CoLab Network

Drug Utilization Study

Long-Term Use of Omalizumab for Chronic Idiopathic Urticaria

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Key Messages

Omalizumab is recommended to treat chronic idiopathic urticaria when patients do not respond to nonsedating H_1 antihistamines.

A drug utilization study was conducted to explore the characteristics of individuals with chronic idiopathic urticaria using omalizumab, as well as the incidence of omalizumab long-term use (i.e., > 24 weeks) in 4 Canadian provinces. These provinces were selected based on where comprehensive community-based prescription drug dispensing data were available (Manitoba, Saskatchewan, and British Columbia), and also included Newfoundland and Labrador based on their interest in this query.

The use of omalizumab for chronic idiopathic urticaria has increased in 4 Canadian provinces (Manitoba, Saskatchewan, British Columbia, and Newfoundland and Labrador) since 2015, when it was first recommended for use in symptomatic, moderate to severe chronic idiopathic urticaria.

In Manitoba, Saskatchewan, and British Columbia, the majority of new treatment episodes exceeded 24 weeks, despite a lack of evidence regarding the use of omalizumab beyond 24 weeks (considered long-term use).

Across jurisdictions, no notable differences were observed in age, sex, or location (urban versus rural) between short-term and long-term recipients of omalizumab.

Further research examining the real-world effectiveness and cost-effectiveness of treatment of chronic idiopathic urticaria using omalizumab beyond 24 weeks is required.

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Abbreviations

CIU	chronic idiopathic urticaria
CDEC	Canadian Drug Expert Committee
DIN	drug information number
NPDUIS	National Prescription Drug Utilization Information System
NA	not applicable

Background

Epidemiology

Chronic idiopathic urticaria (CIU) — also known as chronic spontaneous urticaria — is defined as itchy hives that last for at least 6 weeks, with or without angioedema,[1] that have no apparent external trigger. The condition generally has a prolonged duration of 1 to 5 years (persisting for > 5 years in 11% to 14% of patients), is more common in women, and can have detrimental effects on patients' emotional and physical health-related quality of life.[2]

The economic impact of CIU on both patients and the health care system is significant. In the ASSURE-CSU study, people in Canada who had been living with the condition for longer than 6 months averaged out-of-pocket expenses approaching $1,000 annually.[3]

Treatment

Nonsedating H_1 antihistamines have historically been the mainstay for initial treatment of CIU.[4] In accordance with clinical practice guidelines jointly issued by the European Academy of Allergy and Clinical Immunology, the Global Allergy and Asthma European Network, the European Dermatology Forum, and the World Allergy Organization, maximally tolerated doses of second-generation H_1 antihistamines up to 4 times higher than the approved label dose may be used.[5] However, some patients do not experience a response to H_1 antihistamines, even at supratherapeutic doses, and require additional therapy.[6] For example, 1 study of levocetirizine and desloratadine found that for approximately 15% of patients, neither drug produced a response. [7]

Omalizumab is a humanized, recombinant immunoglobulin G (IgG) monoclonal antibody that binds to immunoglobulin E (IgE) and prevents it from binding to its high-affinity receptor on mast cells and basophils, thereby reducing IgE-induced mast cell and basophil degranulation and the release of histamine and other inflammatory mediators.[8] In 2015, the Canadian Drug Expert Committee (CDEC) recommended that omalizumab be listed for the treatment of adults and adolescents with CIU who remain symptomatic despite H_1 antihistamine treatment, if the following clinical criterion is met:

- moderate to severe CIU that remains symptomatic (presence of hives and/or associated itching) despite 6 months of optimum management with available oral therapies.[9]

For CIU treatment, the drug product monograph authorizes the administration of omalizumab as a 150 mg or 300 mg subcutaneous injection every 4 weeks.[10]

At the time of the recommendation in May 2015, there were no data available to evaluate the efficacy and safety of omalizumab in patients requiring re-treatment, nor for the use of omalizumab beyond 24 weeks. With pan-Canadian Pharmaceutical Alliance (pCPA) negotiations concluding on November 28, 2016, coverage for omalizumab for CIU in Manitoba and Saskatchewan became effective in January 2017 and April 2017, respectively, with prior authorization.[11,12] Coverage became effective in July 2017 in Newfoundland and Labrador.[13] Despite some slight variations, the prior-authorization criteria across these provinces generally pertain to individuals (aged ≥ 12 years) who remain symptomatic despite optimum management with

available oral therapies, with initial drug approval for 24 weeks and subsequent assessment of symptoms and/or treatment efficacy.

More recent international guidelines suggest an initial dose of 300 mg every 4 weeks, recommending that omalizumab be used if control remains inadequate after 2 to 4 weeks of a high dose (i.e., up to 4 times the standard dose) of a second-generation H_1 antihistamine is used, or sooner if symptoms remain intolerable.[14]

Key Take-Away

Nonsedating H_1 antihistamines are the first line of treatment for patients with CIU. However, some patients do not experience a response to them even at higher doses. In such cases, omalizumab can be used. It is recommended for patients with moderate to severe CIU who remain symptomatic despite optimum management with available oral therapies.

Purpose of This Report

The purpose of this report is to relay the findings of a drug utilization study exploring the characteristics of individuals with CIU using omalizumab, as well as the incidence of omalizumab long-term use (i.e., > 24 weeks) in 4 Canadian provinces.

Policy Issues

Omalizumab is being used for the long-term treatment of patients with CIU in the real-world setting. In Newfoundland and Labrador, renewals are approved on a case-by-case basis and criteria include clinical documentation of symptom control for each approval period (i.e., this information is required for the previous 24 weeks for each renewal). However, there is limited evidence for the use of this drug chronically (i.e., beyond 24 weeks), and most federal, provincial, and territorial drug formularies (including Newfoundland and Labrador) specify limits on the duration of approval (i.e., 24 weeks).[11,13] With rising requests for renewals of omalizumab beyond the 24-week period, and no explicit limitation on number of renewals in Newfoundland and Labrador specifically, there is a need for information regarding the incidence of longer-term omalizumab use for CIU across Canada as well as an understanding of this drug's long-term effectiveness. The evidence produced from this query response will be used to inform policy on the use of omalizumab beyond 24 weeks.

Research Questions

1. What is the incidence of omalizumab long-term use (i.e., > 24 weeks) for individuals being treated for CIU?
2. What are the characteristics of patients with CIU who use omalizumab for longer than 24 weeks?

Key Take-Away

The objective of the drug utilization study is to determine real-world omalizumab use patterns in patients with CIU. The focus is on identifying the incidence of use beyond 24 weeks (considered long-term treatment).

Methods

Data Sources

A data request was made to the Canadian Institute for Health Information (CIHI) using their National Prescription Drug Utilization Information System (NPDUIS) database. The request was limited to Manitoba, Saskatchewan, and British Columbia, where full prescription drug data were available (i.e., full coverage of community-based drug dispensations made in the province). Newfoundland and Labrador was also included in the analyses due to interest from this jurisdiction. The details of the Drug Information Numbers (DINs) included in this request, and the provinces from which data were obtained, are outlined in Table 1; drug programs included in the analyses can be found in Table 2.

Table 1: Drugs Included in the NPDUIS Database Search

Name of product	Strength (units per mL)	Product type and size
Omalizumab (DIN: 02260565)	150 mg	Vial
Omalizumab (DIN: 02459787)	75 mg	Prefilled syringe
Omalizumab (DIN: 02459795)	150 mg	Prefilled syringe

DIN = drug information number; NPDUIS = National Prescription Drug Utilization Information System.

Table 2: Provincial Public Drug Plans and Programs With Claims Data Contained Within the NPDUIS Database Within the Requested Time Period (2014 to 2021)

Province	Program
British Columbia	Assurance Program
	Children in the At-Home Program
	Fair PharmaCare
	Residential Care
	Recipients of British Columbia Income Assistance
	Cystic Fibrosis
	Children in the At-Home Program
	Psychiatric Medication Program
	Palliative Care
	Nicotine Replacement Therapies

Province	Program
	Non-adjudicated
Manitoba	Employment and Income Assistance Program
	Palliative Care
	Pharmacare
	Personal Home Care/Nursing Homes
	Non-adjudicated
Newfoundland and Labrador	Foundation Plan
	65 Plus Plan
	Access Plan
	Select Needs/Cystic Fibrosis Plan
	Select Needs/Growth Hormone Plan
	Assurance Plan
Saskatchewan	Universal Program
	Non-adjudicated

NPDUIS = National Prescription Drug Utilization Information System.

Study Design, Data Analysis, and Limitations

Study Design

Study period: Individuals with index episodes during the study period were included and followed for up to 365 days with a maximum follow-up date of December 31, 2021.The study period for each province is outlined in Table 3.

Table 3: Study Period and Reporting Period of Omalizumab Use for CIU by Province

Province	Study period
British Columbia	January 1, 2014, to December 31, 2020
Manitoba	January 1, 2016, to December 31, 2020
Newfoundland and Labrador	January 1, 2014, to December 31, 2020
Saskatchewan	January 1, 2014, to December 31, 2020

Cohort definition: Incident treatment episodes were defined as omalizumab dispensations with no prior dispensing within a 6-month period (≥ 183 days). An individual could have multiple incident treatment episodes (and index dates). The first dispensation of omalizumab following each 6-month gap was treated as an incident treatment index date.

Exclusion criteria: All omalizumab dispensations preceded by dispensations for an inhaler, theophylline, or aminophylline in the 6 months (< 183 days) before (and including) the index date were excluded. This criterion was applied to restrict treatment episodes to individuals being treated for CIU, while excluding those

using omalizumab for asthma management. The number of index dispensations excluded based on the criteria were reported.

Outcome Definition

Omalizumab discontinuation: Omalizumab discontinuation was defined by following each patient forward for subsequent dispensations and allowing gaps between dispensing for up to 8 weeks (≤ 56 days, main definition). This 8-week period was selected to allow for a doubling of the suggested dosing interval of omalizumab for CIU (every 4 weeks). In a sensitivity analysis, discontinuation was defined according to gaps in dispensations of 6 weeks (≤ 42 days, definition 2) and 12 weeks (≤ 84 days, definition 3). Upon discontinuation, the treatment episode discontinuation date was defined as the date of last omalizumab dispensation plus 28 days (because injections are meant to be separated by 4 weeks). Duration of omalizumab use was defined as the number of days between index date and discontinuation date. The maximum follow-up period was 365 days.

Long-term treatment episodes: Treatment episodes with a duration of use of greater than 24 weeks (> 168 days) were defined as long-term incident treatment episodes.

Analysis

The following analyses were conducted:

1. Annual trends in incidence of long-term omalizumab utilization for CIU, stratified by province; population-level rates were also calculated in Manitoba, Saskatchewan, and British Columbia using population estimates obtained from Statistics Canada as the denominator.
2. Duration of use of omalizumab for CIU: the number and percent of all new users of omalizumab for CIU were categorized by duration (≤ 8 weeks, > 8 weeks to ≤ 16 weeks, > 16 weeks to ≤ 24 weeks, > 24 weeks to ≤ 32 weeks, > 32 weeks to ≤ 40 weeks, > 40 weeks to ≤ 48 weeks, and > 48 weeks) and stratified by province.
3. Characteristics of individuals receiving long-term omalizumab for CIU: age (mean [standard deviation (SD)], median [interquartile range (IQR)], age group), sex, and urban or rural location of dispensation were stratified by province and long- versus short-duration recipients; these summary statistics are defined on the index claim for each patient in each episode.

Limitations

1. In Newfoundland and Labrador, only dispensations resulting from claims made to public drug programs were included. Prescriptions that were dispensed but for which the associated drug costs were not submitted to, or not accepted by, the public drug programs in Newfoundland and Labrador were not included. Due to the design of the public drug program (e.g., older adults and low-income families or individuals), there are limited data on claims made by individuals younger than 65 years. As a result, results from this jurisdiction are not population-based. Characteristics of individuals with and without public drug coverage may also differ. Finally, because the overall number of persons

eligible for public drug programs in Newfoundland and Labrador are not available, population adjusted rates could not be calculated.

2. Across the jurisdictions, information on the diagnoses or conditions for which prescriptions were written was also not available. In particular, it was not possible to ascertain whether the recipients of omalizumab identified in these analyses were dispensed omalizumab for CIU, although efforts were made to remove episodes in which the drug was used for the treatment of asthma by excluding individuals who had previously been dispensed an inhaler, aminophylline, or theophylline. Due to this exclusion criteria, some treatment episodes of omalizumab for CIU involving individuals with comorbid asthma may have been excluded. Additionally, other off-label uses of omalizumab may not have been captured in the exclusion criteria, although such uses are likely uncommon and are not often listed in approved prior-authorization criteria.

Findings

Key Take-Aways

The use of omalizumab treatment for CIU has increased since 2015 when it was first recommended for listing on public drug plans; however, there has been a slight decline in use in recent years.

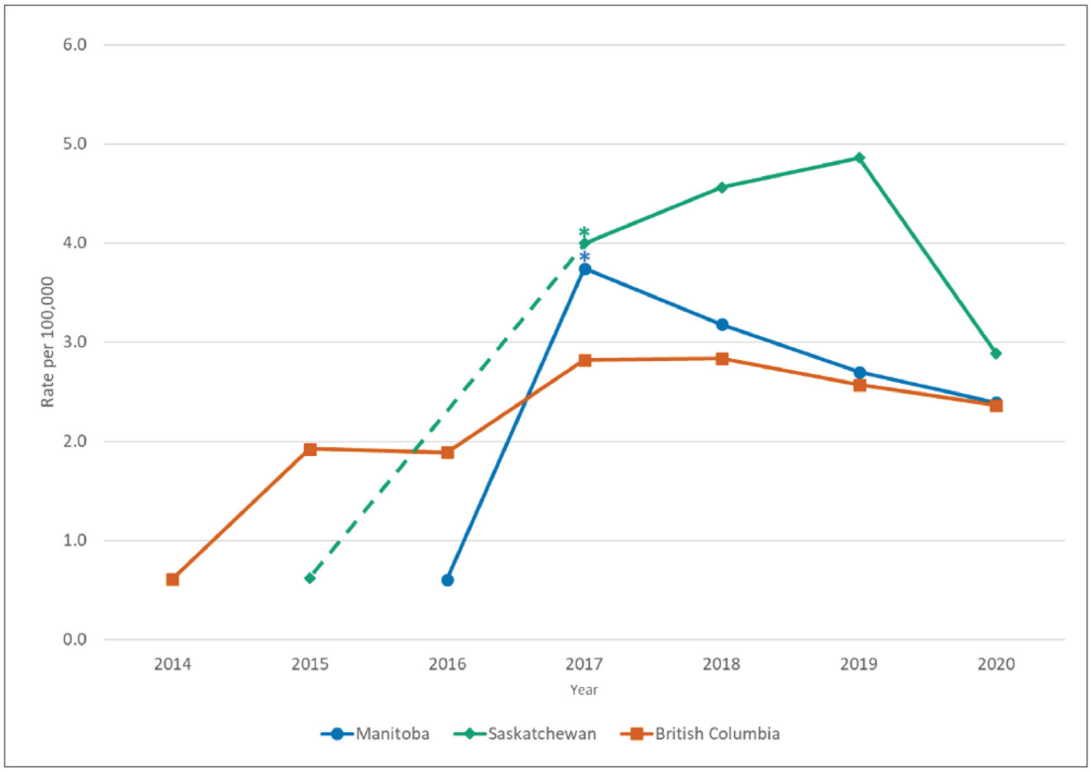
In Manitoba, Saskatchewan, and British Columbia, the majority of those prescribed omalizumab received treatment that exceeded 24 weeks, with many exceeding 48 weeks.

The majority of those prescribed omalizumab for CIU were between the ages of 25 and 64 years, were female, and were dispensed omalizumab at a pharmacy located in an urban area.

Age, sex, and location did not vary for long-term (> 24 weeks) versus short-term (≤ 24 weeks) use of omalizumab across jurisdictions.

Between 2014 and 2020, there were 747 incident treatment episodes of omalizumab for CIU in British Columbia and 203 in Saskatchewan. In Manitoba, where data were only available between 2016 and 2020, there were 171 incident treatment episodes. Finally, in Newfoundland and Labrador, there were 38 incident treatment episodes of omalizumab between 2017 and 2020 among public drug beneficiaries. These incident treatment episodes excluded episodes in which an individual was also dispensed an inhaler, theophylline, or aminophylline in the 6 months before the initiation of omalizumab to restrict to episodes in which omalizumab was being prescribed for CIU and not asthma. This restriction led to the removal of 62 (26.6% of all episodes identified) episodes in Manitoba, 76 (27.2%) in Saskatchewan, 587 (44.0%) episodes in British Columbia and 11 episodes (22.4%) in Newfoundland and Labrador.

Figure 1: Rate of Incident Omalizumab Treatment Episodes for CIU (per 100,000), by Year and Province

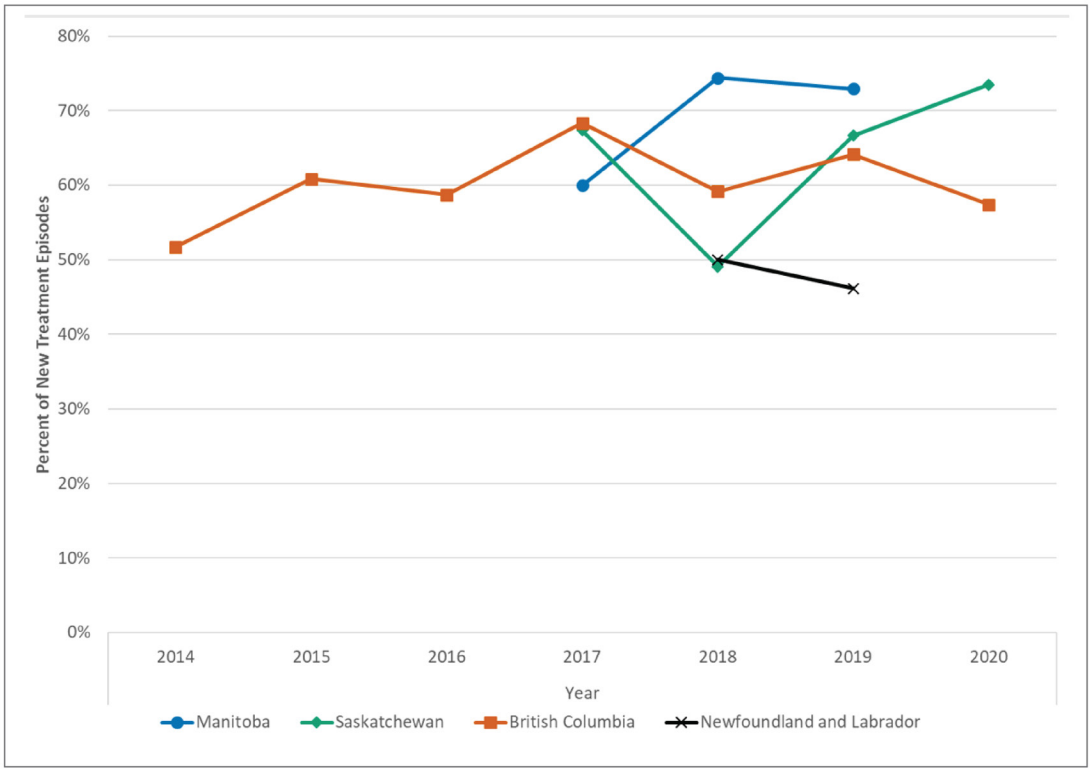


CIU = chronic idiopathic urticaria.

Notes: Asterisks denote the year when the prior authorization was approved in Manitoba and Saskatchewan. Results for Manitoba are not available before 2016.The rates of new treatment episodes of omalizumab for CIU could not be reported for Saskatchewan in 2014 and 2016 due to the suppression of small cells.

In Manitoba, Saskatchewan, and British Columbia, the number and rate of incident treatment episodes of omalizumab for CIU remained relatively low before 2017, after which they began to rise, followed by a decline in more recent years (Figure 1; Appendix 1, Table 8). In Saskatchewan, rates of incident treatment episodes began declining in 2020, while in Manitoba and British Columbia, these declines began in 2018. By 2020, the rate of incident treatment episodes were highest in Saskatchewan (2.9 per 100,000; N = 34) and were similar in Manitoba (2.4 per 100,000; N = 33) and British Columbia (2.4 per 100,000; N = 122). In Newfoundland and Labrador, there were no incident treatment episodes before 2017. Between 2018 and 2020, the number of incident omalizumab treatment episodes was relatively stable (range, 10 to 13 new episodes) (Appendix 1, Table 8).

Figure 2: Percent of New Treatment Episodes of Omalizumab for CIU Exceeding 24 Weeks (Long-Term), by Year and Province



CIU = chronic idiopathic urticaria.

Notes: Due to the suppression of small cell counts and residual disclosure of small cell counts, results in Manitoba could not be reported for 2016 and 2020; results in Saskatchewan could not be reported before 2017; and results in Newfoundland and Labrador could not be reported before 2018 or in 2020.

In the primary analysis, the proportion of incident omalizumab episodes for CIU that led to long-term use (i.e., > 24 weeks) generally exceeded 50% of all episodes but fluctuated over the study period and by province (Figure 2). In British Columbia, where data were available from 2014 to 2020, the percentage was relatively stable, ranging from 51.7% to 68.3%. In Manitoba, where data were only available in later years, percentages were generally slightly higher, reaching 73.0% in 2019 (compared to 64.1% in British Columbia). In Saskatchewan, the long-term omalizumab patterns were similar to British Columbia until 2020, when 73.5% of new episodes led to long-term use. Finally, In Newfoundland and Labrador, among public drug beneficiaries, approximately 50% (range, 46.2% to 50.0%) of incident omalizumab episodes for CIU led to long-term treatment.

Table 4: Incidence of Long-Term Omalizumab Treatment Episodes for CIU Using 3 Definitions of Ongoing Use, by Province (2014 to 2020)

	Manitoba[a]				Saskatchewan				British Columbia				Newfoundland and Labrador			
		Long-term treatment N (%)				Long-term treatment N (%)				Long-term treatment N (%)				Long-term treatment N (%)		
Index year	Episodes, N	8 weeks[b]	6 weeks	12 weeks	Episodes, N	8 weeks[b]	6 weeks	12 weeks	Episodes, N	8 weeks[b]	6 weeks	12 weeks	Episodes, N	8 weeks[b]	6 weeks	12 weeks
2014	NA	NA	NA	NA	< 5	0	0	0	29	15 (51.7)	12 (41.4)	16 (55.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2015	NA	NA	NA	NA	7	S[c]	S	S	92	56 (60.9)	48 (52.2)	62 (67.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2016	8	S	S	S	< 5	< 5	< 5	< 5	92	54 (58.7)	44 (47.8)	61 (66.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2017	50	30 (60.0)	24 (48.0)	37 (74.0)	46	31 (67.4)	21 (45.7)	39 (84.8)	139	95 (68.3)	81 (58.3)	102 (73.4)	5	< 5	< 5	5 (100)
2018	43	32 (74.4)	29 (67.4)	35 (81.4)	53	26 (49.1)	24 (45.3)	29 (54.7)	142	84 (59.2)	74 (52.1)	91 (64.1)	10	5 (50.0)	5 (50.0)	S
2019	37	27 (73.0)	26 (70.3)	30 (81.1)	57	38 (66.7)	32 (56.1)	45 (78.9)	131	84 (64.1)	72 (55.0)	93 (71.0)	13	6 (46.2)	< 5	S
2020	33	S	16 (48.5)	23 (69.7)	34	25 (73.5)	21 (61.8)	26 (76.5)	122	70 (57.4)	57 (46.7)	81 (66.4)	10	< 5	< 5	< 5

CIU = chronic idiopathic urticaria; IQR = interquartile range; NA = not available; S = suppressed; SD = standard deviation.

[a]Results for Manitoba represent data from 2016 to 2020 only.

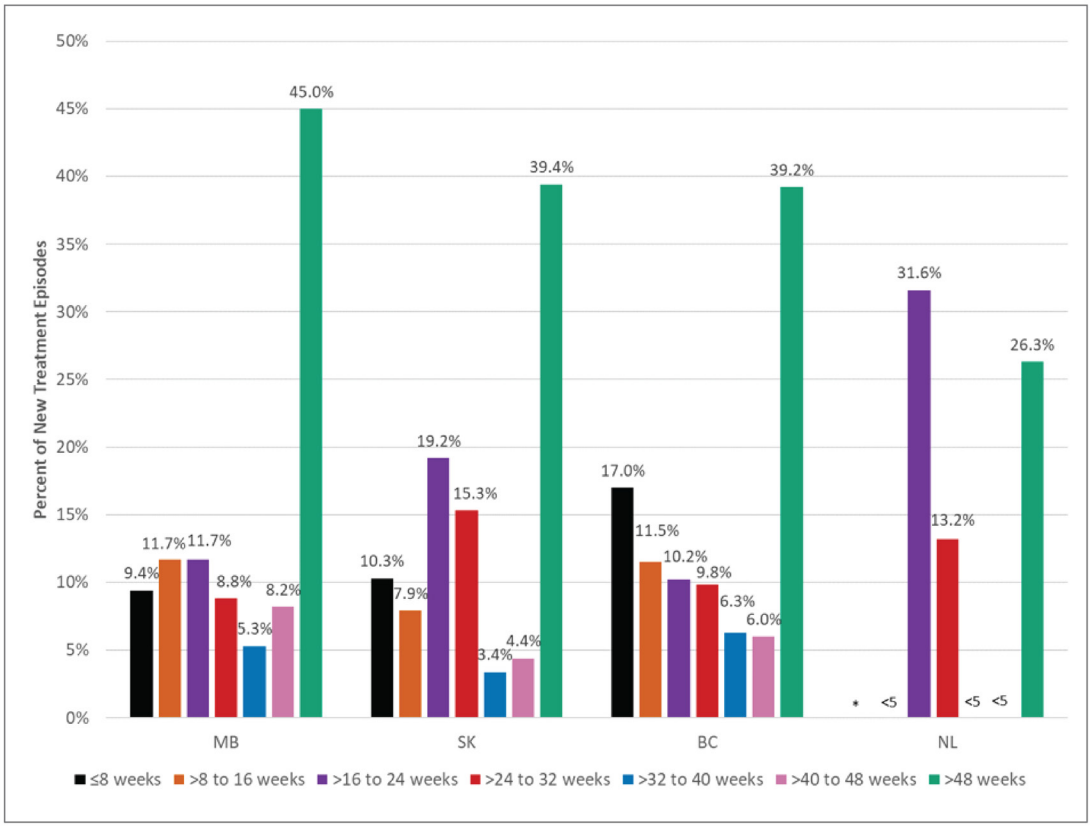
[b]Main definition of ongoing use (i.e., discontinuation was defined according to gaps in dispensations of 8 weeks).

[c]In cases where a single record is suppressed (i.e., it has a cell count less than 5), the subsequent record with the lowest value is also suppressed to prevent residual disclosure, in accordance with CIHI privacy policy.

In sensitivity analyses where alternate dispensation intervals were used to define ongoing use, results were generally consistent, although when using a shorter dispensation interval to define discontinuation (i.e., dispensations at least every 6 weeks), a smaller proportion of incident episodes were considered long-term episodes (range, 41.4% to 70.3%), while the longer dispensation interval definition (i.e., dispensations at least every 12 weeks) led to a larger proportion of incident episodes being considered long-term episodes (range, 54.7% to 84.8%; Table 4).

Among the incident omalizumab treatment episodes identified over the entire study period, approximately two-thirds had a duration of more than 24 weeks (67.3%, n = 115 of 171 in Manitoba; 62.6%, n = 127 of 203 in Saskatchewan; 61.3%, n = 458 of 747 in British Columbia). Importantly, where complete data were available for the entire population, incident treatment episode durations more than 48 weeks in length were most common (Manitoba: 45.0%, n = 77; Saskatchewan: 39.4%, n = 80; British Columbia: 39.2%, n = 293). In British Columbia the second most common duration was 8 weeks or less (17.0%), whereas in Saskatchewan the second most common duration was 16 weeks to 24 weeks (19.2%). In Manitoba, incident treatment

Figure 3: Duration of Incident Omalizumab Treatment Episodes for CIU, by Province (2014 to 2020)



BC = British Columbia; CIU = chronic idiopathic urticaria; MB = Manitoba; NL = Newfoundland and Labrador; SK = Saskatchewan.

Notes: Asterisks indicate that, in cases where a single record is suppressed (i.e., it has a cell count less than 5), the subsequent record with the lowest value is also suppressed to prevent residual disclosure in accordance with CIHI privacy policy. Data for Manitoba are for the years 2016 to 2020 only.

episode durations were relatively evenly distributed for incident episodes of 48 weeks or less. In contrast, in Newfoundland and Labrador, only 26.3% of episodes (n = 10) were longer than 48 weeks in duration, and the most common incident treatment episode duration was 16 weeks to 24 weeks (31.6%).

Table 5: Demographic Characteristics of Recipients of Incident Treatment Episodes of Omalizumab for CIU, by Province (2014 to 2020)

Characteristics on index claim		British Columbia (N = 747)	Manitoba[a] (N = 171)	Saskatchewan (N = 203)
Age	Mean (SD), years	44.8 (15.5)	42.5 (15.8)	43.5 (15.2)
	P value	—	0.09	0.28
	Median (IQR), years	44 (22)	40 (22)	43 (19)
Age categories, N (%)	≤ 24 years	78 (10.4)	22 (12.9)	22 (10.8)
	25 to 44 years	310 (41.5)	76 (44.4)	84 (41.4)
	45 to 64 years	281 (37.6)	58 (33.3)	80 (39.4)
	≥ 65 years	78 (10.4)	15 (8.8)	17 (8.4)
	P value	—	0.59	0.84
Sex, N (%)	Male	251 (33.6)	50 (29.2)	50 (24.6)
	Female	496 (66.4)	121 (70.8)	153 (75.4)
	P value	—	0.27	0.01
Location of dispensation, N (%)	Urban	625 (83.7)	123 (71.9)	135 (66.5)
	Rural	46 (6.2)	S[b]	34 (16.7)
	Missing	76 (10.2)	< 5	34 (16.7)
	P value	—	NE[c]	< 0.01

CIU = chronic idiopathic urticaria; IQR = interquartile range; NE = not estimable; S = suppressed; SD = standard deviation.

[a]Results for Manitoba represent data from 2016 to 2020 only.

[b]In cases where a single record is suppressed (i.e., it has a cell count less than 5), the subsequent record with the lowest value is also suppressed to prevent residual disclosure in accordance with CIHI privacy policy.

[c]P value cannot be estimated due to supressed cell.

Note: P values compare recipient characteristics to those in British Columbia (reference group).

Table 6: Demographic Characteristics of Recipients of Incident Treatment Episodes of Omalizumab for CIU in Newfoundland and Labrador (2014 to 2020)

Characteristics on index claim		Newfoundland and Labrador (N = 38)
Age	Mean (SD), years	45.4 (16.9)
	Median (IQR), years	42 (29)
Age categories, N (%)	< 66 years	5 (13.2)
	≥ 66 years	33 (86.8)
Sex, N (%)	Male	7 (18.4)

Characteristics on index claim		Newfoundland and Labrador (N = 38)
	Female	31 (81.6)
Location of dispense, N (%)	Urban	27 (71.1)
	Rural	11 (28.9)
	Missing	0 (0)

CIU = chronic idiopathic urticaria; IQR = interquartile range, SD = standard deviation.

Note: P values for NL could not be calculated due to small numbers.

The mean ages of those initiating incident episodes of omalizumab for CIU were similar across Manitoba, Saskatchewan, and British Columbia, ranging from 42.5 years in Manitoba to 44.8 years in British Columbia (Table 5). The mean age of individuals initiating an incident episode of omalizumab in Newfoundland and Labrador was also similar at 45.4 years (Table 6).

The majority of recipients of incident omalizumab treatment for CIU were between the ages of 25 and 44 years, with this demographic representing 44.4% (n = 76 of 171) of incident treatment episodes in Manitoba, 41.4% (n = 84 of 203) in Saskatchewan, and 41.5% (n = 310 of 747) in British Columbia (Table 4). When compared to the age distribution in British Columbia, there were no significant differences in age distribution observed in Manitoba or Saskatchewan. In Newfoundland and Labrador, 86.8% (n = 33 of 38) of incident treatment recipients for CIU were aged 66 years or older. This finding likely reflects the population available for analysis in Newfoundland and Labrador, which comprised an older demographic eligible for public drug benefits through the provincial 65Plus Plan.

Across all jurisdictions, the majority of incident treatment episode initiations were for females, ranging from 66.4% (n = 496 of 747) in British Columbia to 81.6% (n = 31 of 38) in Newfoundland and Labrador (Table 5). The sex distribution was similar between Manitoba and British Columbia, but there was a higher prevalence of incident omalizumab treatment for CIU among females in Saskatchewan compared to British Columbia (75.4% versus 66.4%; P = 0.01).

The majority of omalizumab dispensations for CIU were in an urban area, ranging from 66.5% (n = 135 of 203) in Saskatchewan to 83.7% (n = 625 of 747) in British Columbia. However, it is important to note that these percentages do not take into account the relative distribution of populations across rural and urban areas in each province.

Mean age for long-term versus short-term omalizumab incident treatment episode duration did not vary notably within or across jurisdictions. The sex distributions between short-term and long-term incident episode recipients were also similar. The distribution of short-term versus long-term incident treatment episode recipients was similar in each province, with the exception of Manitoba where 62.5% (n = 35 of 56) of short-term recipients were dispensed omalizumab in an urban area, compared with 76.5% (n = 88 of 115) of long-term recipients (Table 7).

Table 7: Demographic Characteristics of Recipients of Incident Treatment Episodes of Omalizumab for CIU (2014 to 2020), by Duration of Use and Province

Characteristics on index claim		Manitoba[a]		Saskatchewan		British Columbia		Newfoundland and Labrador	
		Short-term ≤ 24 weeks (N = 56)	Long-term > 24 weeks (N = 115)	Short-term ≤ 24 weeks (N = 76)	Long-term > 24 weeks (N = 127)	Short-term ≤ 24 weeks (N = 289)	Long-term > 24 weeks (N = 458)	Short-term ≤ 24 weeks (N = 20)	Long-term > 24 weeks (N = 18)
Age, N (%)	Mean (SD), years	41.9 (14.8)	42.7 (16.3)	44.6 (14.2)	42.8 (15.7)	45.1 (16.1)	44.6 (15.1)	44.5 (15.3)	46.4(18.9)
	Median (IQR), years	39 (19)	42 (25)	43.5 (19)	42 (19)	44 (23)	44 (20)	43.5 (21)	42(33)
Age categories, N (%)	≤ 24 years	S[b]	S	< 5	S	33 (11.4)	45 (9.8)	NA	NA
	25 to 44 years	23 (41.1)	53 (46.1)	37 (48.7)	47 (37.0)	114 (39.4)	196 (42.8)	NA	NA
	45 to 64 years	21 (37.5)	37 (32.2)	28 (36.8)	52 (40.9)	109 (37.7)	172 (37.6)	NA	NA
	≥ 65 years	< 5	S	S	S	33 (11.4)	45 (9.8)	NA	NA
	0 to 65 years	NA	NA	NA	NA	NA	NA	< 5	< 5
	≥ 66 years	NA	NA	NA	NA	NA	NA	S	S
Sex, N (%)	Male	17 (30.4)	33 (28.7)	20 (26.3)	30 (23.6)	104 (36.0)	147 (32.1)	< 5	< 5
	Female	39 (69.6)	82 (71.3)	56 (73.7)	97 (76.4)	185 (64.0)	311 (67.9)	S	S
Location of dispensing pharmacy, N (%)	Urban	35 (62.5)	88 (76.5)	53 (69.7)	82 (64.6)	235 (81.3)	390 (85.2)	14 (70.0)	13 (72.2)
	Rural	21 (37.5)	S	13 (17.1)	21 (16.5)	19 (6.6)	27 (5.9)	6 (30.0)	5 (27.8)
	Missing	0	< 5	10 (13.2)	24 (18.9)	35 (12.1)	41 (9.0)	0 (0.0)	0 (0.0)

CIU = chronic idiopathic urticaria; IQR = interquartile range; NA = not applicable; S = suppressed; SD = standard deviation.

[a]Results for Manitoba represent data from 2016 to 2020 only.

[b]In cases where a single record is suppressed (i.e., it has a cell count less than 5), the subsequent record with the lowest value is also suppressed to prevent residual disclosure in accordance with CIHI privacy policy.

Discussion

This analysis found a low rate of incident treatment episodes of omalizumab after its recommendation for use for CIU by CDEC in 2015, although rates increased in the years immediately following its listing on the Manitoba and Saskatchewan provincial drug formularies in 2017. In Manitoba, Saskatchewan, and British Columbia, more than two-thirds of incident treatment episodes were greater than 24 weeks in duration, and approximately 40% of episodes in these provinces were greater than 48 weeks in duration.

The initial increases in rates of treatment could reflect greater awareness of the use of omalizumab for CIU and its availability on drug formularies. Interestingly, in later years, a slight decline in the number of new treatment episodes for CIU was observed. In Newfoundland and Labrador and Saskatchewan, the decline was observed in 2020, which could reflect changes in health care access at the beginning of the COVID-19 pandemic. The reason for the earlier declines observed in Manitoba is unclear.

Although this study did not examine the effectiveness of long-term use of omalizumab for CIU, most incident treatment episodes identified exceeded 24 weeks. It is important to note that the product monograph for omalizumab states that long-term clinical experience with using the drug for longer than 24 weeks is limited,[10] and although some studies suggest safety and effectiveness of longer-term omalizumab use for CIU, these studies are generally restricted to small, retrospective chart reviews or single-centre prospective studies.[15-17] It is therefore possible that prolonged use may not provide optimal therapeutic benefits. Thus, future research is needed to assess the effectiveness of long-term use of omalizumab for CIU in larger population-based cohorts to ensure that resources are being used efficiently. In Manitoba, Saskatchewan, and British Columbia, approximately two-thirds of treatment episodes were more than 24 weeks in duration, compared with approximately 40% in Newfoundland and Labrador. Importantly, treatment durations beyond 48 weeks were common in Manitoba, Saskatchewan, and British Columbia, representing approximately 40% of episodes. The proportion of episodes with a duration longer than 24 weeks varied across provinces, fluctuating from year to year, although there did not appear to be a clear trend in long-term episodes over time. In Newfoundland and Labrador, episode durations between 16 weeks and 24 weeks were most common; however, these data are difficult to interpret due to the high degree of suppression of results for privacy reasons as well as the restriction to publicly funded dispensations only. It is possible that differences in treatment duration were informed by provincial funding criteria. For example, Saskatchewan residents treated with omalizumab are permitted to request an extension for the drug beyond 24 weeks of treatment when complete symptom control is not attained for at least 12 weeks, or if there is only a partial response to treatment.[11] In Newfoundland and Labrador, although the extension criteria are the same, 2 assessments using the Urticaria Assessment Score (1 every 12 weeks) are required for extensions beyond 24 weeks.[13] Differences observed in Newfoundland and Labrador may also be due to the restriction to claims made to public drug programs only, which may have different criteria than private drug plans and out-of-pocket payments that are included in the analyses of other jurisdictions. Furthermore, differences in treatment duration may be influenced by physician prescribing practices, particularly in less populous provinces where a small number of physicians can strongly influence prescribing trends. Nevertheless, the high proportion of incident treatment episodes of omalizumab exceeding 24 weeks suggests that there is a demand for

longer treatment durations which could be influenced by suboptimal disease control at 24 weeks and/or a preference by prescribers to continue treatment among patients who have experienced disease remission with omalizumab treatment. Despite this, these findings suggest a clear need to understand the effectiveness and cost-effectiveness of longer-term omalizumab treatment for CIU in Canada.

Sensitivity analyses that varied with respect to the definition of treatment discontinuation identified some differences in the proportion of episodes identified as long-term episodes, suggesting that although omalizumab is indicated for use every 4 weeks for CIU, it appears to be dispensed less frequently for some patients. Reasons for this lower frequency of administration are unknown, but could include out-of-pocket costs, adverse events, barriers to access, attempts to taper treatment, attempts to maintain patients at the lowest effective dose of treatment, attempts to discontinue the drug followed by a return of symptoms, or a less frequent perceived need for treatment.

Characteristics of incident treatment episode recipients of omalizumab showed that the majority were between the ages of 25 and 64 years, were female, and were dispensed omalizumab at a pharmacy located in an urban area. These characteristics were generally similar among omalizumab recipients with a short-term and long-term duration of use, and are likely more reflective of the characteristics of individuals with CIU,[1] the urban or rural location of residence of the population more generally, and increased access to specialist care in urban settings. Other sociodemographic or clinical characteristics may differentiate short-term and long-term users of omalizumab for CIU. In particular, clinical characteristics including more severe disease,[18] concurrent angioedema,[19] and concurrent inducible urticaria[20] are known risk factors for longer duration of CIU. However, due to limitations in the availability of such data, additional characteristics could not be explored as factors related to longer treatment duration with omalizumab.

Methodological limitations of the analyses were discussed in the Methods section. However, the suppression of small cell values due to privacy restrictions is a notable limitation to the interpretation of the data. As a result, complete understanding of trends presented in this analysis may be somewhat obscured and findings should be interpreted with caution. In addition, the results of this analysis only included 4 Canadian provinces and may not necessarily be generalizable to other jurisdictions within Canada, where coverage of omalizumab for CIU may be different and which may have larger urban populations than 3 of the provinces included in this analysis (i.e., Manitoba, Saskatchewan, and Newfoundland and Labrador).[21]

Conclusion

The incidence of omalizumab treatment episodes for CIU has increased since it was first recommended for listing on drug plans for CIU. The majority of episodes of treatment in Manitoba, Saskatchewan, British Columbia, and Newfoundland and Labrador exceeded 24 weeks, with many episodes exceeding 48 weeks. Further evaluation of the effectiveness and cost-effectiveness of long-term omalizumab treatment as a maintenance therapy for CIU is required. There are no clear demographic (e.g., age, sex, or location of dispensation) factors differentiating short-term and long-term recipients of these treatment episodes that

were identified in this first analysis of this topic using real-world evidence; thus, future work examining additional demographic and clinical characteristics that were unavailable in the data may be warranted.

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Authors

Clinical Review

Tara Gomes assisted with study design and finalizing the data request, oversaw and contributed toward data interpretation and reporting, critically reviewed the report for content, and provided oversight for all Ontario Drug Policy Research Network (ODPRN) staff involved in the project.

Clare Cheng developed the analysis plan for the data request, interpreted results of the analyses, and drafted and revised all sections of the report.

Bisola Hamzat prepared and created figures and tables from data output for interpretation of study results, provided feedback, and revised drafts of the report.

Aaron M. Drucker helped refine methodology, interpreted results of the analysis, and provided critical revisions to the report.

Tony Antoniou complied with CADTH guidelines for reports; reviewed the report and revised drafts; and ensured clarity of messaging, accuracy, and completeness of the report.

Mina Tadrous developed the analysis plan, interpreted results, and provided review and revisions.

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This individual kindly provided comments on this report:

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Conflicts of Interest

Clare Cheng disclosed the following:
Past Employment:
- Canadian Institute for Health Information – Project Lead, Health System Analytics

Aaron M. Drucker disclosed the following:
Dr. Drucker has received compensation from the British Journal of Dermatology (reviewer and section editor), American Academy of Dermatology (guidelines writer), Canadian Dermatology Today (manuscript writer), and CADTH (consultant). Dr. Drucker has received research grants to his institution from the National Eczema Association, Eczema Society of Canada, Canadian Dermatology Foundation, Canadian Institutes for Health Research, US National Institutes of Health, and Physicians' Services Incorporated Foundation.

Mina Tadrous disclosed the following:
Consulting Fees: Health Canada – Drug Shortages

Payment as Advisor or Consultant:
- Green Shield Canada – Data Analytics

Karen Binkley disclosed the following:
Speaking Engagement and Educational Lecture:
- Takeda – Firazyr, Takzhyra

Other – Advisory Board Member:
- Takeda – Firazyr, Takzhyra
- Biocryst – Orladeo

Payment as Advisor or Consultant:
- Medexus – Rupall
- Speaker: Education lectures on angioedema and urticaria

No other conflicts of interest were declared.

Appendix 1: Additional Information

Table 8: Number and Rate of Incident Omalizumab Treatment Episodes for CIU, by Province (2014 to 2020)

Index year	Manitoba[a]			Saskatchewan			British Columbia			Newfoundland and Labrador
	Number of episodes	Population denominator	Rate per 100,000	Number of episodes	Population denominator	Rate per 100,000	Number of episodes	Population denominator	Rate per 100,000	Number of episodes
2014	NA	1,279,014	NA	< 5	1,112,979	NA	29	4,707,103	0.6	0
2015	NA	1,292,227	NA	7	1,120,967	0.6	92	4,776,388	1.9	0
2016	8	1,314,139	0.6	< 5	1,135,987	NA	92	4,859,250	1.9	0
2017	50	1,334,790	3.7	46	1,150,331	4.0	139	4,929,384	2.8	5
2018	43	1,352,825	3.2	53	1,161,767	4.6	142	5,010,476	2.8	10
2019	37	1,369,954	2.7	57	1,172,479	4.9	131	5,094,796	2.6	13
2020	33	1,379,888	2.4	34	1,178,467	2.9	122	5,155,495	2.4	10

CIU = chronic idiopathic urticaria; IQR = interquartile range, NA = not applicable, SD = standard deviation.

[a]Results for Manitoba represent data from 2016 to 2020 only.

Notes: Cell counts less than 5 were suppressed in accordance with the CIHI privacy policy. Population rates were not calculated; new treatment episodes of omalizumab included only those covered by public drug programs in Newfoundland and Labrador. Denominators for rates are obtained from Statistics Canada population estimates.

Note that this table has not been copy-edited.

For more information on CoLab and its work visit **colab.cadth.ca**

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About CADTH: CADTH is a not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs and medical devices in our health care system.

About CoLab: CoLab is a pan-Canadian network of experts in applied research, scientific methods, and data analysis. CoLab members work with CADTH's Post-Market Drug Evaluation Program to produce credible and timely evidence on post-market drug safety and effectiveness.