drug Program • Seniors • Nursing Home Residents • Social Development Clients • Individuals in Licensed Residential Facilities • Children in Care of the Minister of Social and Special Needs Children • Multiple Sclerosis • HIV/AIDS • Cystic Fibrosis • Organ Transplant Recipients • Change Hormone Deficiency New Brunswick Drug Plan Medical Abortion Plan
Newfoundland and Labrador	The Foundation Plan The 65Plus Plan The Access Plan Assurance Plan Select Needs/Cystic Fibrosis Plan Select Needs/Change Hormone Plan

Jurisdiction	Plan/Program Description
Nova Scotia[b]	Diabetic Assistance Pharmacare Program Drug Assistance for Cancer patients Family Pharmacare Program Palliative Drug Care Program Under 65 – Long-Term Care Pharmacare Plan Seniors' Pharmacare Program
Ontario	Ministry of Community and Social Services (MCSS) Ontario Ministry of Health and Long-Term Care (MOHLTC) Drug Benefit Program (ODB)
Prince Edward Island[c]	Diabetes Control Program Family Health Benefit Program Immunization Program High Cost Drugs Program Nursing Home Seniors Drug Cost Assistance Program Sexually Transmitted Diseases (STD) Children-In-Care/Financial Assistance Smoking Cessation Program Catastrophic Drug Program Opioid Replacement Therapy Drug Program Generic Drug Program
Saskatchewan	Universal Program
Yukon	Children's Drug and Optical Plan Chronic Disease Program Pharmacare

NPDUIS = National Prescription Drug Utilization Information System.

Note: In all jurisdictions, people covered by provincial workers' compensation boards or federal drug programs are not eligible for provincial public coverage. In Ontario, individuals who have coverage through the First Nations and Inuit Health Branch (FNIHB) first have their drug claims covered by the Ontario Drug Benefit, with remaining costs covered by FNIHB.

[a]Claims financed through the Income Support, Alberta Adult Health Benefit, Assured Income for the Severely Handicapped, and Alberta Child Health Benefit programs, are not submitted. Claims financed to residents of long-term care facilities are not submitted.

[b]Claims dispensed through the Department of Community Services Drug Programs are not submitted.

[c]Claims dispensed through the Child in Care/Financial Assistance, Seniors Cost Assistance, Diabetes Control, Family Health Benefits, High Cost Drugs, Nursing Home, Quit Smoking, and Sexually Transmitted Diseases programs are included. Claims for all other plans are not submitted.

Appendix 2: Drugs Included in the NPDUIS Database Search

Note that this appendix has not been copy-edited.

Table 7: Drugs Included in the NPDUIS Database Search

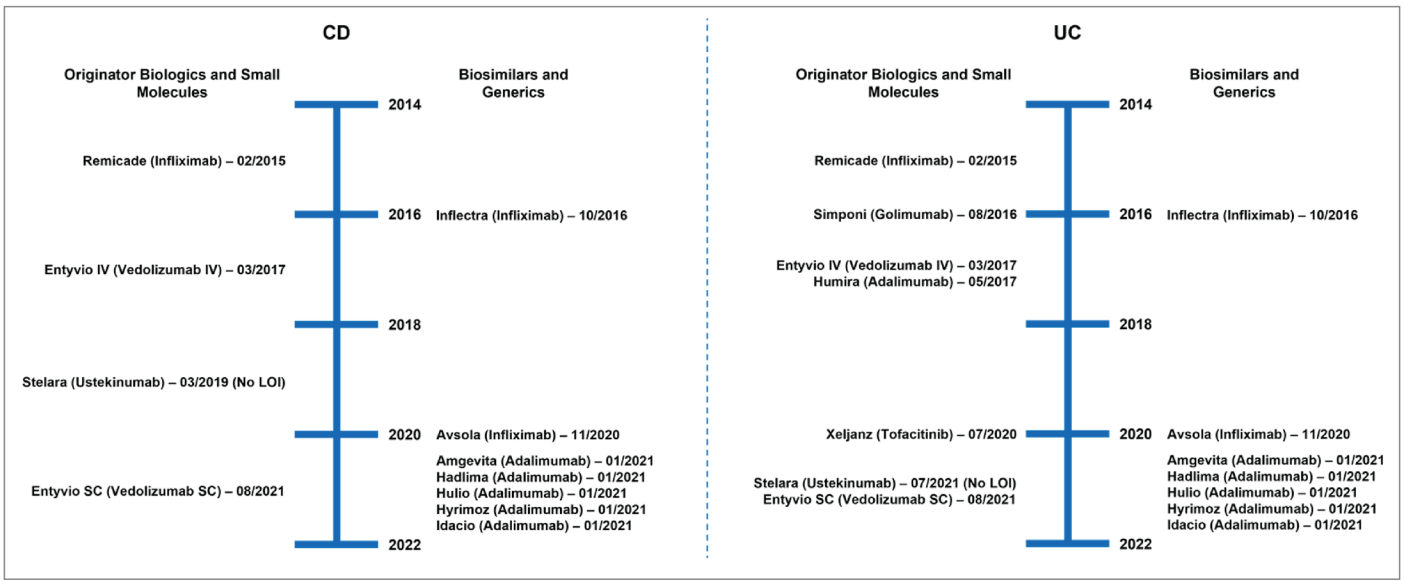
Chemical (Generic Name)	ATC Code
Conventional therapy	
Anti-inflammatory agents	
5-aminosalicylic acid/mesalamine/mesalazine	A07EC02
Olsalazine	A07EC03
Sulfasalazine	A07EC01
Corticosteroids	
Betamethasone	A07EA04
Budesonide	A07EA06
Hydrocortisone	C05AA01
Methylprednisolone	H02AB04
Prednisone	H02AB07
Immunosuppressive agents	
6-mercaptopurine	L01BB02
Azathioprine	L04AX01
Methotrexate	L01BA01
Targeted Immune modulators	
Adalimumab	L04AB04
Infliximab	L04AB02
Golimumab	L04AB06
Tofacitinib	L04AA29
Ustekinumab	L04AC05
Vedolizumab	L04AA33

ATC = Anatomical Therapeutic Chemical; NPDUIS = National Prescription Drug Utilization Information System.

Appendix 3: Timeline for Conclusion of pCPA Negotiations for TIMs Approved for CD and UC Before or During the Study Period

Note that this appendix has not been copy-edited.

Figure 2: Timeline for Conclusion of pCPA Negotiations for TIMs Approved for CD and UC Before or During the Study Period



CD = Crohn disease; LOI = letter of intent; pCPA = pan-Canadian Pharmaceutical Alliance; SC = subcutaneous; UC = ulcerative colitis.

Note: Remicade (infliximab) was approved for the treatment of CD and UC and Humira (adalimumab) was approved for the treatment of CD by Health Canada before pCPA was established. In addition, pCPA negotiations were concluded for Stelara (ustekinumab) without an agreement for both CD and UC.

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Questions or requests for information about this report can be directed to Requests@CADTH.ca.