CoLab Network

CDA-AMC Canada's Drug Agency
L'Agence des médicaments du Canada

March 2025

Drugs Health Technologies Health Systems

Drug Utilization Study

Calcitonin Gene–Related Peptide Inhibitors for Migraine Prophylaxis

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This drug utilization study was conducted by the Alberta Drug and Therapeutic Evaluation Consortium (ADTEC), the CAnadian Network for Advanced Interdisciplinary Methods for comparative effectiveness research (CAN-AIM), and the Institut national d'excellence en santé et en services sociaux (INESSS) through the Post-Market Drug Evaluation (PMDE) CoLab Network.

Key Messages

Calcitonin gene–related peptide (CGRP) inhibitors for migraine prophylaxis (also known as migraine prevention) were first approved in 2018 in Canada for use in individuals whose condition did not respond to conventional migraine therapy.

Further evidence is needed to inform the optimal use of CGRP inhibitors. There is a lack of understanding around trends in use; treatment patterns, including switching from one CGRP inhibitor to another; and outcomes after switching.

This study analyzed data from 6 Canadian provinces and from the US to determine CGRP inhibitor treatment patterns and examine indirect markers of effectiveness (including the use of rescue medications) across subgroups, including those who switch from 1 CGRP inhibitor to another.

The findings indicate that CGRP inhibitor use has increased over time; in recent years, the newer CGRP inhibitors are most commonly dispensed for new and current users of CGRP inhibitors.

The trends suggest that CGRP inhibitor use may continue rising, with a preference for newer medications.

Approximately 5.4% of users of CGRP inhibitors switch to another CGRP inhibitor within a year; 9.3% switch to onabotulinumtoxinA, 12.0% switch to other preventive treatments, and 9.1% discontinue preventive medication within a year.

New users of CGRP inhibitors generally use fewer rescue medications and use health care services less often after starting treatment.

For those who switched to another CGRP inhibitor, the use of rescue medications and health care services was also generally lower in the year after switching.

This study did not find evidence to suggest that those who switched to an alternate CGRP inhibitor experienced lower treatment effectiveness.

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Abbreviations

CGRP	calcitonin gene–related peptide
CIMD	Canadian Index of Multiple Deprivation
ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical Modification
ICD-10-CA	International Classification of Diseases, 10th Revision, Canadian Enhancement
ICD-10-CM	International Classification of Diseases, 10th Revision, Clinical Modification
mAb	monoclonal antibodies
SAC	Statistical Area Classification

Introduction and Rationale

Background

Migraine is a common neurologic disorder characterized by recurrent headaches of moderate-to-severe intensity associated with other symptoms including dizziness and nausea. According to the 2019 Global Burden of Disease, migraine is the most disabling neurologic disorder[1,2] and the second most disabling of all disorders, affecting more than 1 billion people globally,[3] with an estimated prevalence of 8.3% to 10.2% and a cumulative incidence of 12.4% among people living in Canada.[4,5] Migraine is most prevalent in adults between the ages of 20 and 50 years and 3 to 4 times more frequent in women than men.[6] The manifestations of migraine are diverse but typically follow 4 phases: prodrome, aura (which may involve visual disturbances, sensory disturbances, and other neurologic symptoms), headache, and postdrome (marked by exhaustion or confusion), though not all migraine sufferers experience each phase.[7,8] The most common types of migraine are migraine with aura or migraine without aura,[7,8] whereas other less common types include abdominal migraine, hemiplegic migraine, menstrual migraine, retinal migraine, and status migrainosus (a severe migraine with disabling pain and nausea that persists beyond 72 hours).[7,8] If an individual experiences less than 15 headache days per month, this is classified as episodic migraine; chronic migraine is defined as 15 headache days or more per month for longer than 3 months, 8 or more of which have the features of a migraine headache.[9]

The pathophysiology of migraine involves a complex interplay between neuronal and vascular factors, prominently involving the trigeminovascular system.[8] Calcitonin gene–related peptide (CGRP) has been identified as a key neuropeptide in migraine pain signalling;[10] CGRP-mediated neuronal sensitization and glutamate-based signalling contribute to migraine pain.[11] Activation of certain serotonergic receptor subtypes that inhibit CGRP release provides migraine relief; blocking CGRP action is a central target to aborting or preventing migraine.[10,12]

Drug therapy for migraine is divided into rescue medications aimed at stopping migraine development and/or relieving symptoms, and prophylactic treatments aimed at preventing future attacks.[7,8] Rescue medications are taken as soon as migraine symptoms begin, while prophylactic medications are taken regularly to reduce the frequency and severity of future attacks.[7,8] These treatments include both migraine-specific and nonspecific pharmacotherapies. Migraine-specific rescue medications may include CGRP receptor antagonists such as ubrogepant (approved for oral use and Canadian market entry on April 4, 2023, and US market entry on December 23, 2019), zavegepant (not yet approved in Canada; approved in the US on May 10, 2023, for nasal spray), or rimegepant (recently approved in Canada; approved in the US in February 2020 for oral use); ergot derivative drugs (interacting with affinities for serotonin 5-HT, and dopamine and noradrenalin receptors); triptan drugs (targeting serotonin 5-HT1B/1D receptors); and ditans, a newer class of rescue medications specifically targeting the serotonin 5-HT1F receptor (available in the US since 2019 [lasmiditan]; not yet approved in Canada).[13-16] Nonspecific rescue medications include nonprescription and prescription analgesics, combination analgesics, nonsteroidal anti-inflammatory drugs, nausea relief drugs, and narcotics.[17]

Prophylactic migraine pharmacotherapies primarily include off-label use of several drug classes including anticonvulsants, beta-blockers, calcium channel blockers, and antidepressants.[18,19] OnabotulinumtoxinA (Botox) is an injectable pharmacotherapy (available since 2010 and administered by a trained health care provider) indicated for the prevention of chronic migraine through multiple mechanisms, primarily acting on cranial sensory neurons to inhibit nociception transmission by reducing the release of neurotransmitters like CGRP, substance P, and glutamate.[8,19,20] More recently introduced pharmacological migraine prophylaxis includes 2 classes of CGRP inhibitors: monoclonal antibodies (mAbs) targeting CGRP or the CGRP receptor (CGRP mAbs), and CGRP receptor antagonists. The place in therapy of CGRP inhibitors has traditionally been after an individual has experienced inadequate response, intolerance, or contraindication to 2 or more conventional oral migraine prophylactic drugs.[19] However, recent position statements by the American Headache Society and guidelines by the Canadian Headache Society indicate that these therapies should be considered first-line, especially in patients with moderate-to-severe levels of disability.[21,22] Three subcutaneous injection mAb CGRP inhibitors are currently approved (erenumab [Aimovig] [December 4, 2018, and May 17, 2018, market dates in Canada and the US, respectively], galcanezumab [Emgality] [October 2019 and September 2018 market dates in Canada and the US, respectively], and fremanezumab [Ajovy] [August 2020 and September 2018 market dates in Canada and the US, respectively]), along with 1 IV injection (eptinezumab [Vyepti] [August 2022 and February 2020 market dates in Canada and the US, respectively]). CGRP receptor antagonists (gepants) include 2 oral drugs: atogepant [Qulipta] [February 2023 and September 2021 market dates in Canada and the US, respectively] and rimegepant [Nurtec] [May 2021 market date in the US and not approved in Canada currently for prevention of migraine],[14,16] which have a fast onset of action, convenient dosing, and mild to moderate side effects.[19] Of note, atogepant (Qulipta) was not reimbursed in any Canadian jurisdiction until early 2023. For all CGRP inhibitors, coverage varies across commercial health plans in the US.

Main Take-Aways

CGRP inhibitors are a class of drugs used for migraine prevention, typically prescribed after an individual's condition has not responded to 2 or more conventional therapies. If an individual's migraine does not respond well to the first CGRP inhibitor, there is not enough evidence to confirm if switching to a different CGRP inhibitor will provide benefit. If benefit is unlikely, switching may result in unnecessary exposure of individuals to migraine medications, delays in effective treatment or care, and suboptimal medication use. More evidence is needed to inform policies guiding the use of CGRP inhibitors for migraine prevention in individuals who have previously tried a CGRP inhibitor.

Purpose of this Report

Use of CGRP inhibitors was quantified, and treatment patterns between 2018 and 2023 were described, including switching to a subsequent CGRP inhibitor, switching to other migraine preventive medication, and discontinuing treatment. Surrogate markers of migraine symptoms, including use of rescue medications and health care utilization, were determined in subgroups defined by patterns of CGRP inhibitor use. This

report provides preliminary evidence that may inform policies on the use of CGRP inhibitors for migraine prophylaxis.

Policy Issue

While CGRP inhibitors are often effective, their use over time and patterns of use, including switching between different CGRP inhibitors, is not clear. Further, it is not known if switching improves outcomes in individuals experiencing intolerance or suboptimal response to their initial CGRP inhibitor; while some evidence suggests it may, it is not conclusive. Public drug plan reimbursement criteria for CGRP inhibitors have no stipulation regarding prior use of drugs of the same class; switching between CGRP inhibitors is therefore covered by many insurance plans. More data are needed to further inform policies guiding the use of CGRP inhibitors for migraine prophylaxis for individuals who have trialled a previous CGRP inhibitor.

Policy Question

Should CGRP inhibitors be reimbursed upon lack or loss of response to a previous CGRP inhibitor for migraine prophylaxis?

Research Questions

1. What are the treatment patterns of individuals using CGRP inhibitors for migraine prophylaxis between the years 2018 and 2023?
2. How frequently are rescue medications used among individuals treated with CGRP inhibitors for migraine?

Objectives

Research Objectives

The specific objectives of the study are to:

1. describe trends in the overall utilization of CGRP inhibitors for migraine prophylaxis between the years 2018 and 2023 by estimating the annual incidence and prevalence of CGRP inhibitor use between 2018 and 2023 (number and rate) overall, categorized by CGRP inhibitor product, and stratified by age and sex
2. describe the treatment patterns of CGRP inhibitors for migraine prophylaxis between the years 2018 and 2023 by estimating:
    a) fixed follow-up durations: over 1, 2, 3, and 4 years after initial CGRP inhibitor initiation
    b) time from CGRP inhibitor initiation to first treatment break, and probability of a treatment break at a particular interval (e.g., 1 year, 2 years)

   c) time from CGRP inhibitor initiation to switching (to another CGRP inhibitor and to another prophylactic medication) and probability of switching at a particular interval

3. describe the characteristics of users of CGRP inhibitors, health care utilization, and rescue medication use across CGRP inhibitor users, switchers, and discontinuers subgroups, using the following indicators:
   a) sociodemographic characteristics: age, sex, location of residence, and socioeconomic status
   b) overall chronic health burden (Charlson Comorbidity Index) and comorbid conditions
   c) rescue medication use
   d) migraine-related health care utilization.

Methods

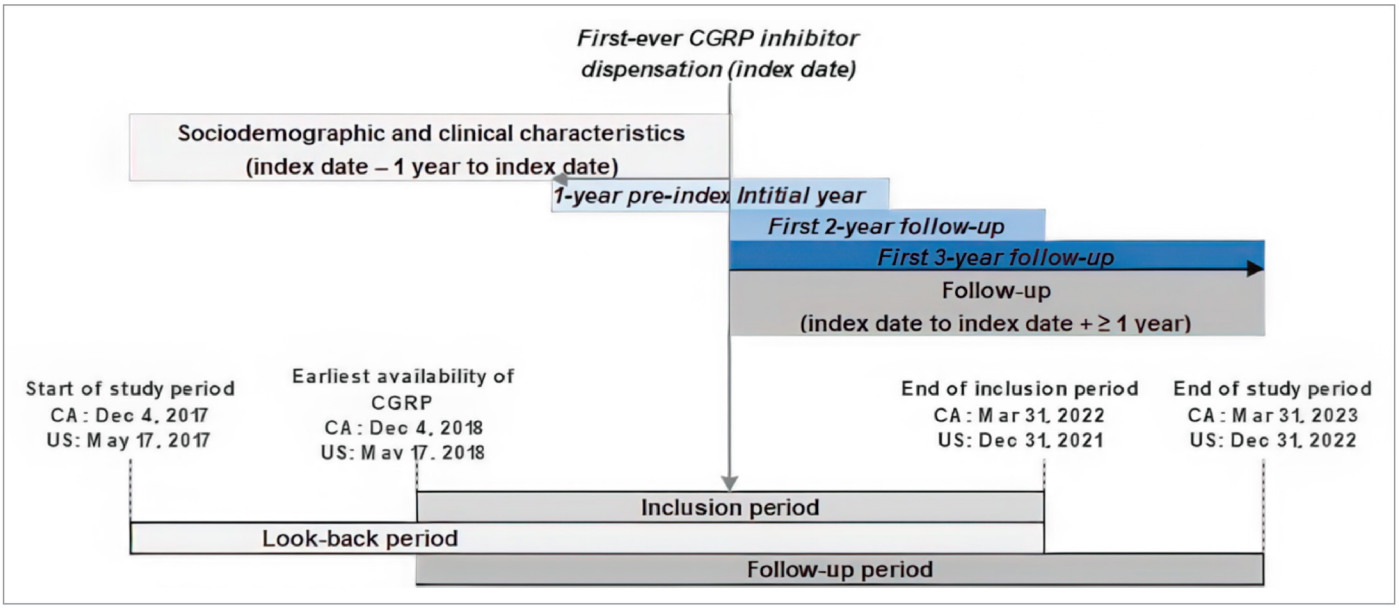
Population and Setting

We examined all individuals aged 18 years and older who received a dispensation for a CGRP inhibitor from 2018 to 2023. Populations were identified using administrative records for community drug dispensations in Alberta, British Columbia, Manitoba, Nova Scotia, Quebec, and Saskatchewan. US CGRP inhibitor recipients were identified using the MarketScan Prescription Database, which contains administrative claims for individuals covered by US commercial, Medicare Supplemental, and Medicaid insurance plans. Dispensations were identified based on anatomic therapeutic chemical code or Drug Identification Number from community pharmacies.

Study Design

We used a descriptive cohort design. The overall study period was from 2017 to 2023, which comprised the inclusion period (December 4, 2018, or May 17, 2018 [the earliest availability of the CGRP inhibitor product in the Canadian or US market, respectively], to March 31, 2023, or December 31, 2022, for Canadian provinces or the US, respectively), and a 1-year look-back period as far back as December 4, 2017 (Canada), or May 17, 2017 (US), for the assessment of characteristics. The index (i.e., cohort entry) date was defined as the earliest dispensation date of a CGRP inhibitor medication (incident or first-ever). The follow-up period was determined as the interval from the index date until the end of provincial health care coverage and/or insurance plan (e.g., relocation out of province, no longer enrolled in an insurance plan, or death) or until the end of data availability (March 31, 2023, for Canada, and December 31, 2022, for the US), whichever occurred first. A schematic representation of the study is outlined in Figure 1.

Figure 1: Study Time Frame for the Base Cohort of Users of CGRP Inhibitors Between 2018 and 2022 (Objective 2)



CA = Canada; CGRP = calcitonin gene–related peptide; Dec = December; Mar = March.

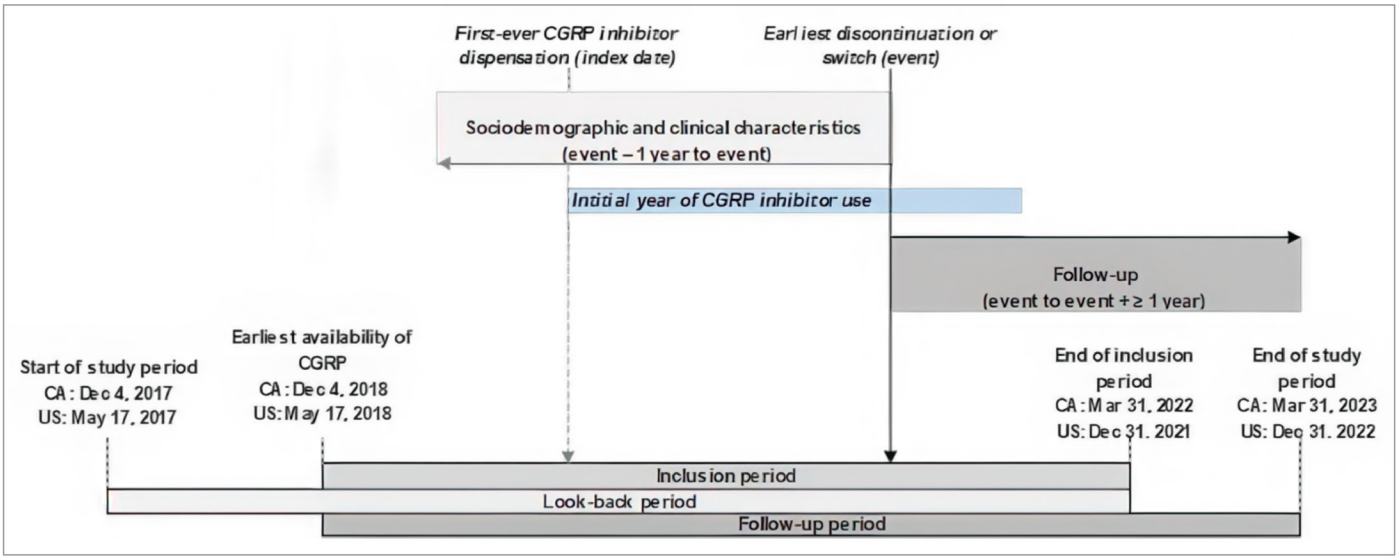
The cohort included adult (aged 18 years or older) residents (with provincial health care coverage and/or health insurance plan) who received 1 or more CGRP inhibitor medication dispensations between December 4, 2018, and March 31, 2023, for Canada, or between May 17, 2018, and December 31, 2022, for the US. Specific eligibility criteria and CGRP inhibitor subgroups are defined in Table 1. Users of CGRP inhibitors are new users with more than a 1-year preindex and postindex date observation. Mutually exclusive subgroups of people who were switchers of CGRP inhibitors and those who were discontinuers of CGRP inhibitors were also defined and included users of CGRP inhibitors who received 1 or more CGRP inhibitor dispensation between December 4, 2018, and March 31, 2022, for Canada data, or between May 17, 2018, and December 31, 2021, for US data, and subsequently discontinued their CGRP inhibitor or switched to another CGRP inhibitor within the first year of initiating CGRP inhibitor treatment, without resuming the initial CGRP inhibitor within the first year of discontinuation or switch. The index date for these subgroups was adjusted to the date of the first dispensation of the second CGRP inhibitor or discontinuation (refer to Figure 2). The follow-up period was determined from the switching date or discontinuation date until the end of provincial health care coverage and/or insurance plan (e.g., relocation out of province, no longer enrolled in an insurance plan, or death) or until the end of data availability (March 31, 2023, for Canada and December 31, 2022, for the US), whichever came first. Additional restrictions on the study cohort were added for specific subanalyses to ensure that all included individuals had sufficient follow-up time.

Table 1: CGRP Inhibitor Subgroup Definitions

Objective	Inclusion criteria
Objective 1	Received ≥ 1 outpatient pharmacy dispensation or infusion procedure record of CGRP inhibitor medication during the period between December 4, 2018, and March 31, 2023, for Canada, or between May 17, 2018, and December 31, 2022, for the US AND was aged 18 years or older at the index date
Objective 2	Received ≥ 1 outpatient pharmacy dispensation or infusion procedure record of CGRP inhibitor medication during the period between December 4, 2018, and March 31, 2022, for Canada, or between May 17, 2018, and December 31, 2021, for the US AND was aged 18 years or older at the index date AND had provincial health care coverage and/or health insurance plan ≥ 1 year after the index date
Objective 3	Received ≥ 1 outpatient pharmacy dispensation or infusion procedure record of CGRP inhibitor medication during the period between December 4, 2018, and March 31, 2022, for Canada, or between May 17, 2018, and December 31, 2021, for the US AND was aged 18 years or older at the index date AND had provincial health care coverage and/or health insurance plan for ≥ 1 year before the index date and ≥ 1 year after the index date
Objective 3 cohorts	
CGRP inhibitor user cohort	Any individual who met criteria for Objective 3 • the index date was the date of dispensation of the first CGRP inhibitor
CGRP inhibitor switcher subcohort	Any individual who met criteria for Objective 3 AND • switched to a second CGRP inhibitor within the first year of treatment without resuming the original CGRP within 1 year of the date of switching • had data for both the 1-year preindex and 1-year postindex periods • the index date was the date of switching to their second CGRP inhibitor. This group is a subset of the CGRP inhibitor user group just defined.
CGRP inhibitor discontinuer subcohort	Any individual who met criteria for Objective 3 AND • discontinued their initial CGRP inhibitor within the first year of treatment without resuming the original CGRP within 1 year of the date of discontinuation • had data for both the 1-year preindex and 1-year postindex periods • the index date was the date of discontinuation. This group is a subset of the CGRP inhibitor user group just defined. Individuals who switch to other prophylactic medication are included in this group.

CGRP = calcitonin gene–related peptide.

Figure 2: Study Time Frame for the CGRP Inhibitor Discontinuer and Switcher Subcohorts (Objective 3)



CA = Canada; CGRP = calcitonin gene–related peptide; Dec = December; Mar = March.

Data Sources

Health administrative and billing databases from Canadian provinces and the US were used.

Canada

Provincial registry data containing demographic information and health plan coverage were used to identify whether individuals had provincial health coverage during their follow-up period, and to determine their location of residence, dates of migration in and out of the province, and vital status. Each individual is assigned a unique person-level identifier (Personal Health Number), which was used to link across datasets. Community pharmacy–dispensed prescription drug data from Canadian provinces was used: Alberta, British Columbia, Manitoba, Nova Scotia, and Saskatchewan datasets contained full population-level data; Quebec data were restricted to dispensation data from the Régie de l'assurance maladie du Québec (contains data for approximately 46% of the population of the province). These databases contain all prescription medication dispensations from outpatient community pharmacies, regardless of payer. Data included the Drug Identification Number, dispensing date, unique patient identifiers such as a provincial health insurance number, age and sex on dispensing date, dose dispensed, and days' supply or local equivalent. Inpatient hospital discharge, ambulatory care (Alberta only), and physician claims data were used to determine overall health burden, comorbidities, and migraine-related health care encounters. Statistics Canada census data (publicly available) were used for population denominators overall by jurisdiction and by age and/or sex.

United States

Prescription, in-hospital, and ambulatorial data from MarketScan, Commercial Claims, and Medicare databases were used. The prescription database (Outpatient Pharmaceutical Claims Table [D]) contained

administrative claims for individuals covered by US commercial, Medicare Supplemental, and Medicaid insurance plans. Data includes the National Drug Code and generic identifiers of the drug dispensed; encrypted unique patient identifiers; and dispensing date, quantity, and number of days' supply. Inpatient (Inpatient Services Table [S]; Inpatient Admissions Table [I]) and outpatient (Outpatient Services Table [O]) databases contain medical claims for procedures and visits; diagnosis information can be obtained using International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM), Current Procedural Terminology (CPT), or Healthcare Common Procedure Coding System (HCPCS). Enrolment tables (A, T) were used to define insured individuals (enrollees). Location of residence and vital status (death) were not available. MarketScan enrollee numbers were used for population denominators.

Key Study Measures

Exposure(s)

The exposures of interest were the receipt of 1 or more CGRP inhibitors, listed in Table 2, during the inclusion period. Users of incident CGRP inhibitors were defined as individuals who received their first-ever dispensation of a CGRP inhibitor within a given year, with no prior CGRP inhibitor dispensations. Users of prevalent CGRP inhibitors were defined as individuals who had 1 or more dispensations of a CGRP inhibitor within the specific year of interest and included both new and continuing users.

Table 2: Approved Indications for Available CGRP Inhibitors for Migraine Prophylaxis

Medication	Indication (approved)	Recommended dose	Earliest market date in Canada	Earliest market date in the US
mAb CGRP				
Erenumab (Aimovig)	Prevention of migraine in adults who have at least 4 migraine days per month	70 mg or 140 mg SC injection once monthly	December 4, 2018	May 22, 2018
Galcanezumab (Emgality)	Prevention of migraine in adults who have at least 4 migraine days per month	Initial (loading) dose of 240 mg (administered as 2 consecutive SC injections of 120 mg) followed by once monthly doses of 120 mg (1 injection)	October 2, 2019	September 27, 2018
Fremanezumab (Ajovy)	Prevention of migraine in adults who have at least 4 migraine days per month	225 mg (1 injection) once monthly or 675 mg (3 separate SC injections of 225 mg one after another) every 3 months	August 4, 2020	September 15, 2018
Eptinezumab (Vyepti)	Prevention of migraine in adults who have at least 4 migraine days per month	100 mg by IV infusion every 3 months Can be increased to 300 mg per infusion if needed	August 17, 2022	February 21, 2020
CGRP receptor antagonist (gepants)				
Atogepant (Qulipta)	Prevention of migraine in adults who have at	10 mg, 30 mg, or 60 mg orally once daily	February 23, 2023	September 30, 2021

Medication	Indication (approved)	Recommended dose	Earliest market date in Canada	Earliest market date in the US
	least 4 migraine days per month			
Rimegepant (Nurtec ODT)	Prevention of episodic migraine in adults	75 mg orally once daily, up to 18 doses per month	March 25, 2024[a]	May 27, 2021

CGRP = calcitonin gene–related peptide; mAb = monoclonal antibody; SC = subcutaneous.

[a]In Canada, rimegepant is only approved for the acute treatment of migraine.

Source: Health Canada Drug Product Database and FDA drug approval document.

Outcomes of Interest

The treatment patterns of users of incident CGRP inhibitors over time were examined using fixed and nonfixed follow-up durations.

1. Fixed follow-up durations:

   The following outcomes were described over the first year of CGRP inhibitor use (incident or first-ever) as well as within the 2-, 3-, and 4-year durations following CGRP inhibitor initiation.

   a) **Non-use of any prophylactic medication** was defined as discontinuation of all prophylactic medication. Any switching or resuming prophylactic treatment would exclude inclusion in this group and merit inclusion in 1 of the following groups.

   b) **Switching from an initial to a subsequent CGRP inhibitor** was defined as a change in CGRP inhibitor medication from the initial (first-ever) CGRP inhibitor to another CGRP inhibitor medication. The switching date was defined as the first dispensing date of the switched-to CGRP inhibitor medication.

   c) **Switching from a CGRP inhibitor to another migraine prophylactic treatment** was defined as a change from a CGRP inhibitor to another prophylactic medication. The switching date was defined as the first dispensing date of the switched-to prophylactic medication.

   d) **Concomitant CGRP inhibitor treatment with other migraine prophylactic treatments** was defined as using another prophylactic medication at the same time as a CGRP inhibitor (including using a second CGRP inhibitor).

   e) **Treatment break** was defined as 120 or more consecutive days without any CGRP inhibitor medications or other migraine prophylactic treatment since the last dispensation end date, followed by the resumption of previously dispensed CGRP inhibitor medications.

The decision method used for classification into these groups is more thoroughly described in Appendix 1, Table 18 and Figure 8.

1. Nonfixed follow-up durations:

   a) Time from CGRP inhibitor initiation to first treatment break or CGRP inhibitor resumption, discontinuation, or first switch (in days per month)

b) Probability of a treatment break or CGRP inhibitor resumption, discontinuation, or first switching at a particular interval (i.e., 1 year, 2 years)

Migraine-related medication use was derived from dispensations of migraine-related medications (both migraine-specific and nonspecific) among users of CGRP inhibitors during the 1-year preindex and 1-year postindex periods based on their first dispensation, and reported as totals, categorized by treatment type (rescue and prophylactic medications), and further subdivided by class. Results for the switcher and discontinuer subcohorts were also derived using the date of switching or the date of discontinuation as the index date when determining the 1-year preindex and postindex periods. Detailed medication classifications are provided in Table 3. Further information regarding these medications can be found in Appendix 1, Table 14.

Migraine-related health care encounters were measured during the 1-year preindex and postindex observation periods (note that the index date varies by subgroup). In Canadian provinces, these encounters were identified using the International Classification of Diseases, 10th Revision, Canadian Enhancement (ICD-10-CA) G43 code in the most responsible diagnosis field for inpatient hospitalizations and ambulatory care visits, and the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) 346 code in any diagnostic field for physician visits. For US data, encounters were identified using the ICD-10-CM G43 code in the main diagnosis field for inpatient claims and in any diagnosis field for outpatient claims.

Table 3: Prescription Migraine Rescue and Prophylactic Medication Classification

Class	Migraine-specific	Approved use	Example drugs	Earliest market date in Canada	Earliest market date in the US
Rescue medications					
Migraine nonspecific					
NSAID	No	Rescue	Diclofenac Ketorolac	NR	NR
Opioids	No	Rescue	Tylenol 3 Tramacet	NR	NR
Migraine-specific					
Triptans	Yes	Rescue	Sumatriptan Zolmitriptan	NR	NR
Ergots	Yes	Rescue	Dihydroergotamine	NR	NR
Gepants (CGRP receptor antagonists)	Yes	Rescue	Ubrogepant (oral use) Rimegepant (oral use) Zavegepant (nasal spray)	April 4, 2023 March 25, 2024 Not yet available	December 23, 2019 March 05, 2020 June 01, 2023
Ditans	Yes	Rescue	Lasmiditan (oral use)	Not yet available	October 11, 2019
Other prophylactic medications					
Antidepressants	No	Preventive	Amitriptyline	NR	NR

Class	Migraine-specific	Approved use	Example drugs	Earliest market date in Canada	Earliest market date in the US
Antiepileptics	No	Preventive	Topiramate	NR	NR
Antihypertensives	No	Preventive	Propranolol	NR	NR
Serotonin and tryptamine antagonist	Yes[a]	Preventive	Pizotifen	1980	1980
OnabotulinumtoxinA (for CM)	Yes	Preventive	Botox	2012	2010

CGRP = calcitonin gene–related peptide; CM = chronic migraine; NR = not reported; NSAID = nonsteroidal anti-inflammatory drug.

Note: Over-the-counter medications are not captured in dispensation records and are not reported.

[a]Although there are other uses for this medication, we assumed that its use among those who have also received a CGRP inhibitor is as a preventive migraine medication.

Population characteristics included sociodemographic and clinical factors. Demographic characteristics included age, sex, and region of residence (urban or rural) on the index date. The region of residence was identified as urban or rural based on the second postal code digit (0 for rural residence) in Alberta, the Statistical Area Classification (SAC) type from the Postal Code Conversion File Plus Version 8A for other Canadian provinces (SAC types 1 to 3 as urban and SAC types 4 to 8 as rural),[23] or as described by Creedon and colleagues for US data.[24] In the US, the Metropolitan Statistical Area variable was used to classify urban and rural areas. For the Canada analysis, socioeconomic status was determined by the Canadian Index of Multiple Deprivation (CIMD)[25] derived from the 2021 Canadian Census of Population at the dissemination area level, which was linked to postal codes and presented based on quintiles. The CIMD includes 4 dimensions of deprivation: residential instability, economic dependency, ethnocultural composition, and situational vulnerability. The burden of co-occurring health conditions was assessed by a longitudinal Charlson Comorbidity Index score based on ICD-10-CA or ICD-10-CM and ICD-9-CM codes of 17 different specific medical conditions weighted according to their potential for influencing mortality measured during the 1-year look-back period using inpatient hospital and physician claims data (details listed in Appendix 1). Specific comorbid conditions associated with migraine (anxiety, asthma, cardiovascular disease, depression, epilepsy, hypertension, and obstructive sleep apnea) were determined over the 1-year look-back period.

Analyses

The annual incidence and prevalence (numbers and rates) of CGRP inhibitor use from 2018 to 2023 were determined and reported by fiscal or calendar year. For the Canadian analysis, annual rates per 100,000 persons were calculated using population estimates from Statistics Canada for denominators. In the US analysis, annual rates per 100,000 insured individuals (enrollees) were used as denominators; the US analysis is therefore not population-based. Incidence and prevalence numbers and rates were stratified by age and sex, with age-specific and sex-specific rates per 100,000 people calculated based on annual population estimates for these strata in Canada, or per 100,000 enrollees for these strata in the US. Age- and sex-adjusted rates (i.e., direct standardization) were also calculated using the annual Canadian or US population by age and sex from Statistics Canada or the MarketScan 2018 population as the standard population structure. Incidence and prevalence numbers were categorized by CGRP inhibitor product (erenumab, galcanezumab, fremanezumab, eptinezumab, atogepant, rimegepant), and proportions for

each product were calculated for the total users of incident and prevalent CGRP inhibitors for each fiscal or calendar year from 2018 to 2022.

Treatment patterns were determined, including the number and proportions of switching, concomitant use, treatment breaks, and discontinuation for the initial year of CGRP inhibitor use as well as within the 2-, 3-, and 4-year periods of observation after incident CGRP inhibitor use. The denominators were adjusted based on the number of participants observable over time. For instance, participants who initiated CGRP inhibitors on April 1, 2020, had their follow-up periods include the initial year (April 1, 2020, to March 31, 2021), the 2-year period (April 1, 2020, to March 31, 2022), and the 3-year period (April 1, 2020, to March 31, 2023), provided they maintained health coverage and/or insurance plans throughout these periods. Kaplan-Meier estimators were used to account for different follow-up durations, with follow-up starting from CGRP inhibitor initiation and ending upon the occurrence of an event (first treatment break, discontinuation, or first switch), loss to follow-up (relocation out of the province or death), or the end of the study period, whichever occurred first. Mean (standard error) and median time from CGRP inhibitor initiation and probability at a particular interval (95% confidence interval) were reported for the first treatment break, discontinuation, and the first switch. Treatment patterns were depicted using Sankey and tree diagrams.

Frequencies of other treatments (prophylactic and rescue), sociodemographics, and clinical characteristics were determined. Characteristics, including rescue medication use, were reported among all users of CGRP inhibitors within 1 year of the (first-ever) index date between December 4, 2018, and March 31, 2022, for Canada, or between May 17, 2018, and December 31, 2021, for the US. Subcohorts (switcher and discontinuer) were also described anchored on the date of the switch or discontinuation, if sample sizes allowed. Descriptive statistics for migraine-related medication dispensations described overall migraine-related medication use. This included the frequency and proportion of users of CGRP inhibitors with at least 1 dispensation of any migraine-related medication (including both prophylactic and rescue medications) during the 1-year preindex period and those with at least 1 dispensation of rescue medication or a prophylactic, specifically, during the same period. The analysis also included the average number of days of supply and the number of rescue medication classes dispensed (categorized into NSAIDs, opioids, triptans, ergots, and ditans), and migraine-related prophylactic medications (categorized into antidepressants, antiepileptics, antihypertensives, and onabotulinumtoxinA). The use of these medications was also reported in the 1-year postindex period. The number and proportion of participants who used rescue medications while actively receiving a CGRP inhibitor were reported for within the 1-year preindex and postindex periods (i.e., excluding periods within the 1-year time frame when individuals had not been dispensed a CGRP inhibitor). Sociodemographic characteristics, such as age (mean, median, and category: 18 to 44 years, 45 to 64 years, 65 years and older), sex (female and male), location of residence (rural and urban), and the CIMD (1 to 5, for Canada only), were reported in counts and percentages. Clinical characteristics included the Charlson Comorbidity Index score, reported in means, standard deviations, medians, and min-max, and categorized by comorbidity level. Counts and percentages of participants with each comorbid condition were calculated. Means, standard deviations, medians, and first and third quartiles for the number of migraine-related health care encounters, and counts and percentages for participants with at least 1 migraine-related health care encounter (including physician visits, outpatient or ambulatory visit, emergency department visits,

and inpatient admissions) were reported for the 1-year preindex and 1-year postindex periods. Data for the Canadian provinces required censoring of small frequency cells and suppressing of other cells that could be used to recalculate a censored cell. Values between 1 and 4 were censored for Nova Scotia, Quebec, Manitoba, Saskatchewan, and British Columbia. Values between 1 and 9 were censored in the results using Alberta data. In some instances, a range of possibility may have been presented for these censored and suppressed values. When aggregating results across provinces, values of censored counts were assumed to be 5 for Alberta and 3 for the other Canadian provinces. Suppressed cells had their values adjusted to match these values for the censored results.

Some results were aggregated across the provinces and presented in tables and figures within the main body of the report or in Appendix 2. Data were analyzed separately for each province and for the US. Tables with the region-specific results are located in Appendix 3.

Results

Main Take-Aways

The use of CGRP inhibitors is increasing over time in Canada and the US, among both new and current users of these treatments. There is a trend for greater use of recently introduced CGRP inhibitors over time, among both new and current users.

Findings estimate that 5.4% of new users switch to an alternate CGRP inhibitor within the first year of use and 33% switch within 4 years. Individuals are more likely to switch to either onabotulinumtoxinA or other nonspecific preventive medications than another CGRP inhibitor within 1 year, with rates of 9.3% and 12.0%, respectively.

Among new users of CGRP inhibitors, the need for rescue medication and the use of health care resources for migraines were generally lower in the first year after starting treatment. For those who switched to another CGRP inhibitor, the use of rescue medications and health care resources for migraines was also generally lower in the year after the switch.

Population Characteristics

A total of 12,851 users of incident CGRP were identified in 6 Canadian provinces (US: 148,100) (Table 4). The most common age group at initiation of a CGRP inhibitor was 18 to 44 years (Canada: 45.6%; US: 52.7%), and females comprised the majority (Canada: 82.4%; US: 85.9%) (Table 4). Demographic characteristics of users of incident CGRP inhibitors, presented annually, are shown in Appendix 3, Tables 17 to 23.

Table 4: Demographic Characteristics of Adults Who Initiated a CGRP Inhibitor

Canada						US	
Region	N	%	Demographic group	N = 12,851	100%	N = 148,100	100%
Canada	12,851[a]	100.0%	Aged 18 to 44 years	5,854	45.6%	78,047	52.7%
AB	5,123	39.9%	Aged 45 to 64 years	5,723	44.5%	66,525	44.9%
BC	3,725	29.0%	Aged 65 years or older	1,274	9.9%	3,528	2.4%
MB	1,055	8.2%	Female	10,561	82.4%	127,165	85.9%
NS	714	5.6%	Male	2,261	17.6%	20,935	14.1%
QC	1,513 to 1,516[a]	11.8%	—	—	—	—	—
SK	719	5.6%	—	—	—	—	—

AB = Alberta; BC = British Columbia; CGRP = calcitonin gene–related peptide; MB = Manitoba; NS = Nova Scotia; QC = Quebec; SK = Saskatchewan.

[a]Quebec's total N required suppressing to prevent the calculation of censored cells. A value of 1,515 was used for the calculation of total N and %.

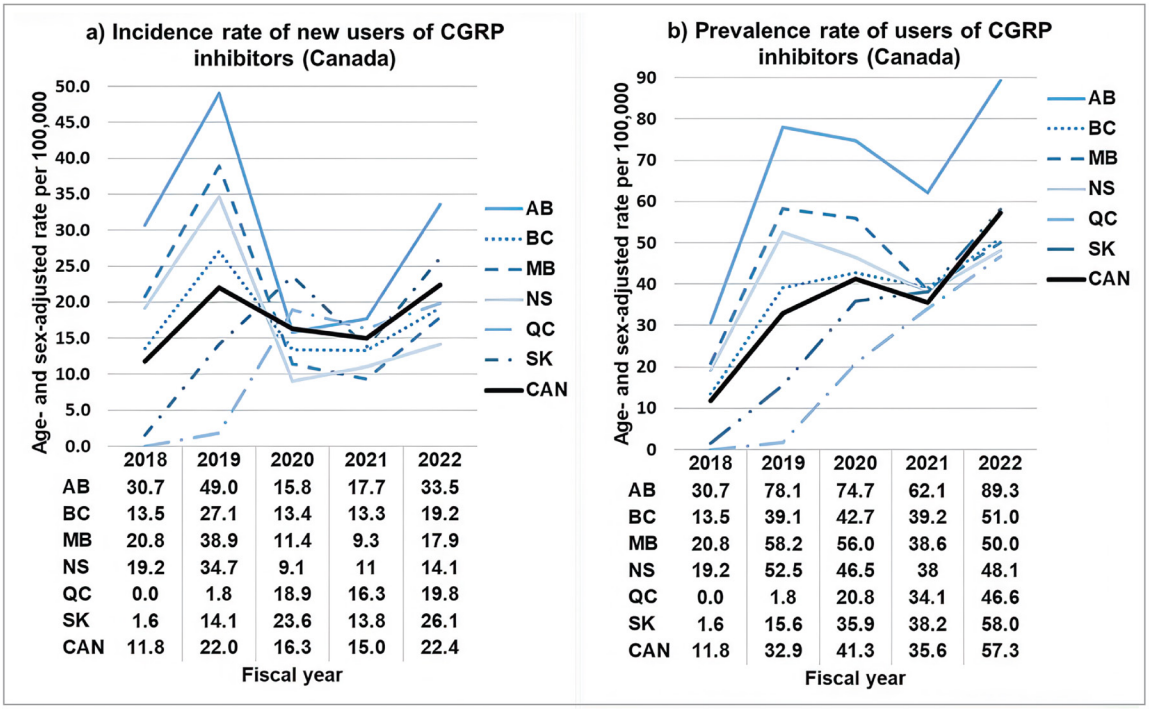
Main Findings

Incident and Prevalent CGRP Inhibitor Dispensation Over Time

In the 6 included Canadian provinces (henceforth shortened to "Canada"), the annual rate of users of incident CGRP inhibitors is shown in Figure 3a the annual rate of prevalent CGRP inhibitor in Figure 3b.

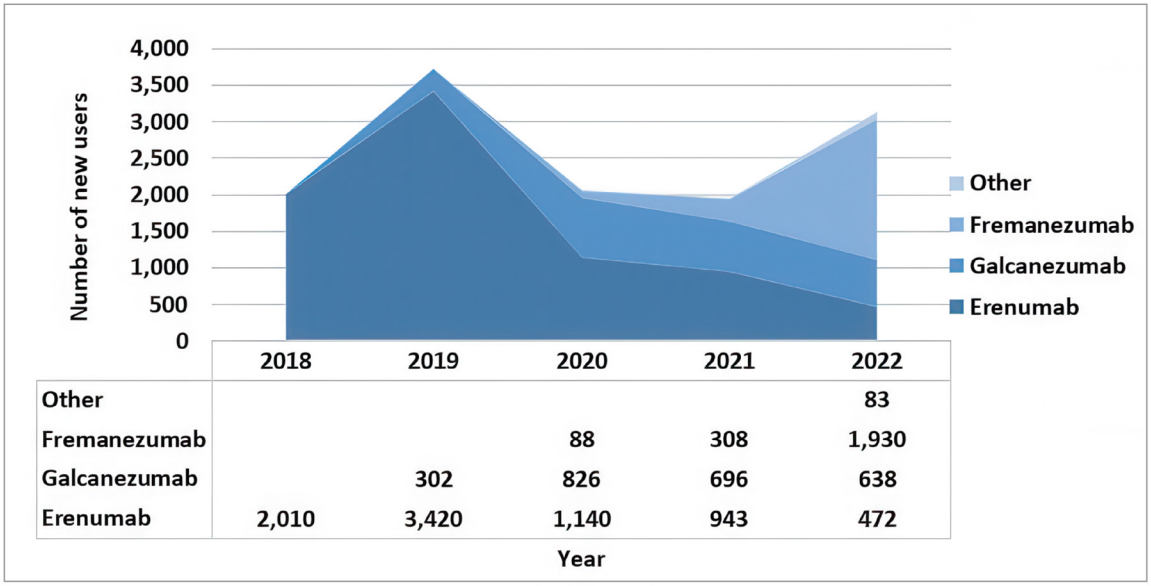
The CGRP inhibitor that was initiated by most users of incident CGRP inhibitors changed over time (Canada: Figure 4; US: Figure 5). As new drugs became available, the proportion receiving erenumab as the first CGRP inhibitor decreased; by the last year of observation, fremanezumab was the most common drug prescribed to users of incident CGRP inhibitors in Canada. Similarly, in the most recent time period in the US, rimegepant and galcanezumab were the most common.

Figure 3: Annual Incidence and Prevalence of Users of CGRP Inhibitors in Canada



AB = Alberta; BC = British Columbia; CAN = Canada; CGRP = calcitonin gene–related peptide; MB = Manitoba; NS = Nova Scotia; QC = Quebec; SK = Saskatchewan.

Figure 4: Annual Users of Incident CGRP Inhibitors, Presented by Drug, Canada



CGRP = calcitonin gene–related peptide.

Table 5: Annual Prevalence of Users of CGRP Inhibitors Presented by Drug Type, Canada

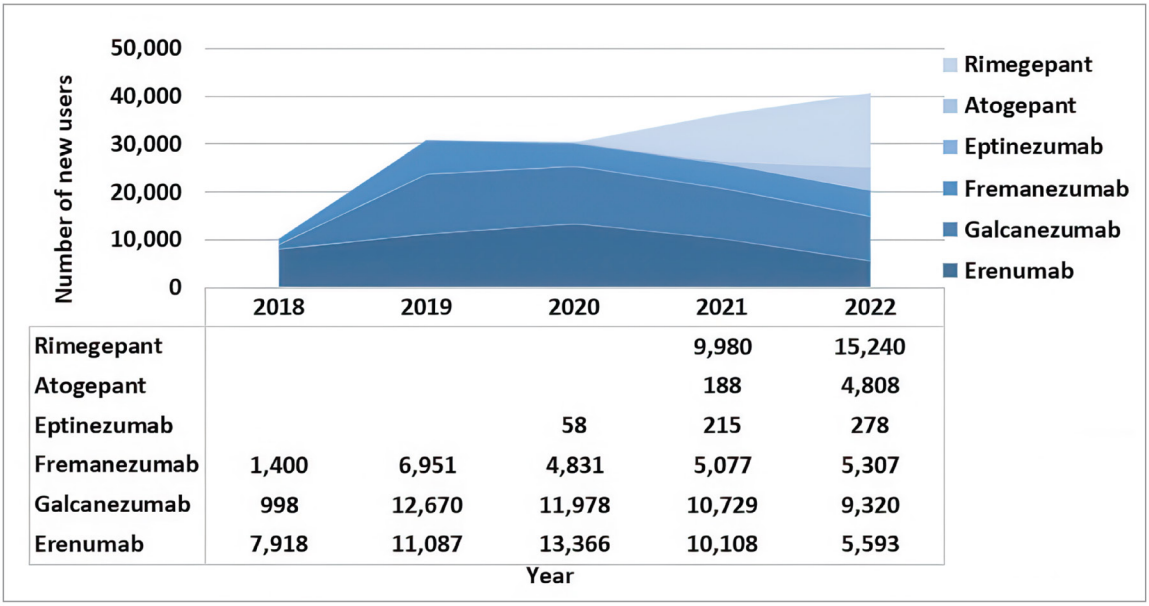
Drug type	2018[a] N = 2,010	2019 N = 5,609	2020 N = 6,306	2021 N = 5,861	2022 N = 8,157
Erenumab	2,010 (100%)	5,285 (94.2%)	4,672 (74.1%)	3,404 (58.1%)	3,157 (38.7%)
Galcanezumab	N/A	620 (11.1%)	1,917 (30.4%)	2,082 (35.5%)	2,119 (26%)
Fremanezumab	N/A	N/A	178 (2.8%)	610 (10.4%)	3,172 (38.9%)
Eptinezumab	N/A	N/A	N/A	N/A	268 (3.3%)
Atogepant	N/A	N/A	N/A	N/A	45 (0.6%)

CGRP = calcitonin gene–related peptide; N/A = not available.

Notes: Individuals can be dispensed more than 1 CGRP inhibitor in a year. The sum of distinct CGRP inhibitors dispensed is greater than the total number of individuals prescribed at least 1 CGRP inhibitor.

[a]Fiscal year is used for Canada; calendar year is used for the US.

Figure 5: Annual Users of Incident CGRP Inhibitors, Presented by Drug, US



CGRP = calcitonin gene–related peptide.

Similar results were observed in users of prevalent CGRP inhibitors (Table 5 and Table 6). In Canada in 2018, erenumab accounted for all use, and in 2022, the most commonly prescribed CGRP inhibitor was fremanezumab. In the US, in 2022, 1 of the more recently introduced CGRP inhibitors (rimegepant) accounted for the greatest use in users of prevalent CGRP inhibitors, followed by galcanezumab.

Table 6: Annual Prevalence of Users of CGRP Inhibitors Presented by Drug Type, US

Drug type	2018[a] N = 10,316	2019 N = 38,299	2020 N = 53,377	2021 N = 69,440	2022 N = 82,624
Erenumab	7,918 (76.8%)	16,057 (41.9%)	22,674 (42.5%)	23,024 (33.2%)	15,449 (18.7%)
Galcanezumab	998 (9.7%)	13,966 (36.5%)	21,274 (39.9%)	23,320 (33.6%)	23,338 (28.2%)
Fremanezumab	1,400 (13.6%)	8,276 (21.6%)	9,321 (17.5%)	11,210 (16.1%)	13,056 (15.8%)
Eptinezumab	N/A	N/A	108 (0.2%)	652 (0.9%)	918 (1.1%)
Atogepant	N/A	N/A	N/A	216 (0.3%)	6,427 (7.8%)
Rimegepant	N/A	N/A	N/A	11,018 (15.9%)	23,436 (28.4%)

CGRP = calcitonin gene–related peptide; N/A = not available.

Notes: Individuals can be dispensed more than 1 CGRP inhibitor in a year. The sum of distinct CGRP inhibitors dispensed is greater than the total number of individuals prescribed at least 1 CGRP inhibitor.

[a]Fiscal year is used for Canada; calendar year is used for the US.

CGRP Inhibitor Treatment Patterns

CGRP inhibitor treatment patterns are reported in Table 7 (each province is reported in Appendix 3, Tables 28 to 35). In Canada, the proportion of users of CGRP inhibitors who switched to a subsequent CGRP inhibitor was 5.4% (US: 10.3%) during the first year after CGRP inhibitor initiation, and 33.1% (US: 35.2%) during the first 4 years. Switching from a CGRP inhibitor to another type of prophylactic migraine medication was the most common switching pattern during the first year after CGRP inhibitor initiation (switched to onabotulinumtoxinA: 9.3%; nonspecific prophylactic: 12.0%). A proportion of people ceased all prophylactic migraine medication (9.1% during the first year after CGRP inhibitor initiation). The Kaplan-Meier analysis found similar patterns for the probability of these events (switch to CGRP inhibitor, switch to onabotulinumtoxinA, discontinuation) at the end of year 1 and year 2 when data were available (Appendix 3, Table 36 to 39).

A Sankey diagram of all users of incident CGRP inhibitors in the US with at least 1 year of follow-up data (Appendix 2, Figure 9) depicting the flow of individuals from their first CGRP inhibitor to their second indicates that a small portion of users of incident CGRP inhibitors switched during the first year, using the US data. Temporal availability of CGRP inhibitors likely influenced patterns of use. This analysis was not done using Canadian data due to the small number of individuals switching (Table 6 and Appendix 3, Tables 28 to 35).

Table 7: Treatment Patterns of CGRP Inhibitors, 2018 to 2023, Canada

Treatment event	Years of follow-up after CGRP inhibitor initiation: End of initial year N = 9,717	End of year 2 N = 7,719	End of year 3 N = 5,670	End of year 4 N = 2,001
Switching from a CGRP inhibitor to another CGRP inhibitor	528 (5.4%)	1,172 (15.2%)	1,225 (21.6%)	662 (33.1%)
Switching from a CGRP inhibitor to onabotulinumtoxinA	908 (9.3%)	1,651 (21.4%)	1,616 (28.5%)	583 (29.1%)

Treatment event	Years of follow-up after CGRP inhibitor initiation			
	End of initial year	End of year 2	End of year 3	End of year 4
	N = 9,717	N = 7,719	N = 5,670	N = 2,001
Switching from a CGRP inhibitor to a nonspecific prophylactic treatment	1,162 (12%)	1,696 (22%)	1,432 (25.3%)	457 (22.8%)
Concomitant CGRP inhibitor treatment and onabotulinumtoxinA	2,253 (23.2%)	2,106 (27.3%)	1,904 (33.6%)	854 (42.7%)
Concomitant CGRP inhibitor treatment and nonspecific prophylactic treatment	3,324 (34.2%)	2,790 (36.1%)	2,059 (36.3%)	749 (37.4%)
Treatment break	91 (0.9%)	161 (2.1%)	141 (2.5%)	67 (3.3%)
Non-use of any prophylactic medication	881 (9.1%)	976 (12.6%)	716 (12.6%)	228 (11.4%)

CGRP = calcitonin gene–related peptide.

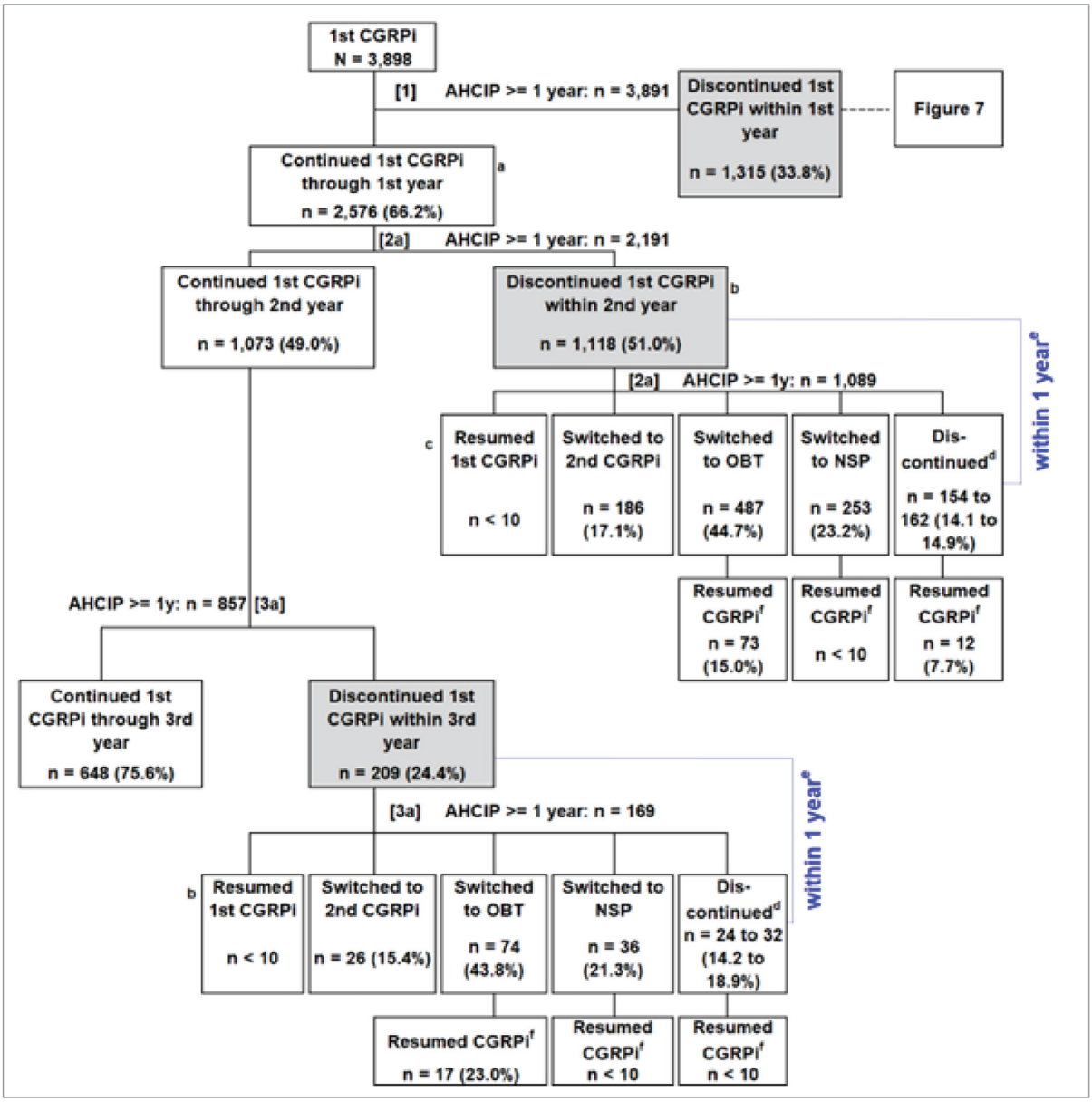
Table 8: Treatment Patterns of CGRP Inhibitors, 2018 to 2023, US

Treatment event	Years of follow-up after CGRP inhibitor initiation			
	End of initial year	End of year 2	End of year 3	End of year 4
	N = 73,258	N = 38,385	N = 17,263	N = 3,477
Switching from a CGRP inhibitor to another CGRP inhibitor	7,537 (10.3%)	6,077 (15.8%)	3,668 (21.2%)	1,224 (35.2%)
Switching from a CGRP inhibitor to onabotulinumtoxinA	7,483 (10.2%)	4,645 (12.1%)	2,344 (13.6%)	568 (16.3%)
Switching from a CGRP inhibitor to a nonspecific prophylactic treatment	22,281 (30.4%)	11,983 (31.2%)	5,183 (30%)	843 (24.2%)
Concomitant CGRP inhibitor treatment and onabotulinumtoxinA	3,741 (5.1%)	3,239 (8.4%)	2,017 (11.7%)	676 (19.4%)
Concomitant CGRP inhibitor treatment and nonspecific prophylactic treatment	10,069 (13.7%)	6,802 (17.7%)	3,466 (20.1%)	783 (22.5%)
Treatment break	1,301 (1.8%)	2,381 (6.2%)	1,939 (11.2%)	508 (14.6%)
Non-use of any prophylactic medication	9,866 (13.5%)	5,242 (13.7%)	1,971 (11.4%)	215 (6.2%)

CGRP = calcitonin gene–related peptide.

Sufficient sample size and data from Alberta allowed granular examination over time of the treatment patterns of users of incident CGRP inhibitors, shown in a flow chart (Figures 6 and 7). The proportion switching to a subsequent CGRP inhibitor in each time period was less common than switching to onabotulinumtoxinA or a nonspecific migraine medication. The proportion of people discontinuing CGRP inhibitors was approximately one-third within 1 year, and two-thirds discontinued within 2 years of initiating a CGRP inhibitor. A minority returned to CGRP inhibitor use after switching to another prophylactic, including around 15% to 23% of those switching to onabotulinumtoxinA and less among those who switched to a nonspecific migraine prophylactic.

Figure 6: CGRP Inhibitor Treatment Pattern for Those Who Continued Treatment at 1 Year, Alberta



AHCIP = Alberta Health Care Insurance Plan; CGRPi = calcitonin gene–related peptide inhibitor; NSP = nonspecific prophylactic; OBT = onabotulinumtoxinA.

Note: [1], [2a], and [3a] indicate analysis layers.

[a]Continued first CGRPi by 1 year: 1 day or more of that CGRP within the last 120 days of the year; may include concomitant use with other CGRPs and drugs.

[b]Definition 2: Discontinued first CGRPi by 1 year: those who did not meet definition 1 may have some events (e.g., concomitant use, switch) before discontinuing first CGRPi.

[c]If multiple events, take the first one; priority order if events happen at the same date: Resumed first CGRPi → switched to second CGRPi → switched to onabotulinumtoxinA; a switch to nonspecific drugs is only considered if none of those 3 events happens.

[d]Includes discontinuation of all migraine prophylactic medications.

[e]The start date of the next event must occur within 1 year from the start date of the previous event.

[f]Resumed any CGRP within 1 year.

Rescue Medication and Health Care Utilization

The direct measure of migraine prophylaxis effectiveness is not available in the accessible data. Surrogate markers of CGRP inhibitor effectiveness included rescue medication use and migraine-related health care use during the 1-year period before and after initiating a CGRP inhibitor (the users subcohort, which includes those who later switched or discontinued), switching to another CGRP inhibitor (the switchers subcohort), or discontinuing a CGRP inhibitor (the discontinuers subcohort).

Rescue Medication Use

Rescue medication dispensation within the 1-year period before and after incident CGRP inhibitor use was measured (Table 9); this was also measured in the number of people who switched and discontinued CGRP inhibitors, anchored on the date of switch or discontinuation. Also shown in Table 9 is the use of migraine rescue medication within these 1-year periods during active treatment with a CGRP inhibitor (if an individual starts or discontinues their CGRP inhibitor within 1 year of the anchor date, then dispensations before starting or after ceasing treatment are not counted). Of all incident CGRP inhibitor use, any migraine, rescue, and migraine-specific rescue medication use was numerically lower in the year after initiation of CGRP inhibitor dispensation; this pattern was also observed in those who switched to a subsequent CGRP inhibitor and those who discontinued CGRP inhibitor use.

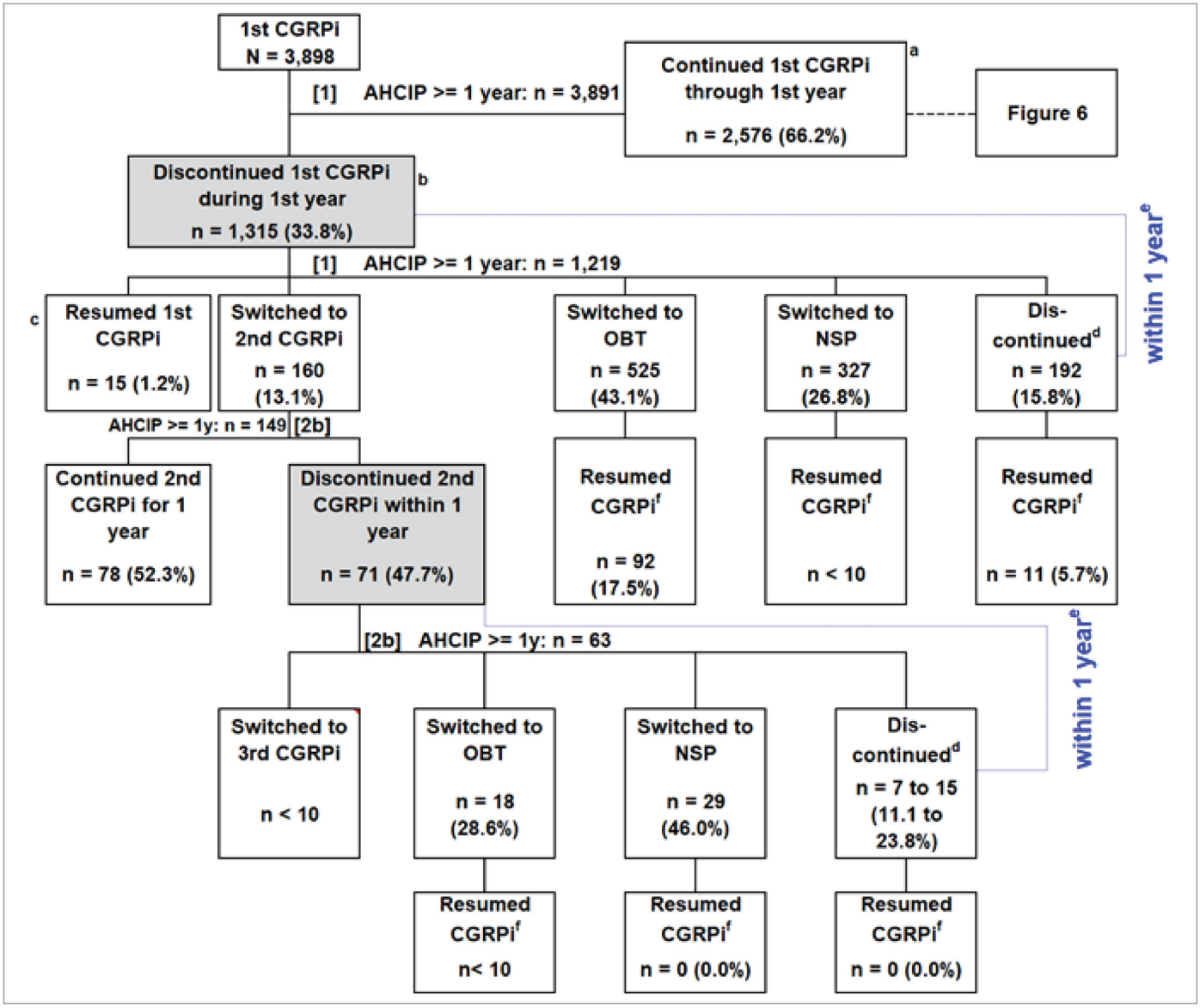
Table 9: Migraine-Related Medication Use During the 1-Year Period Before and After CGRP Inhibitor Initiation

Medication	CGRP inhibitor user cohort		
	1 year before initiation	1 year after initiation	During CGRP inhibitor use
Canada			
	N = 9,556		
Any migraine-related medication	9,130 (95.5%)	8,832 (92.4%)	NR
Any rescue medication	8,129 (85.1%)	7,683 (80.4%)	6,188 (64.8%)
Migraine-specific rescue medication	6,397 (66.9%)	5,756 (60.2%)	4,695 (49.1%)
US			
	N = 55,212		
Any migraine-related medication	51,435 (93.2%)	48,992 (88.7%)	NR
Any rescue medication	47,614 (86.2%)	44,232 (80.1%)	41,746 (75.6%)
Migraine-specific rescue medication	37,223 (67.4%)	32,435 (58.7%)	24,983 (45.3%)

CGRP = calcitonin gene–related peptide; NR = not reported.

Notes: The “During CGRP inhibitor use” column includes people who received medications while under active treatment with a CGRP inhibitor within 1 year of the index date. Therefore, for this outcome, if an individual starts or discontinues their CGRP inhibitor within 1 year of the index date, then dispensations before starting or after ceasing treatment are not counted. Users, switchers, and discontinuers groups and their index dates are defined in Table 1.

Figure 7: CGRP Inhibitor Treatment Pattern for Those Who Discontinued Treatment at 1 Year, Alberta



AHCIP = Alberta Health Care Insurance Plan; CGRPi = calcitonin gene–related peptide inhibitor; NSP = nonspecific prophylactic; OBT = onabotulinumtoxinA.

Note: [1] and [2b] indicate analysis layers.

[a]Continued first CGRPi by 1 year: 1 day or more of that CGRP within the last 120 days of the year, may include concomitant use with other CGRPs and drugs.

[b]Definition 2: Discontinued first CGRPi by 1 year — Those who did not meet definition 1 may have some events (e.g., concomitant use, switch) before discontinuing the first CGRPi.

[c]If multiple events, take the first one; priority order if events happen at the same date: Resumed first CGRPi → switched to second CGRPi → switched to onabotulinumtoxinA; a switch to nonspecific drugs is only considered if none of those 3 events happens.

[d]Includes discontinuation of all migraine prophylactic medications.

[e]The start date of the next event must occur within 1 year from the start date of the previous event.

[f]Resumed any CGRP within 1 year.

Table 10: Migraine-Related Medication Use During the 1-Year Period Before and After CGRP Inhibitor Switch

Medication	CGRP inhibitor switcher subcohort (to another CGRP inhibitor)		
	1 year before switch	1 year after switch	During CGRP inhibitor use after switch
Canada			
	N = 560		
Any migraine-related medication	532 (95%)	517 (92.3%)	NR
Any rescue medication	468 (83.6%)	453 (80.9%)	406 (72.5%)
Migraine-specific rescue medication	357 (63.8%)	327 (58.4%)	299 (53.4%)
US			
	N = 4,048		
Any migraine-related medication	3,876 (95.8%)	3,723 (92%)	NR
Any rescue medication	3,651 (90.2%)	3,378 (83.4%)	3,172 (78.4%)
Migraine-specific rescue medication	3,046 (75.2%)	2,606 (64.4%)	1,955 (48.3%)

CGRP = calcitonin gene–related peptide; NR = not reported.

Notes: The "During CGRP inhibitor use" column includes people who received medications while under active treatment with a CGRP inhibitor within 1 year of the index date. Therefore, for this outcome, if an individual starts or discontinues their CGRP inhibitor within 1 year of the index date, then dispensations before starting or after ceasing treatment are not counted. Users, switchers, and discontinuers groups and their index dates are defined in Table 1.

Table 11: Migraine-Related Medication Use During the 1-Year Period Before and After CGRP Inhibitor Discontinuation

Medication	CGRP inhibitor discontinuer subcohort		
	1-year prediscontinuation	1-year postdiscontinuation	During CGRP inhibitor use
Canada			
	N = 3,276		
Any migraine-related medication	3,031 (92.5%)	2,867 (87.5%)	NR
Any rescue medication	2,596 (79.2%)	2,399 (73.2%)	2,019 (61.6%)
Migraine-specific rescue medication	1,860 (56.8%)	1,571 (48%)	1,335 (40.8%)
US			
	N = 7,078		
Any migraine-related medication	5,580 (78.8%)	4,959 (70.1%)	NR
Any rescue medication	5,265 (74.4%)	4,871 (68.8%)	3,574 (50.5%)
Migraine-specific rescue medication	3,922 (55.4%)	3,090 (43.7%)	2,286 (32.3%)

CGRP = calcitonin gene–related peptide; NR = not reported.

Notes: The "During CGRP inhibitor use" column includes people who received medications while under active treatment with a CGRP inhibitor within 1 year of the index date. Therefore, for this outcome, if an individual starts or discontinues their CGRP inhibitor within 1 year of the index date, then dispensations before starting or after ceasing treatment are not counted. Users, switchers, and discontinuers groups and their index dates are defined in Table 1.

The days' supply of rescue medication for migraine was also measured in the year before and after the index date (incident CGRP inhibitor use by "users," date of switch from 1 CGRP inhibitor to another in "switchers," and date of discontinuation in "discontinuers"). A reduction in days supplied was observed in the incident users and switchers subgroups with variable results for discontinuers in Canada and the US (Table 12).

Table 12: Change in Rescue Medication Days of Supply Between the 1-Year Period Before and After CGRP Inhibitor Initiation, Switch, or Discontinuation

Rescue medications	Users of CGRP inhibitors		Switchers of CGRP inhibitors		Discontinuers of CGRP inhibitors	
	Pre	Post	Pre	Post	Pre	Post
Canada						
Days supplied, mean (had ≥ 1 dispensation)	170.1	160.1	186.4	181.1	173.2	177.6
Change in days supplied (had ≥ 1 dispensation)	−5.9%		−2.8%		2.5%	
Change in days supplied (the full cohort)	−11.0%		−5.9%		−5.3%	
US						
Days supplied, mean (had ≥ 1 dispensation)	162.5	159.0	187.5	185.3	125.4	180.5
Change in days supplied (had ≥ 1 dispensation)	−2.2%		−1.2%		43.9%	
Change in days supplied (the full cohort)	−9.1%		−8.6%		33.2%	

CGRP = calcitonin gene–related peptide.

Notes: Users, switchers, and discontinuers groups, and their index dates are defined in Table 1.

Migraine-Related Health Care Use

In Canada, migraine-related health care resource use was determined only in Alberta (Table 13). Compared with the 1-year period before, all groups had a numerically lower proportion with a migraine-related hospitalization, emergency department visit, ambulatory care visit, or physician visit during the 1-year period after (Table 13). Determined using the number of individuals with 1 or more visit and the average number of visits among that group, the reduction in all migraine-related health care encounters was 19.5% among all new users of CGRP inhibitors in the first year after initiating, compared to 20.9% and 18.0% among the switchers and discontinuers subcohorts in the year after their switch or discontinuation, respectively. The reduction in health service use occurred within all locations of migraine-related encounters within Alberta.

Health care utilization in the US cohort (Appendix 3, Table 56) showed similar results to what was found in Alberta, with the benefit of larger sample for less common outcomes. Overall use of health services was lower in the US data than in Alberta (81.0% of the US cohort had at least 1 migraine-related health care encounter compared to 95.5% of Albertans) and the change over time was greater among the US cohort.

Table 13: Migraine-Related Health Care Resource Use During the 1-Year Period Before and After CGRP Inhibitor Initiation, Switching, or Discontinuation in Alberta

	CGRP inhibitor user		CGRP inhibitor switch		CGRP inhibitor discontinuation	
	1 year before index	1 year after index	1 year before index	1 year after index	1 year before index	1 year after index
Alberta	N = 3,869	N = 3,869	N = 243	N = 243	N = 1,375	N = 1,375
Any migraine-related health care encounter[a]						
Had ≥ 1 visit, n (%)	3,696 (95.5)	3,570 (92.3)	239 (98.4)	231 (95.1)	1,295 (94.2)	1,163 (84.6)
Number of visits						
Mean[a] (SD)	9.6 (10.1)	8.0 (8.8)	11.0 (10.9)	9.0 (10.7)	9.2 (9.0)	8.4 (7.5)
Median[a] (Q1-Q3)	8.0 (4.0 to 12.0)	6.0 (3.0 to 10.0)	8.0 (5.0 to 12.0)	7.0 (4.0 to 10.0)	7.0 (4.0 to 11.0)	7.0 (3.0 to 11.0)
Migraine-related hospitalizations						
Had ≥ 1 visit, n (%)	23 (0.6)	17 (0.4)	< 10	< 10	< 10	< 10
Length of hospital stay (day)						
Mean[b] (SD)	6.1 (7.6)	4.4 (4.8)	3.3 (2.1)	0.0 (0.0)	2.3 (1.5)	2.0 (0.0)
Median[b] (Q1-Q3)	4.0 (1.0 to 8.0)	3.0 (2.0 to 4.0)	4.0 (1.0 to 5.0)	0.0 (0.0 to 0.0)	2.0 (1.0 to 3.0)	2.0 (2.0 to 2.0)
Migraine-related ED visits						
Had ≥ 1 visit, n (%)	520 (13.4)	330 (8.5)	23 (9.5)	12 (4.9)	168 (12.2)	98 (7.1)
Number of visits						
Mean[b] (SD)	3.1 (6.6)	3.3 (6.6)	2.0 (2.4)	1.9 (1.7)	3.2 (7.1)	2.9 (4.1)
Median[b] (Q1-Q3)	1.0 (1.0 to 2.0)	1.0 (1.0 to 2.0)	1.0 (1.0 to 2.0)	1.0 (1.0 to 2.0)	1.0 (1.0 to 2.0)	1.0 (1.0 to 2.0)
Migraine-related ambulatory care visits						
Had ≥ 1 visit, n (%)	610 (15.8)	529 (13.7)	43 (17.7)	40 (16.5)	214 (15.6)	174 (12.7)
Number of visits						
Mean[b] (SD)	3.1 (2.6)	3.4 (2.6)	4.3 (3.5)	4.5 (2.8)	3.3 (2.7)	3.5 (2.9)
Median[b] (Q1-Q3)	2.0 (1.0 to 4.0)	3.0 (2.0 to 4.0)	3.0 (2.0 to 6.0)	4.0 (2.0 to 6.5)	3.0 (2.0 to 4.0)	3.0 (1.0 to 5.0)
Migraine-related physician visits						
Had ≥ 1 visit, n (%)	3,682 (95.2)	3,546 (91.7)	237 (97.5)	229 (94.2)	1,290 (93.8)	1,150 (83.6)
Number of visits						

	CGRP inhibitor user		CGRP inhibitor switch		CGRP inhibitor discontinuation	
	1 year before index	1 year after index	1 year before index	1 year after index	1 year before index	1 year after index
Alberta	N = 3,869	N = 3,869	N = 243	N = 243	N = 1,375	N = 1,375
Mean[b] (SD)	8.7 (8.0)	7.2 (7.2)	10.1 (10.0)	8.2 (9.8)	8.2 (7.2)	7.8 (6.6)
Median[b] (Q1-Q3)	7.0 (4.0 to 11.0)	6.0 (3.0 to 9.0)	8.0 (5.0 to 11.0)	6.0 (3.0 to 9.0)	7.0 (4.0 to 10.0)	7.0 (3.0 to 10.0)

CGRP = calcitonin gene–related peptide; ED = emergency department; Q1-Q3 = first and third quartile; SD = standard deviation.

Note: Users, switchers, and discontinuer groups, and their index dates are defined in Table 1.

[a]Combines all migraine-related health care encounters, including hospitalization, ED, ambulatory, and physician visits.

[b]Means and medians are determined for those with 1 visit or more.

Strengths and Limitations

This study has several strengths. The Canadian component is population-based and includes all dispensations of CGRP inhibitors from community pharmacies within the included 6 included provinces (Alberta, British Columbia, Manitoba, Nova Scotia, Quebec, and Saskatchewan). Use and patterns of use spanned the entire time frame during which CGRP inhibitors have been available in both Canada and the US.

The large representative sample allows for the observation of most outcomes that were measured. In some analyses, Canadian data were limited by sample size; the use of MarketScan data from the US, with a larger number of patients, supplemented Canadian findings.

The study is subject to several limitations. The study could not examine the use of these medications in provinces where community drug dispensation data were not available for analysis (including Ontario). The use of administrative data and algorithms as opposed to medical records may introduce misclassification of the study measures due to potential inaccuracies and incomplete reporting. To address this limitation, validated case-finding algorithms were used when possible. Treatment pattern analysis is complicated, and there may be residual differences due to separate analysts working on the different sources of data.

The prescription drug dispensing databases only provide information on prescription medication dispensations from community pharmacies but may not represent actual medication uptake by individuals. This is particularly relevant to the interpretation of rescue medication use, which may reflect an individual's or physician's desire to have backup treatment options "on hand" after switching to a subsequent CGRP inhibitor (which may be more common among individuals for whom the initial CGRP inhibitor has failed) rather than actual use of rescue medication. These data would also not contain any samples provided directly to patients from clinicians or clinics. Data from Quebec was limited by only including data from those registered to receive medication coverage from the Régie de l'assurance maladie du Québec, which consists of approximately 46% of the population of the province. Additionally, it is not known whether nonspecific prophylactic medications were taken specifically for migraine or other conditions such as

depression, hypertension, or epilepsy. The use of over-the-counter medications and nonpharmacotherapy self-management techniques are not captured within provincial administrative data and the MarketScan data and, therefore, are not reported. However, they may also be common sources of rescue interventions.

Comparisons between CGRP inhibitor "switchers" versus "discontinuers" and "users" may be influenced by the fact that these categories were not mutually exclusive. The availability of additional CGRP inhibitors introduced over time and changing reimbursement policy may have influenced the probability of switching between CGRP inhibitors. "Users" referred to all users of CGRP inhibitors, regardless of their pattern of use. Therefore, for example, they cannot be considered to be "never-switchers." Because there was no control or comparison group, the trends in utilization patterns observed may not be due solely to the effectiveness or tolerability of CGRP inhibitors themselves.

This study used surrogate outcomes to identify potential effectiveness-related determinants of patterns of CGRP inhibitor use; however, it was not designed to causally assess associations between these outcomes and CGRP inhibitor discontinuation or switching, or effectiveness in general. While effectiveness is of interest, limitations inherent in the data sources and study design used do not preclude other factors, such as side effects, convenience, or preference in frequency or route of administration as root causes of these outcomes. This latter element may be an important factor as CGRP inhibitors requiring less frequent administration or available in oral versus subcutaneous form become available over time. The ability to compare CGRP inhibitors was also limited by variation in data period (i.e., date of introduction, duration on market, and eligibility for reimbursement). Another factor is reimbursement by provinces or private insurance, which may drive prescriptions toward medications that are reimbursed. For example, erenumab was not reimbursed by public drug plans in Canada; when subsequent CGRP inhibitors were reimbursed, this may have led to switching. Measuring migraine-related medication use during CGRP inhibitor use is affected by the period during CGRP inhibitor use being less than a full year across the sample, and therefore may account for the reductions seen within and across groups.

Administrative data does not allow direct measurement of symptom control, the main effectiveness outcome. Potential surrogate outcomes of rescue medication use and migraine-specific health care utilization may be proxies but are not validated. Further, given the lag between the initial administration and expected clinical effect, these measures may be influenced by the duration of this lag. The use of physician services may be complicated by individuals visiting their physician to receive new or continuing prescriptions for their CGRP inhibitors. This might have inflated the health service use metric in the preindex year slightly because individuals would need to visit a physician to receive the initial prescription of their CGRP inhibitor; however, this is unlikely to influence other outcomes such as migraine-related emergency department visits.

While we observed a dip in incidence and prevalence in 2020 and 2021, more granular data are needed to determine how the COVID-19 pandemic, which peaked in 2020 and 2021, might have affected prescribing or dispensation patterns or health care utilization.

Conclusions and Implications for Decision- or Policy-Making

Main Take-Aways

The rate of CGRP inhibitor use is increasing over time, with a trend that indicates a preference for newer CGRP inhibitors. The reasons behind this trend are unclear and may involve various factors beyond clinical effectiveness.

Individuals who begin using CGRP inhibitors tend to require moderately less rescue medication and fewer health care resources to manage migraines. This observation also holds true for those who switch from 1 CGRP inhibitor to another, relative to preswitch treatment status.

While we cannot directly assess the effectiveness of these medications, patterns of lower rescue medication and migraine-associated health care resource use suggest that patients switching to a different CGRP inhibitor may experience some benefits.

Summary

This report examines the utilization of CGRP inhibitors across several jurisdictions in North America, including multiple Canadian provinces. Although a relatively small portion of people living in Canada have accessed these medications, there is an increasing rate of dispensation over time. As newer drugs in this class become available, they tend to quickly account for a large proportion of incident and prevalent use. The motivations for switching are not known and may include lack of effectiveness, intolerance or side effects, and convenience or preference; the latter merits consideration because more recently introduced CGRP inhibitors are taken less frequently or have a different route of administration. Medication coverage may also play a role; erenumab did not have public drug plan coverage, unlike subsequent CGRP inhibitors such as fremanezumab. Switching from 1 CGRP inhibitor to another occurred in 5% to 10% of users of CGRP inhibitors at year 1 (Canada and the US respectively) and 33% to 35% after 4 years of follow-up. Approximately 9.3% and 12.0% switched to onabotulinumtoxinA or nonspecific migraine prophylaxis, respectively, within 1 year; 9.1% were not using any prophylactic medications at year 1. Relative to other treatment patterns of prophylactic medication use, switching to a subsequent CGRP inhibitor was, in general, similar and numerically slightly less common than other treatment switching patterns. Overall, less than 50% of users of CGRP inhibitors remained on their initial CGRP medication after 1 year in the US and after 2 years in Canada.

As direct measures of migraine prophylaxis effectiveness and symptoms are not readily accessible, surrogate markers, including migraine rescue medication dispensation and migraine-related health care use, were measured to determine if further analyses may provide evidence on the policy question on merits of switching CGRP inhibitors. However, this focus on putative surrogates of effectiveness may not account for other reasons for switching treatments other than suboptimal clinical responses, as previously noted. The results of this analysis demonstrate, in general, a reduction in users of migraine rescue medication and migraine-related health care use after the initiation of CGRP inhibitors, as well as in individuals that switch from a CGRP inhibitor to a subsequent one. This pattern continues for the discontinuer subcohort in Canada

(but not the US discontinuer subcohort, where an increase in health utilization after discontinuation was noted). No clear, strong signals in these outcomes among the different CGRP inhibitor treatment patterns were detected that would suggest that further analyses using these available data are likely to meaningfully inform the policy question.

While not a primary objective of this study, concomitant use of CGRP inhibitors with other prophylactic medications was noted in Canada. In the first year, approximately 23% of individuals taking a CGRP inhibitor were simultaneously receiving onabotulinumtoxinA treatment and 34% were receiving a nonspecific prophylactic treatment. However, concomitant use as defined (> 30 days) may not accurately account for stopping 1 drug and initiating another with varying expected onset of action and duration of action. While there are some studies that suggest that there is benefit of combined therapy, and this is supported by the Canadian Headache Society,[22,26,27] reimbursement recommendations for CGRP inhibitors currently state they should not be used jointly with onabotulinumtoxinA.[28,29]

Comparison With Existing Literature

Switching Between CGRP Therapies

As described in a recent rapid review by Canada's Drug Agency,[30] several studies suggest that switching may be a valid strategy to improve response and mitigate migraine symptoms, but evidence is limited by small sample sizes and other limitations; as such, these limitations need to be taken into account when interpreting the data. Some studies on people whose migraines do not respond to initial CGRP treatment indicate that significant improvements are possible by switching to a different CGRP inhibitor.[31-38] For example, 1 study found that switching from 1 CGRP inhibitor mAb to another mAb with a different mode of action provided a sustained reduction in monthly headache days and improved clinical outcomes in nearly half of the individuals whose migraines initially did not respond to the first treatment.[33] Another study found that 42% of individuals whose migraines did not respond to the first mAb responded to a second mAb, while 28.6% of individuals' migraines responded to the third mAb tested.[35] One more study found that switching between CGRP mAbs led to improvements in quality-of-life measures and reduced headache-related disability; however, individuals who underwent multiple switches experienced diminishing returns in terms of headache days and quality-of-life improvements.[38] Individuals who switched due to the ineffectiveness of therapy rather than the side effects showed significant improvements in headache frequency and disability scores.[34]

Also, switching from a CGRP receptor antibody (erenumab) to a CGRP ligand antibody (such as galcanezumab or fremanezumab) was associated with improved outcomes for some individuals.[36,39,40] One study of individuals switching from erenumab to fremanezumab found that about one-third of people whose migraines did not previously respond showed a significant reduction in migraine days, and this study also highlighted the issue of delayed responses to these medications.[36] Furthermore, switching to eptinezumab (the most recently approved mAb) showed effectiveness in individuals resistant to other CGRP mAbs.[41] Some studies showed that switching from erenumab to galcanezumab or fremanezumab led to a 30% or more response rate in one-third of individuals after 3 months[31] or to the maintenance of current health outcomes with fewer injections.[42]

Conclusion

CGRP inhibitors are a newer medication class for migraine prophylaxis and can offer significant reductions in disability and improvements in quality of life. Since the original clinical trials, additional real-world studies have found these medications to be effective and tolerable, and they provide some evidence to support longer treatment and suggest there is some potential for switching between CGRP medications when treatment goals are not met.[42-44] This study provides evidence on trends in the use of CGRP inhibitors over time in Canada and the US, with increasing rates of use of CGRP inhibitors over time and the trend for more recently introduced CGRP inhibitors to comprise a major proportion of both incident and prevalent dispensation. Among users of CGRP inhibitors, switching to a subsequent CGRP inhibitor does occur, although this treatment pattern occurs in a similar or lower proportion of individuals compared to other treatment patterns (including switching to onabotulinumtoxinA or nonspecific migraine prophylaxis) within 1 year of initiation. Putative surrogate markers of effectiveness among those who switch from 1 CGRP inhibitor to a subsequent CGRP inhibitor are similar to surrogate markers of effectiveness among those using CGRP inhibitors for the first time. While this suggests the possibility of improved effectiveness after switching, moderate differences in surrogate outcome magnitudes and limitations of these outcomes to validly represent migraine symptom reduction and disease burden warrants cautious interpretation. As such, without more direct, validated measures of effectiveness, additional analyses of available administrative data are unlikely to provide more evidence directly related to the policy question.

Authors and Contributors

Authors

Jason R. Randall was involved in the conception and design of the study, was involved in the acquisition of data and coordination of analysis, and was the lead writer for all versions of the report drafts.

Huong Luu contributed to the development of the study protocol and statistical analysis plan, data analysis, interpretation of the study results, discussion, and revision of the report.

Khanh Vu participated in developing the study protocol, conducted the data analysis for Alberta and Nova Scotia, provided Canadian Institute for Health Information SAS codes and technical support for data analysis, and participated in report writing and revising.

Cristiano S. Moura contributed to the conception and design, analysis and interpretation of the study results, and drafting and revising the report.

Houssem Missaoui provided suggestions and feedback on the final version of the protocol and the report, conducted data extraction and analysis related to the province of Quebec, and delivered comprehensive and detailed results specific to the province of Quebec.

Karen Martins contributed to the interpretation of the study results, including key messages and conclusions, and contributed to revising the report.

Hassan Behlouli contributed to the analysis and interpretation of the study results and to the drafting and revising of the report.

Sarah Treit contributed to the creation and editing of the figures, the editing of the text, and the interpretation and communication of the results.

Devin Manning was the local data expert for Nova Scotia, provided leadership for data access and data analysis in Nova Scotia, and reviewed the final report to ensure the discussion accurately reflected Nova Scotia results.

Zhaoyu Liu contributed to the conception and design, the acquisition of data, the analysis and interpretation of the study results, and the drafting and revising of the report.

Farnaz Amoozegar contributed to the interpretation of study results, including key messages and conclusions, revised the report critically for intellectual content, and added clinical perspective and experience.

Daniel Dutton served as the Primary Investigator for the Nova Scotia section, provided leadership for data access and data analysis in Nova Scotia, and reviewed the final report to ensure the discussion accurately reflected Nova Scotia results.

Jean-Luc Kaboré contributed to the protocol revision, review of the analyses, and review of the report.

Sasha Bernatsky contributed to the conception and study design, acquisition of data, the analysis and interpretations of the study results, and drafting and revising the report.

Scott Klarenbach was the overall principal investigator, oversaw the development of the protocol, provided feedback on the analysis, and revised and approved the report and its conclusions.

Contributors

Marina G. Birck contributed to the conception and study design, contributed to early data analysis, and provided methodological support.

Autumn Neville provided project management support, data acquisition, copy-editing, and language editing.

This project was selected as part of a pilot for early engagement with patients, clinicians, and drug manufacturers. We thank the contributors from each of these impacted groups for providing feedback and expertise throughout this project.

Patient Partner

We thank **Beth Kidd** for providing input into the direction of the research, drawing from lived experience, and providing valuable contributions to this report.

Content Experts

These individuals kindly provided comments on this report:

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Professor, Division of Neurology, Department of Clinical Neurological Sciences, Schulich School of Medicine and Dentistry, Western University

Mohammed Wasif Hussain, MBBS, FRCPC

Associate Clinical Professor, University of Alberta

Drug Manufacturers

All CGRP inhibitor drug manufacturers were contacted, and we acknowledge the following 2 who contributed their feedback: AbbVie Canada and Lundbeck Canada.

Additional Acknowledgements

We thank the participants of this study. This study is based in part on anonymized raw data from Alberta Health and Alberta Health Services (AHS), which was provided by the Alberta Strategy for Patient Oriented Research Unit housed within AHS. The interpretation and conclusions contained herein are those of the researchers and do not necessarily represent the views or opinions of the Government of Alberta or AHS. Scott Klarenbach was supported by the Kidney Health Research Chair and the Division of Nephrology at the University of Alberta. Additional data and analytic support was provided by the Canadian Institute for Health Information (CIHI), CAnadian Network for Advanced Interdisciplinary Methods (CAN-AIM), and the Institut national d'excellence en santé et en services sociaux (INESSS). The data that support CAN-AIM's findings are available from the Merative™ MarketScan® Research Database; however, restrictions apply to the availability of these data, which were used under license for the present study and are not publicly available. Portions of the data used in this report were made available by Health Data Nova Scotia of Dalhousie University. Although this research is based on data obtained from the Nova Scotia Department of Health and Wellness, the observations and opinions expressed are those of the authors and do not represent those of either Health Data Nova Scotia or the Department of Health and Wellness.

Parts of this material are based on data and information provided by CIHI. However, the analyses, conclusions, opinions, and statements expressed herein are those of the author and not necessarily those of CIHI.

Conflicts of Interest

Jason R. Randall disclosed the following:

Current employment

- Real World Evidence Unit, University of Alberta (2022 to 2025): various drugs and technologies

Involvement with projects or scientific advice

- RE0047 Biologic Drugs for Asthma
- HC0071 Trends in Opioids in Canada
- HC0098 Long-Acting Injectable Antipsychotics
- OS0011 PCSK9 Inhibitors in Familial Hypercholesterolemia

Huong Luu disclosed the following:

Involvement with projects or scientific advice

- HC0098 Long-Acting Injectable Antipsychotics
- OS0011 PCSK9 Inhibitors in Familial Hypercholesterolemia

Khanh Vu disclosed the following:

Involvement with projects or scientific advice

- HC0098 Long-Acting Injectable Antipsychotics

Cristiano S. Moura disclosed the following:

Employment

- Medlior — Health Outcome Research

Houssem Missaoui disclosed the following:

Involvement with projects or scientific advice

- HC0069 Outpatient Paxlovid and Remdesivir Utilization in Canada
- HC0071 Trends in Opioids in Canada
- HC0096 Hydromorphone Prescriptions Trends

Karen Martins disclosed the following:

- Member of the Alberta Real World Evidence Consortium, which conducts investigator-initiated research projects and receives funding from industry

Involvement with projects or scientific advice

- HT0042 Nirmatrelvir-Ritonavir as Treatment of COVID-19
- RE0047 Biologic Drugs for Asthma
- HC0098 Long-Acting Injectable Antipsychotics

Devin Manning disclosed the following:

Involvement with projects or scientific advice

- HC0073 Oral Fluoroquinolones in Canada — Utilization
- HC0086 Long-Acting Inhalable Drugs for Chronic Obstructive Pulmonary Disease
- HC0099 Drug Utilization in Patients With Major Neurocognitive Disorder
- OS0001 Opioid Use and Diverticulitis

Zhaoyu Liu disclosed the following:

Involvement with projects or scientific advice

- HC0071 Trends in Opioids in Canada
- HC0098 Long-Acting Injectable Antipsychotics
- OS0011 PCSK9 Inhibitors in Familial Hypercholesterolemia

Farnaz Amoozegar disclosed the following:

Educational lectures

- AbbVie, Eli Lilly, Lundbeck, Aralez — 2023, migraine topics

Writing articles or editorials

- Lundbeck 2022 to 2023

Organizing conferences

- Spinal CSF Leak Canada Charity — Spinal CSF Leak, 2024

Payment as advisor or consultant — providing advice on the use of migraine medications

- Pfizer, AbbVie, ICEBM, Teva, Eli Lilly — 2023, migraine

Research funding or grants

- Canadian Institute of Health Research (CIHR) — 2019 to 2024
- Pfizer, AbbVie, Eli Lilly, Teva — 2021 to 2024, migraine
- Spinal CSF Leak Canada Charity — Spinal CSF Leak 2023 to 2024

Daniel Dutton disclosed the following:

Involvement with projects or scientific advice

- HC0073 Oral Fluoroquinolones in Canada — Utilization
- HC0086 Long-Acting Inhalable Drugs for Chronic Obstructive Pulmonary Disease
- HC0099 Drug Utilization in Patients With Major Neurocognitive Disorder

Jean-Luc Kaboré disclosed the following:

Involvement with projects or scientific advice

- HC0069 Outpatient Paxlovid and Remdesivir Utilization in Canada
- HC0071 Trends in Opioids in Canada

Sasha Bernatsky disclosed the following:

- GlaxoSmithKline (GSK) — newly named subinvestigator of phase 4 observational study comparing Health Canada–approved medication Benlysta

Scott Klarenbach disclosed the following:

Research funding or grants paid to institution

- Real World Evidence Unit/Consortium (RWEU/RWEC) (with funding from Bayer) — outcomes in diabetic kidney disease
- RWEU/RWEC with funding from Alberta Innovates (with contribution from Pfizer) — Paxlovid utilization overall, and eligibility and use among those with severe COVID-19 outcomes
- RWEU/RWEC with funding from Intuitive — comparison of acute outcomes between various surgical approaches
- RWEU/RWEC with funding from Mallinckrodt — extracorporeal photopheresis therapy use and patient characteristics
- Alberta Drug and Technology Evidence Consortium with funding from Canada's Drug Agency — CoLab PMDE Core Network Partner
- RWEU/RWEC through the University Hospital Foundation (UHF) (funding to UHF from Roche) — pathways of care for multiple sclerosis, DMT use in patients with multiple sclerosis
- RWEU/RWEC with funding from Allergan — health care resource use in subjects with migraine, pathways of care post stroke, economic impact of discontinuing or reducing injection frequency of botulinum toxin for the treatment of chronic migraine
- RWEU/RWEC with funding from Purdue — analgesia use in trauma
- RWEU/RWEC funding through Moderna — risk factors for severe COVID-19 related outcomes in an endemic era in Alberta
- RWEU/RWEC with funding from University Hospital Foundation (funding to UHF from Novo Nordisk) — health care resources use in patients with obesity

Involvement with projects or scientific advice

- HT0042 Nirmatrelvir-Ritonavir as Treatment of COVID-19
- RE0047 Biologic Drugs for Asthma
- HC0098 Long-Acting Injectable Antipsychotics
- OS0011 PCSK9 Inhibitors in Familial Hypercholesterolemia

Beth Kidd disclosed the following:

Employment

- Health Coalition of Alberta — patient advocacy

Volunteer member

- Canada's Drug Agency — Acting Chair of the Patient and Community Advisory Committee
- Dementia Network Calgary — Strategic Council
- Migraine Warriors Alberta — coadministrator of a virtual patient support group
- Research Canada — Board of Directors

Involvement with projects or scientific advice

- RD0071 CGRP Inhibitors for Migraine Prophylaxis

Paul Cooper disclosed the following:

Participation in advisory board meetings

- Teva — fremanezumab
- AbbVie — ubrogepant and atogepant
- AbbVie — onabotulinumtoxinA
- Novartis — erenumab
- Lundbeck — eptinezumab
- Pfizer — rimegepant

Educational lectures

- Teva — anti-CGRP monoclonal antibodies
- Lilly — treatment of migraine
- Switching Calcitonin Gene–Related Peptide Inhibitors for Migraine Prophylaxis 23/33

Authors:

Speaker training session

- Lundbeck — eptinezumab
- Canada's Drug Agency — participated in reviews of erenumab and galcanezumab

Involvement with projects or scientific advice:

- RD0071 CGRP Inhibitors for Migraine Prophylaxis

Wasif Hussain disclosed the following:

Speaking engagements:

- AbbVie/Allergan — Botox, ubrogepant, atogepant
- Miravo — Cambia, Suvexx

- Eli Lilly — galcanezumab
- Lundbeck — eptinezumab
- Teva — fremanezumab

Payment as advisor or consultant — advisory boards

- AbbVie/Allergan — Botox, ubrogepant, atogepant
- Eli Lilly — galcanezumab
- Lundbeck — eptinezumab
- Miravo — Cambia, Suvexx
- Eisai — lecanemab

Involvement with projects or scientific advice:

- RD0071 CGRP Inhibitors for Migraine Prophylaxis

No other conflicts of interest were declared.

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Appendix 1: Additional/Supporting Information

Please note that this appendix has not been copy-edited.

Table 14: Migraine-Related Medications

Drug Class	Therapy	ATC code	DIN code (Canada)	NDC (unless otherwise specified; e.g., HCPCS) (US)*
CGRP preventive				
Monoclonal antibody CGRP (mAb CGRP)	erenumab	N02CD01	02479613, 02487306 02479605 (approved on 2018 to 08 to 01, no market date information), 02487292 (approved on 2019 to 04 to 11, no market date information),	55513084001, 55513084100, 55513084101, 55513084301, 55513084201, 55513084300, 55513084002, 55513084102
	galcanezumab	N02CD02	02491060, 02491087, 02505134	00002237727, 00002143601, 00002143627, 00002237711, 00002143611, 00002311501, 00002143661, 00002237701, 00002311509
	fremanezumab	N02CD03	02497859, 02509474	51759020411, 51759020222, 51759020410, 51759020211, 51759020210
	eptinezumab	N02CD05	02510839, 02542269 (approved on 2023 to 10 to 18, no market date information)	67386013051, 67386013091 HCPCS: C9063, J3032
Gepants (CGRP antagonists)	atogepant	N02CD07	02533979, 02533987, 02533995	00074709530, 00074709430, 00074709604, 00074709404, 00074709630
	rimegepant	N02CD06	02543605 (marketed on 2024 to 03 to 25, not within the inclusion period)	72618300002, 72618300101, 72618300102
Rescue medications				
Nonspecific				
NSAIDs	diclofenac	M01AB05	excluding rectal route of administration: 02231506, 02231508, 02261928, 02261936, 00632732, 00632724	Generic name (oral, EV, IM, if applicable)
	ibuprofen	M01AE01	—	Generic name (oral, EV, IM, if applicable)
	naproxen	M01AE02	excluding rectal route of administration: 02017237	Generic name (oral, EV, IM, if applicable)

Drug Class	Therapy	ATC code	DIN code (Canada)	NDC (unless otherwise specified; e.g., HCPCS) (US)*
	ketorolac	M01AB15	—	Generic name (oral, EV, IM, if applicable)
Opioids	Any (including codeine, hydromorphone, morphine, oxycodone, tramadol, buprenorphine)	N02A	—	Generic name (oral, EV, IM, if applicable)
Migraine-specific				
Triptans	almotriptan	N02CC05	—	Generic name (oral, EV, IM, if applicable)
	eletriptan	N02CC06	—	Generic name (oral, EV, IM, if applicable)
	frovatriptan	N02CC07	—	Generic name (oral, EV, IM, if applicable)
	naratriptan	N02CC02	—	Generic name (oral, EV, IM, if applicable)
	rizatriptan	N02CC04	—	Generic name (oral, EV, IM, if applicable)
	sumatriptan (nasal spray, oral, subcutaneous)	N02CC01	—	Generic name (oral, EV, IM, nasal, if applicable)
	zolmitriptan (oral, nasal spray)	N02CC03	—	Generic name (oral, EV, IM, nasal, if applicable)
Ergots	dihydroergotamine (DHE) (nasal spray) / DHE mesylate (IV, intramuscular, subcutaneous)	N02CA01	—	Generic name (oral, EV, IM, nasal, if applicable)
Gepants (CGRP antagonist)	ubrogepant (oral)	N02CD04	02532530, 02532581	00023649802, 00023650101, 00023650130, 00023649830, 00023650102, 00023649804, 00023649801, 00023650110, 00023649810, 00023649816, 00023650116
	zavegepant (nasal spray)	NA	NA	00069350001, 00069350002
	rimegepant	NA	NA	72618300002, 72618300101, 72618300102
Ditans	lasmitidan (oral use)	NA	NA	00002431208, 00002431261, 00002431262, 00002449108, 00002449161, 00002449162

Drug Class	Therapy	ATC code	DIN code (Canada)	NDC (unless otherwise specified; e.g., HCPCS) (US)*
Other preventive				
Nonspecific				
Antidepressants	amitriptyline (tricyclic)	N06AA09	—	Generic name (oral, EV, IM, if applicable)
	nortriptyline (tricyclic)	N06AA10	—	Generic name (oral, EV, IM, if applicable)
	desvenlafaxine (SNRI)	N06AX23	—	Generic name (oral, EV, IM, if applicable)
	venlafaxine (SNRI)	N06AX16	—	Generic name (oral, EV, IM, if applicable)
Antiepileptics	gabapentin	N03AX12	—	Generic name (oral, EV, IM, if applicable)
	topiramate	N03AX11	—	Generic name (oral, EV, IM, if applicable)
	lamotrigine	N03AX09	—	Generic name (oral, EV, IM, if applicable)
	divalproex sodium / sodium valproate	N03AG01	—	Generic name (oral, EV, IM, if applicable)
Antihypertensives	atenolol (beta-blocker)	C07AB03	—	Generic name (oral, EV, IM, if applicable)
	metoprolol tartrate (beta-blocker)	C07AB02	—	Generic name (oral, EV, IM, if applicable)
	nadolol (beta-blocker)	C07AA12	—	Generic name (oral, EV, IM, if applicable)
	propranolol (beta-blocker)	C07AA05	—	Generic name (oral, EV, IM, if applicable)
	timolol (beta-blocker)	C07AA06	—	Generic name (oral, EV, IM, if applicable)
	candesartan (angiotensin II antagonist)	C09CA06	—	Generic name (oral, EV, IM, if applicable)
	verapamil	C08DA01	—	
Calcium antagonist	flunarizine	N07CA03	—	NA
Migraine-specific				
OnabotulinumtoxinA	onabotulinumtoxinA		01981501, 02456117, 02460203, 02324032, 02371081	54868412300; 00023114501; 00023114502; 00023392102; 00023392103; 00023391950; 00023923201 HCPCS: J0585

Drug Class	Therapy	ATC code	DIN code (Canada)	NDC (unless otherwise specified; e.g., HCPCS) (US)*
Serotonin and tryptamine antagonist	pizotifen	N02CX01		NA

ATC = anatomic therapeutic chemical; CGRP = calcitonin gene–related peptide; DHE = dihydroergotamine; DIN = Drug Identification Number; EV = extracellular vesicle; HCPCS = Prescription Claim of Administration Claim; IM = intramuscular; mAb = monoclonal antibody; SNRI = Serotonin–norepinephrine reuptake inhibitor; NDC = National Drug Code; NSAID = nonsteroidal anti-inflammatory drug.

Table 15: Diseases and Their Associated Codes and Weights Included in the Charlson Comorbidity Index

Disease	ICD-9-CM codes	ICD-10-CA codes	ICD-10-CM codes	Weight
Myocardial infarction	410, 412	I21, I22, I25.2	I21, I22, I25.2	1
Congestive heart failure	398, 402, 425, 428	I09.9, I11.0, I13.0, I13.2, I25.5, I42.0, I42.5, I42.6, I42.7, I42.8, I42.9, I43, I50, P29.0	I11.0, I13.0, I13.2, I25.5, I42.0, I42.5, I42.6, I42.7, I42.8, I42.9, I43, I50, P29.0	1
Peripheral vascular disease	440, 441, 443, 447, 557	I70, I71, I73.1, I73.8, I73.9, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9	I70, I71, I73.1, I73.8, I73.9, I77.1, I79.0, I79.1, I79.8, K55.1, K55.8, K55.9, Z95.8, Z95.9	1
Cerebrovascular disease	430, 431, 432, 433, 434, 435, 436, 437, 438	G45, G46, I60, I61, I62, I63, I64, I65, I66, I67, I68, I69, H34.0	G45, G46, I60, I61, I62, I63, I64, I65, I66, I67, I68, H34.0-H34.2	1
Dementia	290, 294, 331	F00, F01, F02, F03, G30, F05.1, G31.1	F01, F02, F03, F04, F05, G30, F06.1, F06.8, G13.2, G13.8, G30, G31.0-G31.2, G91.4, R41.81, R54	1
Chronic pulmonary disease	416, 490, 491, 492, 493, 494, 495, 496, 500, 501, 502, 503, 504, 505	J40, J41, J42, J43, J44, J45, J46, J47, J60, J61, J62, J63, J64, J65, J66, J67, I27.8, I27.9, J68.4, J70.1, J70.3	J40, J41, J42, J43, J44, J45, J46, J47, J60, J61, J62, J63, J64, J65, J66, J67, J68.4, J70.1, J70.3	1
Connective tissue disease	446, 710, 714, 725	M05, M32, M33, M34, M06, M31.5, M35.1, M35.3, M36.0	M05, M06, M31.5, M32, M33, M34, M35.1, M35.3, M36.0	1
Peptic ulcer disease	531, 532, 533, 534	K25, K26, K27, K28	K25, K26, K27, K28	1
Mild liver disease	070, 570, 571, 573	B18, K73, K74, K70.0, K70.1, K70.2, K70.3, K70.9, K71.7, K71.3, K71.4, K71.5, K76.0, K76.2, K76.3, K76.4, K76.8, K76.9, Z94.4	B18, K73, K74, K70.0, K70.1, K70.2, K70.3, K70.9, K71.7, K71.3, K71.4, K71.5, K76.0, K76.2, K76.3, K76.4, K76.8, K76.9, Z94.4	1
Moderate/severe liver disease	456, 572	K70.4, K71.1, K72.1, K72.9, K76.5, K76.6, K76.7, I85.0, I85.9, I86.4, I98.2	K70.4, K71.1, K72.1, K72.9, K76.5, K76.6, K76.7, I85.0, I86.4	3
Diabetes (without complication)	250	E10.0, E10.l, E10.6, E10.8, E10.9, E11.0, E11.1, E11.6, E11.8, E11.9, E12.0, E12.1, E12.6, E12.8, E12.9, E13.0, E13.1, E13.6, E13.8, E13.9,	E08-E11, E13 with E**.0x, E**.1x, E**.6x, E**.8x, E**.9x	1

Disease	ICD-9-CM codes	ICD-10-CA codes	ICD-10-CM codes	Weight
		E14.0, E14.1, E14.6, E14.8, E14.9		
Diabetes (with complication)	250	E10.2, E10.3, E10.4, E10.5, E10.7, E11.2, E11.3, E11.4, E11.5, E11.7, E12.2, E12.3, E12.4, E12.5, E12.7, E13.2, E13.3, E13.4, E13.5, E13.7, E14.2, E14.3, E14.4, E14.5, E14.7	E08-E11, E13 with E**.2, E**.3, E**.4, E**.5	2
Hemiplegia and paraplegia	334, 342, 343, 344	G81, G82, G04.1, G11.4, G80.1, G80.2, G83.0, G83.1, G83.2, G83.3, G83.4, G83.9	G81, G82, G04.1, G11.4, G80.0-G80.2, G83	2
Moderate or severe renal disease	403, 582, 583, 585, 586, 588, V56	N18, N19, N05.2, N05.3, N05.4, N05.5, N05.6, N05.7, N25.0, I12.0, I13.1, N03.2, N03.3, N03.4, N03.5, N03.6, N03.7, Z49.0, Z49.1, Z49.2, Z94.0, Z99.2	N18.1-N18.6, N18.9, N19, N03, N05, I12.0, I12.9, I13.0, I13.2, I13.10, I13.11, N25, Z49, Z94.0, Z99.2	2
Cancer	140 to 165, 170 to 172, 174 to 176, 179 to 195, 200 to 208, 238	C00-C26, C30-C34, C37-C41, C43, C45-C58, C60-C76, C81-C85, C88, C90- C97	C00-C29, C30-C34, C37-C41, C43, C45-C58, C60-C63, C76, C80.1, C81-C85, C88, C90-C99	2
Metastatic carcinoma	196, 197, 198, 199	C77, C78, C79, C80	C77-C79, C80.0, C80.2	6
HIV/AIDS	042, 043, 044	B20, B21, B22, B24	B20	6

ICD-9-CM = International Classification of Diseases, ninth revision, clinical modification; ICD-10-CA = International Classification of Diseases, 10th revision, Canadian enhancement; ICD-10-CM = International Classification of Diseases, 10th revision, Clinical Modification.

To be considered as having 1 of the listed diseases, a person must have had 1 or more hospitalizations (associated ICD-10-CA code listed in any diagnostic field) or 2 or more physician claims (associated ICD-9-CM codes listed in any diagnostic field) of the corresponding ICD within 1 year. For the US, ICD-10-CM is used for inpatient and outpatient claims.

Table 16: Case Definitions Using Administrative Data to Identify Comorbid Conditions, Canada

Comorbidity	Algorithm	ICD-9-CM codes	ICD-10-CA codes	Other codes	Source
Anxiety	1 hospitalization or 2 claims OR 1 claim and 2 prescription dispensations in ≤ 1 year	300.0, 300.2	F40, F41	ATC codes: N05BA06, N05BA12	[45]
Asthma	1 hospitalization or 3 ambulatory care visits in ≤ 1 year		J45		[46]
Cardiovascular disease (any of the following)					

Comorbidity	Algorithm	ICD-9-CM codes	ICD-10-CA codes	Other codes	Source
Atrial fibrillation	1 hospitalization or 2 claims in ≤ 1 year	427.3	I48.0		46-50
Chronic heart failure	1 hospitalization or 2 claims in ≤ 1 year	398.9, 402, 404, 425.4 to 425.9, 428	I09.9, I25.5, I42.0, I42.5–I42.9, I43, I50		—
Coronary artery disease	1 hospitalization or 1 ambulatory care visit or 1 procedure or 2 claims in ≤ 1 year	410 to 413	I20–I25	Procedure codes: 1.IJ.57. GQ, 1.IJ.50, 1.IL.35, 1.IJ.76	—
Peripheral artery disease	1 hospitalization or 1 ambulatory care visit or 1 claim in any year	440.2	I70.2		—
Stroke	1 most responsible stroke hospitalization or emergency department OR 1 other diagnosis stroke and 1 most responsible z-code hospitalization or ambulatory care* in any years		G45 (excluding subcode G45.4), H34.0, H34.1, I60, I61, I62.9, I63, I64, I67.6; Z50 (excluding subcodes Z50.2, Z50.3, Z50.4), Z54.8, Z54.9, *only Z51.5 applies to ambulatory care		—
Depression	1 hospitalization or 2 claims in ≤ 1 year	300.4, 311	F32-F33, F34.1		51,52
Epilepsy	1 hospitalization or 2 claims in ≤ 1 year	345	G40, G41		53
Hypertension	1 hospitalization or 2 claims in ≤ 1 year	401 to 405	I10–I13, I15		46
Obstructive sleep apnea	1 hospitalization or 2 claims in ≤ 1 year	780.5	G47.3		54

ATC = anatomic therapeutic chemical.

Table 17: Case Definitions Using Administrative Data to Identify Comorbid Conditions, US

Comorbidity	Algorithm	ICD-10-CM codes	Other codes	Source
Anxiety	1 hospitalization or 2 claims OR 1 claim and 2 prescription dispensations in ≤ 1 year	F40, F41	Generic name: Lorazepam, alprazolam	—
Asthma	1 hospitalization or 3 ambulatory care visits in ≤ 1 year	J45		—
Cardiovascular disease (any of the following)			ICD-9-PCS: 0066, 3601, 3602, 3603, 3605, 3606, 3607, 3609, 361, 3610, 3611, 3612, 3613, 3614, 3615, 3616, 3617, 3619, 362, 0210 ICD-10-PCS: 0270346, 027034Z, 0270356, 027035Z, 0270366, 027036Z, 0270376, 027037Z, 02703D6, 02703DZ, 02703ZZ, 0270046, 0271346, 027134Z, 0271356, 027135Z, 0271366, 027136Z, 0271376, 027137Z, 02713D6, 02713DZ, 02714E6, 02713EZ, 02714EZ, 02723FZ, 02733GZ, 02713E6, 02723F6, 02733G6, 0272366, 0273376, 027236Z, 027337Z, 02C03ZZ, 02C13ZZ, 02C23ZZ, 02C33ZZ, 02C03Z6, 02C13Z6, 02C23Z6, 02C33Z6, 021009W, 02100A3, 02100A8, 02100A9, 02100AC, 02100AF, 02100AW CPT: 33510 to 33514, 33516 to 33519, 33520 to 33523, 33530, 33533 to 33536, 33572, 33545, 37184, 37185, 37186, 37187, 37188, 92920 to 92921, 92924 to 92925, 92928 to 92929, 92933 to 92934, 92937 to 92938, 92941, 92943 to 92944, 92973, 92980 to 92982, 92984, 92995 to 92996 HCPCS: C9600 - C9606, G0290 - G0291	—
Atrial fibrillation	1 hospitalization or 2 claims in ≤ 1 year	I48.0		[55-57]
Chronic heart failure	1 hospitalization or 2 claims in ≤ 1 year	I09.9, I25.5, I42.0, I42.5–I42.9, I43, I50		—
Coronary artery disease	1 hospitalization or 1 ambulatory care visit or 1 procedure or 2 claims in ≤ 1 year	I20–I25		—

Comorbidity	Algorithm	ICD-10-CM codes	Other codes	Source
Peripheral artery disease	1 hospitalization or 1 ambulatory care visit or 1 claim in any years	I70.2		—
Stroke	1 most responsible stroke hospitalization or emergency department OR 1 other diagnosis stroke and 1 most responsible z-code hospitalization or ambulatory care* in any years	G45 (excluding subcode G45.4), H34.0, H34.1, I60, I61, I62.9, I63, I64, I67.6; Z50 (excluding subcodes Z50.2, Z50.3, Z50.4), Z54.8, Z54.9, *only Z51.5 applies to ambulatory care		—
Depression	1 hospitalization or 2 claims in ≤ 1 year	F32-F33, F34.1		51,52
Epilepsy	1 hospitalization or 2 claims in ≤ 1 year	G40, G41		53
Hypertension	1 hospitalization or 2 claims in ≤ 1 year	I10–I13, I15		46
Obstructive sleep apnea	1 hospitalization or 2 claims in ≤ 1 year	G47.3		54

HCPCS = Prescription Claim of Administration Claim.

Table 18: Treatment Pattern Detailed Treatment Event Definitions

Treatment event	Definition
Non-use of any prophylactic medication	Defined as discontinuation of any prophylactic medication for 120 days or more. Determining this involved 2 steps. The end dates of prophylactic dispensations were determined by adding days' supply to the dispensation date. Then discontinuation was defined as having > 120 consecutive days after the end date without any additional prophylactic migraine medication dispensations (any prophylactic treatment dispensation during the 120 period would define inclusion in 1 of the following groups).
Treatment break	Defined as > 120 consecutive days without any CGRP inhibitor medications or other migraine prophylactic treatment since the last dispensation end date, followed by the resumption of previously dispensed CGRP inhibitor medications. Subjects would be considered in the 'nonuse' group during the treatment break if it occurred over the end of the analysis year, but would be updated to be included the treatment break group (and not the nonuse group) during the analysis period when they resumed their CGRP treatment.
Switching from an initial to a subsequent CGRP inhibitor	Defined as a change in CGRP inhibitor medication from the initial (first-ever) CGRP inhibitor to another CGRP inhibitor medication. The user discontinues their initial CGRP inhibitor as previously described (> 120 consecutive days in a follow-up period without a dispensation of the initial CGRP inhibitor). Dispensations of the second CGRP inhibitor can start before the end date of the CGRP inhibitor as long as they overlap with the initial CGRP inhibitor for less than 31 consecutive days. The switching date was defined as the first dispensing date of the switched-to CGRP inhibitor medication.
Switching from a CGRP inhibitor to another migraine prophylactic treatment	Defined as a change from a CGRP inhibitor to another prophylactic medication. The user discontinues their CGRP inhibitor as previously described (> 120 consecutive days in a follow-up period without a dispensation). Dispensations of the second CGRP inhibitor can start before the end date of the CGRP inhibitor as long as they overlap with the initial CGRP inhibitor for less than 31 consecutive days. The switching date was defined as the first dispensing date of the switched-to prophylactic medication.
Concomitant CGRP inhibitor treatment with other migraine prophylactic treatments	Defined as using another prophylactic medication at the same time as a CGRP inhibitor (including using a second CGRP inhibitor). The 2 treatments were required to have ≥ 31 consecutive days of overlapping use. The periods of use for each medication were determined using the dispensation date as the start date and estimating the end date of the dispensations by adding the days' supply of the dispensation to the start date. These periods were then examined to determine if a period of 31 days or more consecutive days of treatment overlap occurred between the 2 medications. The dispensation date of the additional medication immediately before the period of overlap was used as the date of this event. Concomitant treatment and switching categories are not mutually exclusive. Individuals may begin using another prophylactic concomitantly and then be classified as a switch as well if they discontinue the CGRP inhibitor. Similarly, users may experience a switch to another prophylactic and then later begin using a CGRP concomitantly and be counted in both groups.

Figure 8: Treatment Pattern Analysis Guideline

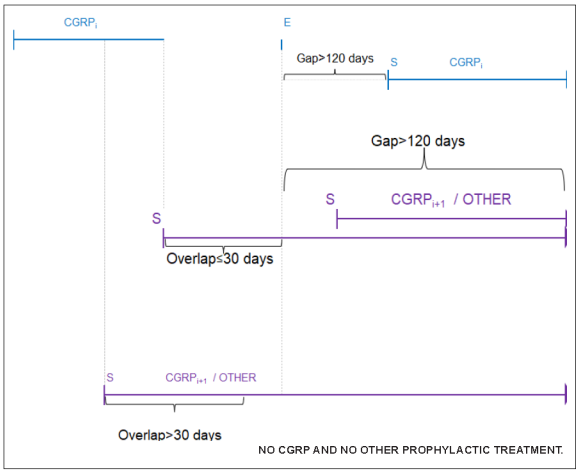
Treatment Patterns

Treatment Break: Dispensation / Claim [from Start date (S) to End date(E)] >120 consecutive days without any CGRP inhibitor or other migraine prophylactic treatment, and followed by the resumption of previously dispensed CGRP inhibitor.

Switching to Another CGRP Inhibitor/Other Migraine Prophylactic Treatment: Starting another CGRP inhibitor / other migraine prophylactic treatment either after stopping (for >120 days) the previously dispensed CGRP inhibitor or within 30 consecutive days before the stopping date (i.e., considered an early switch before exhausting the supply of the previously dispensed treatment).

Concurrent Use With Another CGRP Inhibitor/Other Prophylactic Treatment: Starting a new CGRP inhibitor / other migraine prophylactic treatment while overlapping with the previously dispensed CGRP inhibitor treatment for >30 consecutive days (i.e., to rule out early refill or early switching)

Treatment discontinuation: >120 consecutive days without any CGRP inhibitor or other migraine prophylactic treatment, and does not qualify for switching / treatment break / treatment resumption.



Other Definitions and Notes

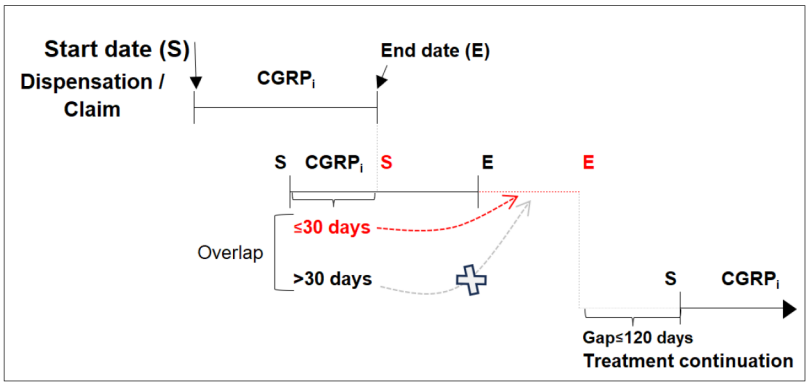
"For each CGRP inhibitor dispensation or claim:

Start date = Dispensation date

End date = Dispensation date + number of days supplied / typical treatment effect duration for the supply

For injection products, the number of days supplied is recorded as the typical treatment effect duration for the supply (e.g., the typical treatment effect duration for each dose multiplied by the number of doses supplied), or as the quantity of doses (sometimes). For example, the number of days supplied can be recorded as either 28/30 or 1 if 1 dose of erenumab is supplied; or recorded as either 90 or 3 if 3 doses of erenumab are supplied. Details regarding the typical treatment effect duration for each dose are as follows: erenumab with 70 or 140 mg/dose for 30 days; galcanezumab with loading dose of 240 mg or monthly dose of 120 mg for 30 days; fremanezumab with 225 mg/dose for 30 days; fremanezumab with 675 mg/dose for 90 days; eptinezumab with 100 mg/dose for 90 days; atogepant with 10, 30, or 60 mg/dose for 1 day; and preventive rimegepant with 75 mg/dose for 2 days and/or the number of doses per month ≤18 [US only, as of May 27, 2021 – differentiated from rescue rimegepant (the average daily dose =75mg and/or the number of doses per month ≤9)].is ≤120 consecutive days, this is considered as the patient staying on the treatment (treatment continuation)."

On average, a 3-month supply is typical, but this can vary depending on the doctor and frequency of follow-up visits. We assume that the maximum supply prescribed for CGRP inhibitors for migraine prophylactic treatment is 6 months. Therefore:



If the number of days supplied ≤7, then End date = (Dispensation date + the number of days supplied*typical treatment effect duration for each day supplied); for the first dispensation of galcanezumab only: if 2≤ number of days supplied ≤7, then End date = [Dispensation date + 30 + (the number of days supplied - 2)*30], if number of days supplied =1, then End date = [Dispensation date + 30]. If the number of days supplied >7, then End date = (Dispensation date + number of days supplied).

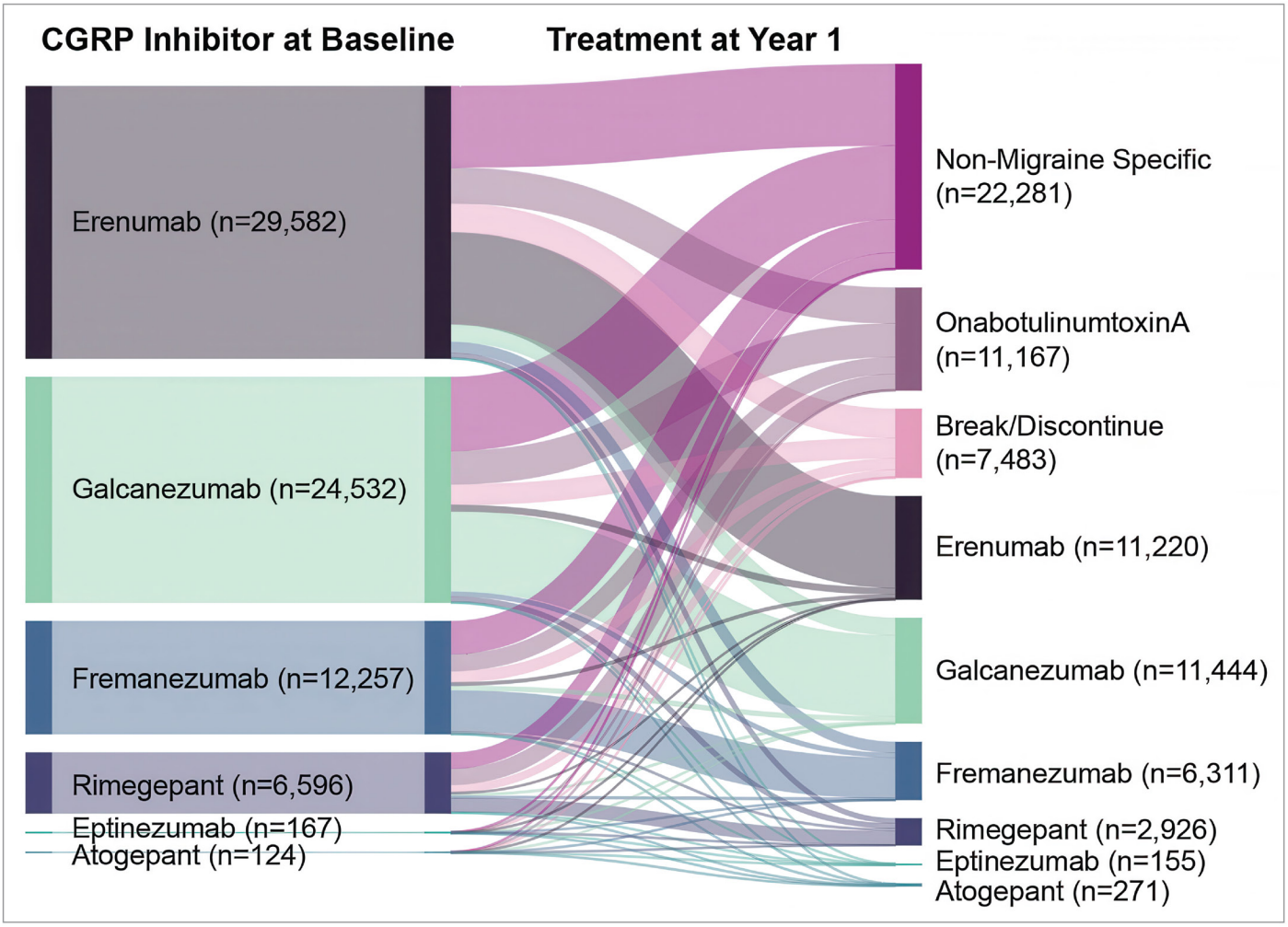
There are dispensations of the same CGRP that overlap. If the overlap is ≤30 consecutive days, the overlapping is determined as an early refill. Therefore, we adjust the end date of the subsequent dispensation as follows: End date = (dispensation date + number of days supplied / typical treatment effect duration for the supply + the number of overlapping days). If the overlap is >30 consecutive days, this will be considered as a change in dose. Therefore, no adjustment of the end date is needed.

Note that if the gap between two dispensations/claims of the same CGRP is ≤120 consecutive days, this is considered as the patient staying on the treatment (treatment continuation)."

Appendix 2: Additional Results

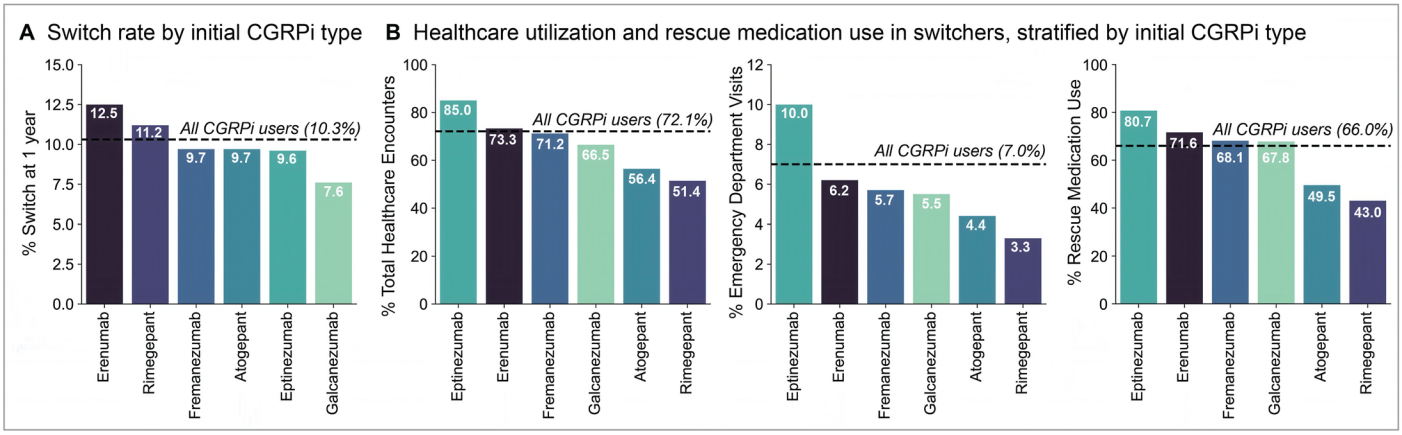
Please note that this appendix has not been copy-edited.

Figure 9: Sankey Diagram of Switching From First to Second CGRP Inhibitor Compared to Other Treatment Events Within the First Year of Treatment in the US



CGRP = calcitonin gene–related peptide.

Figure 10: Rate of Switching (A) and Health care Utilization (B) in Switchers, Stratified by Initial CGRP Inhibitor Type in the US



CGRPi = calcitonin gene–related peptide inhibitor.
Differences in baseline use by drug type means that more common drugs have larger influence over the average represented by the dashed line.

Table 19: Socioeconomic Status by Users, Switchers, and Discontinuers Cohorts in Canada

Deprivation quintile	CGRP inhibitor users cohort 8,666	CGRP inhibitor switchers subcohort 540	CGRP inhibitor discontinuers subcohort 3,227
Economic dependency			
Q1	1,143 (13.2%)	31 (5.7%)	326 (10.1%)
Q2	1,732 (20%)	108 (20%)	605 (18.7%)
Q3	1,936 (22.3%)	135 (25%)	733 (22.7%)
Q4	2,050 (23.7%)	141 (26.1%)	841 (26.1%)
Q5	1,647 (19%)	117 (21.7%)	645 (20%)
Missing/Invalid	158 (1.8%)	8 (1.5%)	77 (2.4%)
Ethnocultural composition			
Q1	2,968 (34.2%)	199 (36.9%)	1,045 (32.4%)
Q2	1,815 (20.9%)	101 (18.7%)	687 (21.3%)
Q3	1,485 (17.1%)	86 (15.9%)	565 (17.5%)
Q4	1,216 (14%)	75 (13.9%)	455 (14.1%)
Q5	1,024 (11.8%)	71 (13.1%)	398 (12.3%)
Missing/Invalid	158 (1.8%)	8 (1.5%)	77 (2.4%)
Residential instability			
Q1	2,047 (23.6%)	138 (25.6%)	722 (22.4%)
Q2	1,692 (19.5%)	101 (18.7%)	631 (19.6%)

Deprivation quintile	CGRP inhibitor users cohort 8,666	CGRP inhibitor switchers subcohort 540	CGRP inhibitor discontinuers subcohort 3,227
Q3	1,719 (19.8%)	100 (18.5%)	638 (19.8%)
Q4	1,674 (19.3%)	96 (17.8%)	613 (19%)
Q5	1,403 (16.2%)	97 (18%)	549 (17%)
Missing/Invalid	158 (1.8%)	8 (1.5%)	74 (2.3%)

CGRP = calcitonin gene–related peptide; Q = quintile; SD = standard deviation.

Notes: Q1 is the highest income/socioeconomic status and Q5 is the lowest. Users include all users of CGRP inhibitors based on the date of their first dispensation. Switchers include those that switched to a second CGRP within the first year of initiating CGRP treatment without returning to the original CGRP inhibitor within 1 year of the date of switching. Date of switching is used to determine 1-year periods. The discontinuers subcohort includes those who discontinued CGRP inhibitor treatment within the first year of initiating CGRP treatment without returning to the original CGRP inhibitor within 1 year of the date of switching. Date of discontinuation is used to determine 1-year periods.

Table 20: Other Prophylactic Medication Use Within 1 Year Before and After Initiation, Switch, or Discontinuation of a CGRP Inhibitor

Prophylactic medications	Users subcohort		Switchers subcohort		Discontinuers subcohort	
	1 year before	1 year after	1 year before	1 year after	1 year before	1 year after
Canada						
N	**N = 9,556**		**N = 560**		**N = 3,271**	
Overall						
Had ≥ 1 dispensation, n (%)	8,098 (84.7%)	7,735 (80.9%)	492 (87.9%)	466 (83.2%)	2,830 (86.5%)	2,653 (75.6%)
Nonspecific						
Had ≥ 1 dispensation, n (%)	7,034 (73.6%)	5,771 (60.4%)	380 (67.9%)	351 (62.7%)	2,232 (68.2%)	2,145 (61.1%)
Number of days supplied						
Mean (SD)[a]	412.9 (282.8)	392.5 (256.5)	381.4 (289.5)	408.3 (252.9)	358.3 (290)	385.7 (264.3)
Average of medians[a]	346.8	343.9	316.1	349	284.8	314.9
Specific						
Had ≥ 1 dispensation, n (%)	3,694 (38.7%)	2,778 (29.1%)	215 (38.4%)	184 (32.9%)	1,147 (35.1%)	1,371 (39.1%)
Number of injections						
Mean (SD)[a]	3.2 (1.3)	3.1 (1.3)	3.4 (1.7)	3.2 (1.7)	3 (1.4)	3.2 (1.3)
Average of medians[a]	3	2.9	3.8	3	3	2.9
US						
	N = 55,212		**N = 4,048**		**N = 7,078**	

Overall						
Overall						
Had ≥ 1 dispensation, n (%)	34,313 (62.2%)	30,151 (54.6%)	2,807 (69.3%)	2,536 (62.7%)	1,979 (28.0%)	744 (10.5%)
Nonspecific						
Had ≥ 1 dispensation, n (%)	30,976 (56.1%)	26,737 (48.4%)	2,532 (62.6%)	2,213 (54.7%)	1,811 (25.6%)	642 (9.1%)
Number of days supplied						
Mean (SD)[a]	282.1 (242.0)	306.8 (223.9)	308.5 (229.0)	342.3 (240.2)	100.1 (93.9)	240.1 (397.7)
Median (Q1-Q3)[a]	210 (90 to 400)	300 (120 to 390)	287.5 (120 to 420)	330 (150 to 450)	60 (30 to 120)	90 (30 to 240)
Specific						
Had ≥ 1 dispensation, n (%)	8,478 (15.4%)	8,169 (14.8%)	766 (18.9%)	846 (20.9%)	242 (3.4%)	185 (2.6%)
Number of injections						
Mean (SD)[a]	3.0 (1.3)	2.9 (1.3)	2.8 (1.4)	3.0 (1.3)	1.9 (1.0)	3.0 (2.9)
Median (Q1-Q3)[a]	3 (2 to 4)	3 (2 to 4)	3 (2 to 4)	3 (2 to 4)	2 (1 to 2)	2 (1 to 3)

CGRP = calcitonin gene–related peptide; Q1-Q3 = first and third quartile; SD = standard deviation.

Notes: Users include all users of CGRP inhibitors based on the date of their first dispensation. Switchers include those that switched to a second CGRP within the first year of initiating CGRP treatment without returning to the original CGRP inhibitor within 1 year of the date of switching. Date of switching is used to determine 1-year periods. The discontinuers subcohort includes those who discontinued CGRP inhibitor treatment within the first year of initiating CGRP treatment without returning to the original CGRP inhibitor within 1 year of the date of switching. Date of discontinuation is used to determine 1-year periods.

[a]Means and medians are calculated for those with 1 or more dispensations.

Appendix 3: Additional Data Tables

Please note that this appendix has not been copy-edited.

Table 21: Annual Incidence and Prevalence Users of CGRP Inhibitors, 2018 to 2022 (Alberta)

Fiscal year	2018[a]	2019	2020	2021	2022
Incidence					
Overall, n (rate per 100,000 inhabitants/ enrollees)	1,047 (31.4)	1,688 (49.9)	559 (16.3)	629 (18.2)	1,200 (34.1)
By product, n (% of CGRP new users)					
Erenumab	1,047 (100.0)	1,567 (92.8)	290 (51.9)	288 (45.8)	182 (15.2)
Galcanezumab	0 (0.0)	121 (7.2)	244 (43.6)	261 (41.5)	360 (30.0)
Fremanezumab	0 (0.0)	0 (0.0)	25 (4.5)	80 (12.7)	584 (48.7)
Eptinezumab	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	63 (5.3)
Atogepant	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	11 (0.9)
Rimegepant	N/A	N/A	N/A	N/A	N/A
By age, n (rate per 100,000 inhabitants/ enrollees)					
18 to 44	481 (28.4)	773 (45.3)	288 (16.8)	338 (19.8)	622 (35.9)
45 to 64	492 (45.1)	784 (71.3)	240 (21.7)	263 (23.7)	484 (43.3)
65+	74 (13.5)	131 (22.7)	31 (5.1)	28 (4.4)	94 (14.1)
By sex, n (rate per 100,000 inhabitants/ enrollees)					
Female	887 (53.4)	1,376 (81.6)	470 (27.5)	527 (30.6)	982 (55.8)
Male	160 (9.6)	312 (18.4)	89 (5.2)	102 (5.9)	218 (12.4)
Age- and sex-adjusted rate per 100,000 inhabitants	30.7 (28.8 to 32.6)	49.0 (46.6 to 51.3)	15.8 (14.5 to 17.2)	17.7 (16.3 to 19.1)	33.5 (31.6 to 35.4)
Prevalence					
Overall, n (rate per 100,000 inhabitants/ enrollees)	1,047 (31.4)	2,694 (79.6)	2,598 (75.8)	2,180 (63.2)	3,165 (89.9)
By product, n (% of CGRP users)					
Erenumab	1,047 (100.0)	2,564 (95.2)	2,004 (77.1)	1,256 (57.6)	1,168 (36.9)
Galcanezumab	0 (0.0)	290 (10.8)	722 (27.8)	824 (37.8)	965 (30.5)
Fremanezumab	0 (0.0)	0 (0.0)	59 (2.3)	194 (8.9)	1,056 (33.4)
Eptinezumab	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	240 (7.6)
Atogepant	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	29 (0.9)
Rimegepant	N/A	N/A	N/A	N/A	N/A

Fiscal year	2018[a]	2019	2020	2021	2022
By age, n (rate per 100,000 inhabitants/ enrollees)					
18 to 44	481 (28.4)	1,237 (72.5)	1,166 (68.0)	1,009 (59.2)	1,429 (82.4)
45 to 64	492 (45.1)	1,254 (114.0)	1,233 (111.4)	1,034 (93.1)	1,469 (131.4)
65+	74 (13.5)	203 (35.1)	199 (32.8)	137 (21.5)	267 (40.0)
By sex, n (rate per 100,000 inhabitants/ enrollees)					
Female	887 (53.4)	2,229 (132.1)	2,170 (127.0)	1,842 (107.0)	2,638 (150.0)
Male	160 (9.6)	465 (27.4)	428 (24.9)	338 (19.5)	527 (29.9)
Age- and sex-adjusted rate per 100,000 inhabitants	30.7 (28.8 to 32.6)	78.1 (75.1 to 81.1)	74.7 (71.8 to 77.6)	62.1 (59.5 to 64.7)	89.3 (86.2 to 92.4)

CGRP = calcitonin gene–related peptide; N/A = not available.

[a]Fiscal year is used for Canada.

Table 22: Annual Incidence and Prevalence of Users of CGRP Inhibitors in British Columbia

Fiscal year	2018[a]	2019	2020	2021	2022
Incidence					
Overall, n (rate per 100,000 inhabitants/ enrollees)	570 (13.76)	1,156 (27.37)	577 (13.48)	574 (13.26)	848 (19.14)
By product, n (% of CGRP new users)					
Erenumab	570 (100%)	1,017 (87.98%)	206 (35.70%)	246 (42.86%)	145 (17.10%)
Galcanezumab	0 (0%)	139 (12.02%)	324 (56.15%)	227 (39.55%)	135 (15.92%)
Fremanezumab	0 (0%)	0 (0%)	47 (8.15%)	101 (17.60%)	566 (66.75%)
Eptinezumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	< 5
Atogepant	0 (0%)	0 (0%)	0 (0%)	0 (0%)	< 5
Rimegepant	0 (0%)	0 (0%)	0 (0%)	US only	US only
By age, n (rate per 100,000 inhabitants/ enrollees)					
18 to 44	236 (13.00)	505 (27.12)	271 (14.37)	275 (14.46)	438 (22.22)
45 to 64	280 (19.80)	550 (38.94)	256 (18.18)	259 (18.45)	329 (23.47)
65+	54 (5.92)	101 (10.64)	50 (5.06)	40 (3.91)	81 (7.65)
By sex, n (rate per 100,000 inhabitants/ enrollees)					
Female	471 (22.35)	918 (42.73)	474 (21.75)	473 (21.46)	691 (30.61)
Male	99 (4.87)	238 (11.47)	103 (4.90)	101 (4.75)	157 (7.22)
Age- and sex-adjusted rate per 100,000 inhabitants	13.52	27.07	13.42	13.27	19.19

Fiscal year	2018[a]	2019	2020	2021	2022
Prevalence					
Overall, n (rate per 100,000 inhabitants/ enrollees)	570 (13.76)	1,671 (39.56)	1,840 (42.98)	1,697 (39.20)	2,252 (50.83)
By product, n (% of CGRP users)					
Erenumab	570 (100%)	1,520 (90.96%)	1,186 (64.46%)	850 (50.09%)	806 (35.79%)
Galcanezumab	0 (0%)	265 (15.86%)	725 (39.40%)	712 (41.96%)	633 (28.11%)
Fremanezumab	0 (0%)	0 (0%)	86 (4.67%)	220 (12.96%)	951 (42.23%)
Eptinezumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	10 (0.44%)
Atogepant	0 (0%)	0 (0%)	0 (0%)	0 (0%)	13 (0.58%)
Rimegepant	0 (0%)	0 (0%)	0 (0%)	US only	US only
By age, n (rate per 100,000 inhabitants/ enrollees)					
18 to 44	236 (13.00)	705 (37.86)	761 (40.36)	693 (36.44)	956 (48.51)
45 to 64	280 (19.80)	806 (57.07)	899 (63.86)	839 (59.77)	1,061 (75.70)
65+	54 (5.92)	160 (16.85)	180 (18.23)	165 (16.12)	235 (22.20)
By sex, n (rate per 100,000 inhabitants/ enrollees)					
Female	471 (22.35)	1,344 (62.55)	1,502 (68.93)	1,400 (63.53)	1,857 (82.25)
Male	99 (4.87)	327 (15.76)	338 (16.08)	297 (13.97)	395 (18.18)
Age- and sex-adjusted rate per 100,000 inhabitants	13.52	39.11	42.71	39.18	51.03

CGRP = calcitonin gene–related peptide.

[a]Fiscal year is used for Canada.

Table 23: Annual Incidence and Prevalence of Users of CGRP Inhibitors in Manitoba

Fiscal year	2018[a]	2019	2020	2021	2022
Incidence					
Overall, n (rate per 100,000 inhabitants/ enrollees)	219 (20.93)	415 (39.11)	124 (11.60)	102 (9.43)	195 (17.77)
By product, n (% of CGRP new users)					
Erenumab	219 (100%)	388 (93.49%)	S	49 (48.04%)	29 (14.87%)
Galcanezumab	0 (0%)	27 (6.51%)	73 (58.87%)	32 (31.37%)	38 (19.49%)
Fremanezumab	0 (0%)	0 (0%)	< 5	21 (20.59%)	128 (65.64%)
Eptinezumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Atogepant	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Rimegepant	0 (0%)	0 (0%)	0 (0%)	US only	US only

Fiscal year	2018[a]	2019	2020	2021	2022
By age, n (rate per 100,000 inhabitants/ enrollees)					
18 to 44	95 (18.97)	194 (38.13)	68 (13.30)	57 (11.01)	91 (17.22)
45 to 64	104 (30.81)	174 (51.62)	46 (13.69)	38 (11.33)	87 (26.03)
65+	20 (9.62)	47 (21.85)	10 (4.50)	7 (3.07)	17 (7.25)
By sex, n (rate per 100,000 inhabitants/ enrollees)					
Female	181 (34.36)	345 (64.59)	98 (18.20)	81 (14.89)	164 (29.73)
Male	38 (7.31)	70 (13.29)	26 (4.90)	21 (3.91)	31 (5.68)
Age- and sex-adjusted rate per 100,000 inhabitants	20.76	38.91	11.44	9.33	17.88
Prevalence					
Overall, n (rate per 100,000 inhabitants/ enrollees)	219 (20.93)	620 (58.44)	599 (56.03)	417 (38.57)	544 (49.59)
By product, n (% of CGRP users)					
Erenumab	219 (100%)	593 (95.65%)	444 (74.12%)	198 (47.48%)	189 (34.74%)
Galcanezumab	0 (0%)	46 (7.42%)	219 (36.56%)	184 (44.12%)	144 (26.47%)
Fremanezumab	0 (0%)	0 (0%)	19 (3.17%)	52 (12.47%)	244 (44.85%)
Eptinezumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	8 (1.47%)
Atogepant	0 (0%)	0 (0%)	0 (0%)	0 (0%)	< 5
Rimegepant	0 (0%)	0 (0%)	0 (0%)	US only	US only
By age, n (rate per 100,000 inhabitants/ enrollees)					
18 to 44	95 (18.97)	279 (54.83)	270 (52.82)	192 (37.10)	243 (45.98)
45 to 64	104 (30.81)	273 (80.99)	263 (78.29)	188 (56.04)	245 (73.31)
65+	20 (9.62)	68 (31.62)	66 (29.72)	37 (16.21)	56 (23.89)
By sex, n (rate per 100,000 inhabitants / enrollees)					
Female	181 (34.36)	513 (96.05)	488 (90.63)	343 (63.07)	451 (81.75)
Male	38 (7.31)	107 (20.31)	111 (20.92)	74 (13.77)	93 (17.05)
Age- and sex-adjusted rate per 100,000 inhabitants	20.76	58.22	55.99	38.64	50.02

CGRP = calcitonin gene–related peptide; S = suppressed.

[a]Fiscal year is used for Canada

Table 24: Annual Incidence and Prevalence of Users of CGRP Inhibitors in Nova Scotia

Fiscal year	2018[a]	2019	2020	2021	2022
Incidence					
Overall, n (rate per 100,000 inhabitants/enrollees)	157 (19.7)	284 (35.1)	67 (8.2)	89 (10.7)	117 (13.7)
By product, n (% of CGRP new users)					
Erenumab	157 (100.0)	284 (100.0)	58 (86.6)	S	S
Galcanezumab	0 (0.0)	0 (0.0)	9 (13.4)	24 (27.0)	27 (23.1)
Fremanezumab	0 (0.0)	0 (0.0)	0 (0.0)	< 5	54 (46.2)
Eptinezumab	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	< 5
Atogepant	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
By age, n (rate per 100,000 inhabitants/enrollees)					
18 to 44	56 (17.8)	103 (32.1)	24 (7.3)	43 (13.0)	61 (17.6)
45 to 64	95 (33.1)	158 (55.2)	36 (12.6)	41 (14.5)	44 (15.6)
65+	6 (3.1)	23 (11.3)	7 (3.3)	5 (2.3)	12 (5.3)
By sex, n (rate per 100,000 inhabitants/enrollees)					
Female	131 (32.0)	227 (54.7)	56 (13.3)	74 (17.4)	90 (20.6)
Male	26 (6.7)	57 (14.5)	11 (2.7)	15 (3.7)	27 (6.5)
Age- and sex-adjusted rate per 100,000 inhabitants	19.2 (16.2 to 22.3)	34.7 (30.6 to 38.7)	9.1 (6.9 to 11.2)	11.0 (8.7 to 13.3)	14.1 (11.5 to 16.6)
Prevalence					
Overall, n (rate per 100,000 inhabitants/enrollees)	157 (19.7)	431 (53.2)	384 (46.7)	314 (37.7)	405 (47.4)
By product, n (% of CGRP users)					
Erenumab	157 (100.0)	430 (99.8)	366 (95.3)	267 (85.0)	247 (61.0)
Galcanezumab	0 (0.0)	< 5	33 (8.6)	48 (15.3)	74 (18.3)
Fremanezumab	0 (0.0)	0 (0.0)	0 (0.0)	7 (2.2)	95 (23.5)
Eptinezumab	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	10 (2.5)
Atogepant	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rimegepant	N/A	N/A	N/A	N/A	N/A
By age, n (rate per 100,000 inhabitants/enrollees)					
18 to 44	57 (18.1)	152 (47.4)	134 (41.0)	117 (35.2)	155 (44.7)
45 to 64	94 (32.7)	249 (87.1)	222 (78.0)	180 (63.7)	217 (77.0)
65+	6 (3.1)	30 (14.8)	28 (13.3)	17 (7.8)	33 (14.6)

Fiscal year	2018[a]	2019	2020	2021	2022
By sex, n (rate per 100,000 inhabitants/enrollees)					
Female	131 (32.0)	351 (84.5)	314 (74.7)	264 (62.0)	332 (76.1)
Male	26 (6.7)	80 (20.3)	70 (17.4)	50 (12.3)	73 (17.5)
Age- and sex-adjusted rate per 100,000 inhabitants	19.3 (16.2 to 22.3)	52.5 (47.5 to 57.5)	46.5 (41.8 to 51.1)	38.0 (33.8 to 42.3)	48.1 (43.4 to 52.8)

CGRP = calcitonin gene–related peptide, S = suppressed.

[a]Fiscal year is used for Canada.

Table 25: Annual Incidence and Prevalence Users of CGRP Inhibitors in Quebec

Fiscal year	2018[a]	2019	2020	2021	2022
Incidence					
Overall, n (rate per 100,000 inhabitants/enrollees)	< 5	50 (1.46)	512 (14.6)	428 (12.08)	522 (14.54)
By product, n (% of CGRP new users)					
Erenumab	< 5	50 (100%)	416 (81.25%)	235 (54.90%)	54 (10.35%)
Galcanezumab	0 (0%)	0 (0%)	86 (16.80%)	109 (25.47%)	45 (8.62%)
Fremanezumab	0 (0%)	0 (0%)	10 (1.95%)	84 (19.63%)	423 (81.03%)
Eptinezumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Atogepant	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Rimegepant	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
By age, n (rate per 100,000 inhabitants/enrollees)					
18 to 44	< 5	10 (1.23)	137 (16.54)	130 (15.75)	178 (21.75)
45 to 64	0	24 (2.98)	237 (29.41)	194 (24.2)	209 (26.23)
65+	0	16 (1.12)	138 (9.34)	104 (6.84)	135 (8.59)
By sex, n (rate per 100,000 inhabitants/enrollees)					
Female	0	45 (2.5)	436 (23.72)	346 (18.61)	436 (23.13)
Male	< 5	5 (0.31)	76 (4.56)	82 (4.87)	86 (5.04)
Age- and sex-adjusted rate per 100,000 inhabitants	0.00	1.76	18.89	16.25	19.84
Prevalence					
Overall, n (rate per 100,000 inhabitants/enrollees)	< 5	51 (1.49)	559 (15.95)	908 (25.62)	1266 (35.27)
By product, n (% of CGRP users)					
Erenumab	< 5	51 (100%)	464 (83.01%)	630 (69.38%)	553 (43.68%)

Fiscal year	2018[a]	2019	2020	2021	2022
Galcanezumab	0 (0%)	0 (0%)	95 (16.99%)	192 (21.15%)	188 (14.85%)
Fremanezumab	0 (0%)	0 (0%)	11 (1.97%)	108 (11.89%)	576 (45.5%)
Eptinezumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Atogepant	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Rimegepant	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
By age, n (rate per 100,000 inhabitants/enrollees)					
18 to 44	< 5	11 (1.35)	147 (17.74)	246 (29.81)	348 (42.51)
45 to 64	0	24 (2.98)	258 (32.02)	412 (51.39)	534 (67.01)
65+	0	16 (1.12)	154 (10.43)	250 (16.43)	384 (24.42)
By sex, n (rate per 100,000 inhabitants/ enrollees)					
Female	0	45 (2.5)	478 (26)	761 (40.93)	1058 (56.14)
Male	< 5	6 (0.37)	81 (4.86)	147 (8.73)	208 (12.2)
Age- and sex-adjusted rate per 100,000 inhabitants	0	1.8	20.81	34.05	46.64

CGRP = calcitonin gene–related peptide.

[a]Fiscal year is used for Canada.

Table 26: Annual Incidence and Prevalence of Users of CGRP Inhibitors in Saskatchewan

Fiscal year	2018[a]	2019	2020	2021	2022
Incidence					
Overall, n (rate per 100,000 inhabitants/ enrollees)	14 (1.57)	129 (14.31)	214 (23.63)	125 (13.76)	237 (25.77)
By product, n (% of CGRP new users)					
Erenumab	14 (100%)	114 (88.37)	121 (56.54%)	63 (50.40%)	29 (12.24%)
Galcanezumab	0 (0%)	15 (11.63)	S	43 (34.40%)	33 (13.92%)
Fremanezumab	0 (0%)	0 (0%)	< 5	19 (15.20%)	175 (73.84%)
Eptinezumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Atogepant	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Rimegepant	0 (0%)	0 (0%)	0 (0%)	US only	US only
By age, n (rate per 100,000 inhabitants/ enrollees)					
18 to 44	6 (1.41)	75 (17.47)	114 (26.52)	70 (16.30)	112 (25.71)
45 to 64	S	49 (17.08)	91 (32.00)	50 (17.71)	104 (36.97)
65+	< 5	5 (2.70)	9 (4.70)	5 (2.54)	21 (10.36)

Fiscal year	2018[a]	2019	2020	2021	2022
By sex, n (rate per 100,000 inhabitants/ enrollees)					
Female	8 (1.80)	109 (24.30)	174 (38.58)	105 (23.19)	186 (40.57)
Male	6 (1.34)	20 (4.42)	40 (8.80)	20 (4.39)	51 (11.06)
Age- and sex-adjusted rate per 100,000 inhabitants	1.57	14.14	23.56	13.76	26.11
Prevalence					
Overall, n (rate per 100,000 inhabitants/ enrollees)	14 (1.57)	142 (15.76)	326 (35.99)	345 (37.97)	525 (57.09)
By product, n (% of CGRP users)					
Erenumab	14 (100%)	127 (89.44%)	208 (63.80%)	203 (58.84%)	194 (36.95%)
Galcanezumab	0 (0%)	16 (11.27%)	S	122 (35.36%)	115 (21.90%)
Fremanezumab	0 (0%)	0 (0%)	< 5	29 (8.41%)	250 (47.62%)
Eptinezumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Atogepant	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Rimegepant	0 (0%)	0 (0%)	0 (0%)	US only	US only
By age, n (rate per 100,000 inhabitants/ enrollees)					
18 to 44	6 (1.41)	80 (18.63)	174 (40.48)	175 (40.76)	239 (54.86)
45 to 64	S	54 (18.83)	135 (47.47)	152 (53.85)	246 (87.45)
65+	< 5	8 (4.33)	17 (8.88)	18 (9.13)	40 (19.74)
By sex, n (rate per 100,000 inhabitants/ enrollees)					
Female	8 (1.80)	116 (25.86)	267 (59.19)	281 (62.06)	422 (92.04)
Male	6 (1.34)	26 (5.74)	59 (12.98)	64 (14.04)	103 (22.34)
Age- and sex-adjusted rate per 100,000 inhabitants	1.57	15.59	35.91	38.19	58.04

CGRP = calcitonin gene–related peptide; S = suppressed.

[a]Fiscal year is used for Canada.

Table 27: Annual Incidence and Prevalence Users of CGRP Inhibitors, 2018 to 2022 (US)

Year	2018	2019	2020	2021	2022
Incidence					
Overall, n (rate per 100,000 enrollees)	10,316 (46.9)	30,708 (150.1)	30,233 (157.5)	36,297 (190.5)	40,546 (217.0)
By product, n (% of CGRP new users)					
Erenumab	7,918 (76.80%)	11,087 (36.1%)	13,366 (44.2%)	10,108 (27.9%)	5,593 (13.80%)

Year	2018	2019	2020	2021	2022
Galcanezumab	998 (9.7%)	12,670 (41.3%)	11,978 (39.6%)	10,729 (29.6%)	9,320 (23.0%)
Fremanezumab	1,400 (13.60%)	6,951 (22.60%)	4,831 (16.00%)	5,077 (14.00%)	5,307 (13.10%)
Eptinezumab	0 (0%)	0 (0%)	58 (0.20%)	215 (0.60%)	278 (0.70%)
Atogepant	0 (0)	0 (0)	0 (0)	188 (0.50%)	4,808 (11.90%)
Rimegepant	0 (0)	0 (0)	0 (0)	9,980 (27.50%)	15,240 (37.6%)
By age, n (rate per 100,000 enrollees)					
18 to 44	4,638 (39.1)	15,395 (138)	16,101 (158.4)	19,724 (193.1)	22,189 (223.4)
45 to 64	5,383 (60.3)	14,793 (179.3)	13,464 (177.1)	15,726 (213.2)	17,159 (243.3)
65+	295 (24.3)	520 (49.3)	668 (46.8)	847 (57.8)	1,198 (70.7)
By sex, n (rate per 100,000 inhabitants/enrollees)					
Female	8,826 (77)	26,270 (246.2)	26,034 (260.3)	31,228 (314.8)	34,807 (356.4)
Male	1,490 (14.2)	4,438 (45.3)	4,199 (45.7)	5,069 (55.5)	5,739 (64.4)
Age- and sex-adjusted rate per 100,000 enrollees	41.9	129.3	137.2	166.8	192.3
Prevalence					
Overall, n (rate per 100,000 enrollees)	10,316	38,299	53,377	69,440	82,624
	(46.9)	(187.2)	(278)	(364.4)	(442.3)
By product, n (% of CGRP users)					
Erenumab	7,918 (76.8%)	16,057 (42.0%)	22,674 (42.5%)	23,024 (33.2%)	15,449 (18.7%)
Galcanezumab	998 (9.7%)	13,966 (36.5%)	21,274 (39.9%)	23,320 (33.6%)	23,338 (28.3%)
Fremanezumab	1,400 (13.6%)	8,276 (21.6%)	9,321 (17.5%)	11,210 (16.1%)	13,056 (15.8%)
Eptinezumab	0 (0)	0 (0)	108 (0.20%)	652 (0.90%)	918 (1.10%)
Atogepant	0 (0)	0 (0)	0 (0)	216 (0.31%)	6,427 (7.78%)
Rimegepant	0 (0)	0 (0)	0 (0)	11,018 (15.9%)	23,436 (28.4%)
By age, n (rate per 100,000 enrollees)					

Year	2018	2019	2020	2021	2022
18 to 44	4,638	18,578	26,048	34,512	40,895
	(39.1)	(166.5)	(256.2)	(337.9)	(411.7)
45 to 64	5,383	18,936	26,064	33,429	39,400
	(60.3)	(229.5)	(342.8)	(453.3)	(558.6)
65+	295	785	1,265	1,499	2,329
	(24.3)	(74.4)	(88.5)	(102.4)	(137.4)
By sex, n (rate per 100,000 enrollees)					
Female	8,826	32,772	45,916	59,932	71,360
	(77)	(307.2)	(459)	(604.1)	(730.6)
Male	1,490	5,527	7,461	9,508	11,264
	(14.2)	(56.5)	(81.1)	(104.1)	(126.4)
Age- and sex-adjusted rate per 100,000 enrollees	41.9	163.3	242.7	317.6	390.8

CGRP = calcitonin gene–related peptide.

Table 28: Treatment Patterns of CGRP Inhibitors, 2018 to 2023 (Alberta)

Treatment year	Initial year	Over 2-year follow-up	Over 3-year follow-up	Over 4-year follow-up
N	3,891	3,241	2,673	1,029
Switching from a CGRP inhibitor to another CGRP inhibitor, n (%)				
Overall	214 (5.5)	505 (15.58)	577 (21.59)	353 (34.31)
Erenumab	178 (4.57)	475 (14.66)	561 (20.99)	353 (34.31)
Galcanezumab	S	S	16 (0.60)	0 (0.00)
Fremanezumab	< 10	< 10	0 (0.00)	0 (0.00)
Eptinezumab	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Atogepant	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Rimegepant	NR	NR	NR	NR
Switching from a CGRP inhibitor to OnabotulinumtoxinA, n (%)	483 (12.41)	937 (28.91)	934 (34.94)	332 (32.26)
Switching from a CGRP inhibitor to nonspecific prophylactic treatment, n (%)	359 (9.23)	591 (18.24)	546 (20.43)	190 (18.46)
Concomitant CGRP inhibitor treatment and OnabotulinumtoxinA, n (%)	1,429 (36.73)	1,319 (40.7)	1,216 (45.49)	529 (51.41)
Concomitant CGRP inhibitor treatment and nonspecific prophylactic treatment, n (%)	1,207 (31.02)	1,073 (33.11)	892 (33.37)	382 (37.12)
Treatment break, n (%)	23 (0.59)	64 (1.97)	60 (2.24)	25 (2.43)

Treatment year	Initial year	Over 2-year follow-up	Over 3-year follow-up	Over 4-year follow-up
Total prophylactic discontinuation, n (%)	295 (7.58)	339 (10.46)	300 (11.22)	102 (9.91)

CGRP = calcitonin gene–related peptide; NR = not reported; S = suppressed.

Table 29: Treatment Patterns of CGRP Inhibitors, British Columbia

Treatment year	Initial year	Over 2-year follow-up	Over 3-year follow-up	Over 4-year follow-up
N	2,877	2,304	1,730	581
Switching from a GCRP inhibitor to another CGRP inhibitor, n (%)	209 (7.26%)	412 (17.89%)	427 (24.74%)	207 (36.00%)
Switching from a CGRP inhibitor to onabotulinumtoxinA, n (%)	285 (9.91%)	424 (18.41%)	402 (23.29%)	144 (25.04%)
Switching from a CGRP inhibitor to nonspecific prophylactic treatment, n (%)	403 (14.01%)	558 (24.23%)	481 (27.87%)	149 (25.91%)
Concomitant CGRP inhibitor treatment and onabotulinumtoxinA, n (%)	475 (16.51%)	463 (20.10%)	424 (24.57%)	201 (34.96%)
Concomitant CGRP inhibitor treatment and nonspecific prophylactic treatment, n (%)	908 (31.56%)	768 (33.35%)	624 (36.15%)	211 (36.70%)
Treatment break, n (%)	< 5	5 (0.22%)	6 (0.35%)	< 5
Total prophylactic discontinuation, n (%)	33 (1.15%)	49 (2.13%)	44 (2.55%)	27 (4.70%)

CGRP = calcitonin gene–related peptide.

Table 30: Treatment Patterns of CGRP Inhibitors, Manitoba

Treatment year	Initial year	Over 2-year follow-up	Over 3-year follow-up	Over 4-year follow-up
N	860	758	634	223
Switching from a GCRP inhibitor to another CGRP inhibitor, n (%)	50 (5.81%)	147 (19.39%)	155 (24.45%)	70 (31.67%)
Switching from a CGRP inhibitor to onabotulinumtoxinA, n (%)	37 (4.30%)	69 (9.10%)	81 (12.78%)	39 (17.65%)
Switching from a CGRP inhibitor to nonspecific prophylactic treatment, n (%)	155 (18.02%)	299 (39.45%)	288 (45.43%)	99 (44.80%)
Concomitant CGRP inhibitor treatment and onabotulinumtoxinA, n (%)	49 (5.70%)	47 (6.20%)	47 (7.41%)	23 (10.41%)
Concomitant CGRP inhibitor treatment and nonspecific prophylactic treatment, n (%)	406 (47.21%)	360 (47.49%)	313 (49.37%)	112 (50.68%)
Treatment break, n (%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Total prophylactic discontinuation, n (%)	7 (0.81%)	9 (1.19%)	13 (2.05%)	6 (2.71%)

CGRP = calcitonin gene–related peptide.

Table 31: Treatment Patterns of CGRP Inhibitors, Nova Scotia

Treatment year	Initial year	Over 2-year follow-up	Over 3-year follow-up	Over 4-year follow-up
N	589	503	430	153
Switching from a GCRP inhibitor to another CGRP inhibitor, n (%)				
Overall	9 (1.53)	29 (5.77)	35 (8.14)	25 (16.34)
By initial CGRP inhibitor product type				
Erenumab	S	S	35 (8.14)	25 (16.34)
Galcanezumab	< 5	< 5	0 (0.00)	0 (0.00)
Fremanezumab	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Eptinezumab	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Atogepant	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Switching from a CGRP inhibitor to onabotulinumtoxinA, n (%)	91 (15.45)	170 (33.8)	170 (39.53)	65 (42.48)
Switching from a CGRP inhibitor to nonspecific prophylactic treatment, n (%)	55 (9.34)	76 (15.11)	67 (15.58)	16 (10.46)
Concomitant CGRP inhibitor treatment and onabotulinumtoxinA, n (%)	220 (37.35)	209 (41.55)	192 (44.65)	98 (64.05)
Concomitant CGRP inhibitor treatment and nonspecific prophylactic treatment, n (%)	180 (30.56)	148 (29.42)	128 (29.77)	38 (24.84)
Treatment break, n (%)	8 (1.36)	15 (2.98)	17 (3.95)	6 (3.92)
Total prophylactic discontinuation, n (%)	33 (5.6)	45 (8.95)	43 (10.00)	10 (6.54)

CGRP = calcitonin gene–related peptide, S = suppressed.

Table 32: Treatment Patterns of CGRP Inhibitors, Quebec

Treatment year	Initial year	Over 2-year follow-up	Over 3-year follow-up	Over 4-year follow-up
N	1,018	556	48	NR
Switching from a GCRP inhibitor to another CGRP inhibitor, n (%)				
Overall	36 (3.54%)	45 (8.09%)	8 (16.67%)	NR
By initial CGRP inhibitor product type				
Erenumab	26 (72.22%)	36 (80.00%)	8 (100%)	NR
Galcanezumab	S	9 (20.00%)	0	NR
Fremanezumab	< 5	0	0	NR
Eptinezumab	0	0	0	NR
Atogepant	0	0	0	NR

Treatment year	Initial year	Over 2-year follow-up	Over 3-year follow-up	Over 4-year follow-up
Switching from a CGRP inhibitor to onabotulinumtoxinA, n (%)	9 (0.88%)	13 (2.34%)	< 5	NR
Switching from a CGRP inhibitor to nonspecific prophylactic treatment, n (%)	108 (10.61%)	74 (13.31%)	7 (14.58%)	NR
Concomitant CGRP inhibitor treatment and onabotulinumtoxinA, n (%)	36 (3.54%)	28 (5.04%)	< 5	NR
Concomitant CGRP inhibitor treatment and nonspecific prophylactic treatment, n (%)	424 (41.65%)	282 (50.72%)	33 (68.75%)	NR
Treatment break, n (%)	9 (0.88%)	9 (1.62%)	0	NR
Total prophylactic discontinuation, n (%)	65 (6.39%)	37 (6.65%)	< 5	NR

CGRP = calcitonin gene–related peptide; NR = not reported; S = suppressed.

Table 33: Treatment Patterns of CGRP Inhibitors, Saskatchewan

Treatment year	Initial year	Over 2-year follow-up	Over 3-year follow-up	Over 4-year follow-up
N	482	357	155	15
Switching from a GCRP inhibitor to another CGRP inhibitor, n (%)	10 (2.07%)	34 (9.52%)	23 (16.08%)	7 (50.00%)
Switching from a CGRP inhibitor to onabotulinumtoxinA, n (%)	30 (6.22%)	38 (10.64%)	26 (18.18%)	< 5
Switching from a CGRP inhibitor to nonspecific prophylactic treatment, n (%)	82 (17.01%)	98 (27.45%)	43 (30.07%)	< 5
Concomitant CGRP inhibitor treatment and onabotulinumtoxinA, n (%)	44 (9.13%)	40 (11.20%)	22 (15.38%)	< 5
Concomitant CGRP inhibitor treatment and nonspecific prophylactic treatment, n (%)	199 (41.29%)	159 (44.54%)	69 (48.25%)	6 (42.86%)
Treatment break, n (%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Total prophylactic discontinuation, n (%)	11 (2.28%)	15 (4.20%)	7 (4.90%)	< 5

CGRP = calcitonin gene–related peptide.

Table 34: Treatment Patterns of CGRP Inhibitors, 2018 to 2023 (US)

Treatment year	Initial year	Over 2-year follow-up	Over 3-year follow-up	Over 4-year follow-up
N	73,258	38,385	17,263	3,477
Switching from an initial to a subsequent CGRP inhibitor, n (%)				
Overall	7,537 (10.3%)	6,077 (15.8%)	3,668 (21.3%)	1,224 (35.2%)
By initial CGRP inhibitor product type				
Erenumab	3,709 (49.2%)	3,386 (55.7%)	1,921 (52.4%)	1,016 (83.0%)

Treatment year	Initial year	Over 2-year follow-up	Over 3-year follow-up	Over 4-year follow-up
Galcanezumab	1,875 (24.9%)	1,598 (26.3%)	981 (26.7%)	78 (6.4%)
Fremanezumab	1,184 (15.7%)	1,089 (17.9%)	766 (20.9%)	130 (10.6%)
Eptinezumab	16 (0.2%)	4 (0.1%)	NR	NR
Atogepant	12 (0.2%)	NR	NR	NR
Rimegepant	741 (9.8%)	NR	NR	NR
Switching from a CGRP inhibitor to OnabotulinumtoxinA, n (%)	7,483 (10.2%)	4,645 (12.1%)	2,344 (13.6%)	568 (16.3%)
Switching from a CGRP inhibitor to non-migraine-specific prophylaxis, n (%)	22,281 (30.4%)	11,983 (31.2%)	5,183 (30.0%)	843 (24.3%)
Concomitant CGRP inhibitor treatment and onabotulinumtoxinA, n (%)	3,741 (5.1%)	3,239 (8.4%)	2,017 (11.7%)	676 (19.4%)
Concomitant use of CGRP inhibitor treatment and non-migraine-specific prophylaxis, n (%)	10,069 (13.7%)	6,802 (17.7%)	3,466 (20.1%)	783 (22.5%)
Treatment break, n (%)	1,301 (1.8%)	2,381 (6.2%)	1,939 (11.2%)	508 (14.5%)
Total prophylactic discontinuation, n (%)	9,866 (13.5%)	5,242 (13.7%)	1,971 (11.4%)	215 (6.2%)

CGRP = calcitonin gene–related peptide; NR = not reported.

Table 35: Treatment Pattern (1-Year Follow-Up) According to Initial CGRP Inhibitors (US)

Initial year drug	Initial CGRP					
	Erenumab	Galcanezumab	Fremanezumab	Eptinezumab	Atogepant	Rimegepant
N	**29,582**	**24,532**	**12,257**	**167**	**124**	**6,596**
Switching to a subsequent CGRP inhibitor, n (%)						
Overall	3,709 (12.5%)	1,875 (7.6%)	1,184 (9.7%)	16 (9.6%)	12 (9.7%)	741 (11.2%)
Erenumab	—	707 (37.7%)	378 (31.9%)	1 (6.3%)	1 (8.3%)	165 (22.3%)
Galcanezumab	1,916 (51.7%)	—	498 (42.1%)	2 (12.5%)	1 (8.3%)	266 (35.9%)
Fremanezumab	1,191 (32.1%)	514 (27.4%)	—	1 (6.3%)	1 (8.3%)	187 (25.2%)
Eptinezumab	22 (0.6%)	35 (1.9%)	18 (1.5%)	—	2 (16.7%)	14 (1.9%)
Atogepant	42 (1.1%)	48 (2.6%)	36 (3.0%)	0 (0)	—	109 (14.7%)
Rimegepant	538 (14.5%)	571 (30.5%)	254 (21.5%)	11 (68.8%)	7 (58.3%)	—
Switching to onabotulinumtoxinA, n (%)	3,163 (10.7%)	2,226 (9.1%)	1,229 (10.0%)	26 (15.6%)	15 (12.1%)	824 (12.5%)

Initial year drug	Initial CGRP					
	Erenumab	Galcanezumab	Fremanezumab	Eptinezumab	Atogepant	Rimegepant
Switching to non-migraine-specific prophylaxis, n (%)	8,861 (30.0%)	8,029 (32.7%)	3,580 (29.2%)	46 (27.5%)	28 (22.6%)	1,737 (26.3%)
Concomitant treatment with onabotulinumtoxinA, n (%)	1,668 (5.6%)	998 (4.1%)	654 (5.3%)	26 (15.6%)	5 (4.0%)	390 (5.9%)
Concomitant treatment with non-migraine-specific prophylaxis, n (%)	4,130 (14.0%)	3,461 (14.1%)	1,872 (15.3%)	30 (18.0%)	14 (11.3%)	562 (8.5%)
Treatment break, n (%)	462 (1.6%)	344 (1.4%)	194 (1.6%)	3 (1.8%)	1 (0.81%)	297 (4.5%)
Total prophylactic discontinuation, n (%)	3,419 (11.6%)	3,297 (13.4%)	1,653 (13.5%)	13 (7.8%)	32 (25.8%)	1,452 (22.0%)

CGRP = calcitonin gene–related peptide.

Notes: Individuals on rimegepant were included as of May 27, 2021, onwards and only for dispenses with 30 or more days' supply.

Table 36: Longitudinal Treatment Patterns of CGRP Inhibitors, 2018 to 2023 (Alberta)

Statistic	Time from CGRP inhibitor initiation (years)		Probability of event[b]	
	Mean (SE)	Q1 time	At 1 year (95% CI)	At 2 years (95% CI)
First switch from an initial to a subsequent CGRP inhibitor	3.46 (0.02)[a]	3.33	7.4% (6.6% to 8.2%)	16.3% (15.2% to 17.6%)
First switch from a CGRP inhibitor to onabotulinumtoxinA	3.22 (0.02)[a]	2.22	12.7% (11.7% to 13.7%)	23.8% (22.5% to 25.2%)
First treatment break	3.46 (0.01)[a]	NE	1.7% (1.3% to 2.1%)	2.4% (2.0% to 3.0%)
Total prophylactic discontinuation	3.33 (0.01)[a]	NE	5.6% (4.9% to 6.4%)	8.6% (7.7% to 9.5%)

CGRP = calcitonin gene–related peptide; CI = confidence interval; NE = not estimable; Q1 = quartile 1; SE = standard error.

Note: Median is unobserved, Q1 reported instead if possible.

[a]The mean survival time and its standard error were underestimated because the largest observation was censored and the estimation was restricted to the largest event time.

[b]Cumulative probabilities of event at 1 and 2 years.

Table 37: Longitudinal Treatment Patterns of CGRP Inhibitors, 2018 to 2023 (Nova Scotia)

Statistic	Time from CGRP inhibitor initiation (years)		Probability of event[b]	
	Mean (SE)	Q1 time	At 1 year (95% CI)	At 2 years (95% CI)
First switch from an initial to a subsequent CGRP inhibitor	3.79 (0.03)[a]	N/A	1.9% (1.0% to 3.3%)	7.0% (5.1% to 9.4%)
First switch from a CGRP inhibitor to onabotulinumtoxinA	2.85 (0.05)[a]	1.47	17.8% (15.0% to 21.2%)	29.0% (25.5% to 32.9%)
First treatment break	2.42 (0.01)[a]	N/A	2.4% (1.4% to 4.0%)	4.0% (2.7% to 6.0%)
Total prophylactic discontinuation	3.59 (0.03)[a]	N/A	5.4% (3.9% to 7.6%)	7.8% (5.9% to 10.3%)

CGRP = calcitonin gene–related peptide; CI = confidence interval; NE = not estimable; Q1 = quartile 1; SE = standard error.

Note: Median is unobserved, Q1 reported instead if possible.

[a]The mean survival time and its standard error were underestimated because the largest observation was censored and the estimation was restricted to the largest event time.

[b]Cumulative probabilities of event at 1 and 2 years.

Table 38: Longitudinal Treatment Patterns of CGRP Inhibitors, 2018 to 2023 (Quebec)

Statistic	Time from CGRP inhibitor initiation (years)		Probability of event[b]	
	Mean (SE)	Median	At 1 year (95% CI)	At 2 years (95% CI)
First switch from an initial to a subsequent CGRP inhibitor	3.68 (0.03)[a]	NE	0.04 (0.03 to 0.05)	0.10 (0.08 to 0.12)
First switch from a CGRP inhibitor to onabotulinumtoxinA	3.97 (0.02)[a]	NE	0.02 (0.01 to 0.02)	0.03 (0.02 to 0.04)
First treatment break	3.39 (0.04)[a]	NE	0.01 (0.01 to 0.02)	0.02 (0.01 to 0.02)
Total prophylactic discontinuation	3.80 (0.03)[a]	NE	0.05 (0.94 to 0.96)	0.07 (0.06 to 0.09)

CGRP = calcitonin gene–related peptide; CI = confidence interval; NE = not estimable; SE = standard error.

[a]The mean survival time and its standard error were underestimated because the largest observation was censored and the estimation was restricted to the largest event time.

[b]Cumulative probabilities of event at 1 and 2 years.

Table 39: Longitudinal Treatment Patterns of CGRP Inhibitors, 2018 to 2023 (US)

Statistic	Time from CGRP inhibitor initiation (in days)		Probability of event[b]	
	Mean (SE)	Q1	At 1 year (95% CI)	At 2 years (95% CI)
First switch from an initial to a subsequent CGRP inhibitor	3.47 (< 0.01)[a]	NE	11.3% (11.1% to 11.5%)	16.8% (16.6% to 17.1%)
First switch from a CGRP inhibitor to onabotulinumtoxinA	3.61 (< 0.01)[a]	NE	11.9% (11.7% to 12.1%)	13.4% (13.2% to 13.6%)
First treatment break	3.87 (< 0.01)[a]	NE	2.4% (2.3% to 2.5%)	4.8% (4.6% to 5.0%)
Total prophylactic discontinuation	3.22 (< 0.01)[a]	4.31 (4.25 to 4.36)	15.7% (15.4% to 15.9%)	29.3% (29.0% to 29.7%)

CGRP = calcitonin gene–related peptide; CI = confidence interval; NE = not estimable; Q1 = quartile 1; SE = standard error.

Note: Median is unobserved, Q1 reported instead if possible.

[a]The mean survival time and its standard error were underestimated because the largest observation was censored and the estimation was restricted to the largest event time.

[b]Cumulative probabilities of event at 1 and 2 years.

Table 40: Migraine-Related Medication Use (Alberta)

	CGRP inhibitor users subcohort		CGRP inhibitor switchers subcohort		CGRP inhibitor discontinuers subcohort	
	1 year before index	1 year after index	1 year before index	1 year after index	1 year before index	1 year after index
N	**3,869**		**243**		**1,375**	
Any migraine-related medication						
Had ≥ 1 dispensation, n (%)	3,788 (97.9)	3,654 (94.4)	229 (94.2)	228 (93.8)	1,312 (95.4)	1,260 (91.6)
Acute rescue medications						
Overall						
Had ≥ 1 dispensation, n (%)	3,398 (87.8)	3,196 (82.6)	193 (79.4)	195 (80.2)	1,150 (83.6)	1,079 (78.5)
Number of days supplied						
Mean (SD)[a]	177.8 (215.2)	168.0 (211.8)	192.8 (239.3)	174.2 (237.3)	186.0 (226.3)	192.6 (234.2)
Median (Q1-Q3)[a]	101.0 (36.0 to 240.0)	87.5 (30.0 to 222.0)	115.0 (29.0 to 257.0)	90.0 (29.0 to 216.0)	97.0 (31.0 to 264.0)	100.0 (30.0 to 270.0)
Number of classes dispensed, n (%)						
1	1,433 (42.2)	1,528 (47.8)	92 (47.7)	94 (48.2)	502 (43.7)	563 (52.2)

	CGRP inhibitor users subcohort		CGRP inhibitor switchers subcohort		CGRP inhibitor discontinuers subcohort	
	1 year before index	1 year after index	1 year before index	1 year after index	1 year before index	1 year after index
N	**3,869**		**243**		**1,375**	
2	1,370 (40.3)	1,236 (38.7)	66 (34.2)	73 (37.4)	459 (39.9)	377 (34.9)
≥ 3	595 (17.5)	432 (13.5)	35 (18.1)	28 (14.4)	189 (16.4)	139 (12.9)
Nonspecific						
Had ≥ 1 dispensation, n (%)	2,471 (63.9)	2,250 (58.2)	130 (53.5)	140 (57.6)	874 (63.6)	799 (58.1)
By class, n (%)						
NSAIDs	1,644 (42.5)	1,405 (36.3)	85 (35.0)	82 (33.7)	537 (39.1)	436 (31.7)
Opioids	1,640 (42.4)	1,506 (38.9)	93 (38.3)	101 (41.6)	618 (44.9)	599 (43.6)
Migraine-specific						
Had ≥ 1 dispensation, n (%)	2,633 (68.1)	2,354 (60.8)	148 (60.9)	137 (56.4)	819 (59.6)	696 (50.6)
By class, n (%)						
Triptans	2,604 (67.3)	2,329 (60.2)	145 (59.7)	S	806 (58.6)	686 (49.9)
Ergots	101 (2.6)	81 (2.1)	10 (4.1)	< 10	34 (2.5)	23 (1.7)
Ditans	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rescue medications dispensed during CGRP inhibitor use, n (%)						
Had ≥ 1 dispensation	NR	2,924 (75.6)	151 (62.1)	175 (72.0)	896 (65.2)	NR
Had ≥ 1 dispensation of nonspecific rescue medications	NR	1,938 (50.1)	94 (38.7)	118 (48.6)	601 (43.7)	NR
Had ≥ 1 dispensation of migraine-specific medications	NR	2,149 (55.5)	110 (45.3)	125 (51.4)	592 (43.1)	NR
Triptans	NR	2,130 (55.1)	S	S	584 (42.5)	NR
Ergots	NR	62 (1.6)	< 10	< 10	20 (1.5)	NR
Ditans	0	0	0	0	0	0
Prophylactic medications						
Overall						
Had ≥ 1 dispensation, n (%)	3,447 (89.1)	2,960 (76.5)	201 (82.7)	196 (80.7)	1,154 (83.9)	1,095 (79.6)

	CGRP inhibitor users subcohort		CGRP inhibitor switchers subcohort		CGRP inhibitor discontinuers subcohort	
	1 year before index	1 year after index	1 year before index	1 year after index	1 year before index	1 year after index
N	**3,869**		**243**		**1,375**	
Nonspecific						
Had ≥ 1 dispensation, n (%)	2,887 (74.6)	2,377 (61.4)	169 (69.5)	162 (66.7)	953 (69.3)	863 (62.8)
Number of days supplied						
Mean (SD)[a]	376.4 (291.7)	388.7 (295.7)	398.7 (304.2)	419.7 (298.1)	355.3 (303.7)	394.8 (311.7)
Median (Q1-Q3)[a]	321.0 (150.0 to 514.0)	330.0 (180.0 to 530.0)	330.0 (170.0 to 600.0)	360.0 (180.0 to 558.0)	294.0 (120.0 to 480.0)	330.0 (164.0 to 547.0)
Number of classes dispensed, n (%)						
1	1,577 (54.6)	1,551 (65.3)	97 (57.4)	99 (61.1)	560 (58.8)	517 (59.9)
2	1,061 (36.8)	686 (28.9)	62 (36.7)	52 (32.1)	332 (34.8)	286 (33.1)
≥ 3	249 (8.6)	140 (5.9)	10 (5.9)	11 (6.8)	61 (6.4)	60 (7.0)
By class						
Antidepressants	1,561 (40.3)	1,187 (30.7)	93 (38.3)	89 (36.6)	482 (35.1)	424 (30.8)
Antiepileptics	1,650 (42.6)	1,191 (30.8)	82 (33.7)	84 (34.6)	526 (38.3)	444 (32.3)
Antihypertensives	1,156 (29.9)	912 (23.6)	73 (30.0)	60 (24.7)	372 (27.1)	380 (27.6)
Calcium antagonist	84 (2.2)	54 (1.4)	< 10	< 10	29 (2.1)	23 (1.7)
OnabotulinumtoxinA						
Had ≥ 1 dispensation, n (%)	2,089 (54.0)	1,586 (41.0)	117 (48.1)	104 (42.8)	671 (48.8)	636 (46.3)
Number of injections						
Mean (SD)[a]	3.3 (1.3)	3.2 (1.4)	3.6 (1.8)	3.2 (1.5)	3.1 (1.5)	3.2 (1.4)
Median (Q1-Q3)[a]	3.0 (3.0 to 4.0)	3.0 (2.0 to 4.0)	4.0 (2.0 to 4.0)	3.0 (2.0 to 4.0)	3.0 (2.0 to 4.0)	3.0 (2.0 to 4.0)

CGRP = calcitonin gene–related peptide; NR = not reported; NSAID = nonsteroidal anti-inflammatory drug; Q1-Q3 = first and third quartiles; SD = standard deviation.

[a]Means and medians are calculated for those with 1 or more dispensations.

Table 41: Migraine-Related Medication Use (British Columbia)

Time period	CGRP inhibitor users subcohort		CGRP inhibitor switchers subcohort		CGRP inhibitor discontinuers subcohort	
	1 year before index	1 year after index	1 year before index	1 year after index	1 year before index	1 year after index
Total Number of Individuals	2,877		229		1,117	
Any migraine-related medication						
Had ≥ 1 dispensation, n (%)	2,632	2,582	220	214	993	923
Acute rescue medications						
Overall						
Had ≥ 1 dispensation, n (%)	2,360	2,263	201	191	848	773
Number of days supplied						
Mean (SD)[a]	173.35 (200.52)	160.03 (201.45)	191.05 (218.90)	186.15 (221.55)	170.47 (208.74)	170.36 (211.87)
Median (Q1-Q3)[a]	100 (37 to 231)	78 (29.5 to 213)	112 (38 to 262)	97 (33 to 278.5)	87 (30 to 240)	87 (30 to 234)
Number of classes dispensed, n (%)						
1	1,071	1,209	88	101	409	425
2	964	784	72	60	324	261
≥ 3	325	270	41	30	115	87
Nonspecific						
Had ≥ 1 dispensation, n (%)	1,621	1,502	154	129	595	537
By class, n (%)						
NSAIDs	964	805	89	71	338	272
Opioids	1,095	1,066	114	98	427	402
Migraine-specific						
Had ≥ 1 dispensation, n (%)	1,885	1,696	149	138	629	522
By class, n (%)						
Triptans	1,856	1,667	147	136	621	515
Ergots	70	60	7	7	21	22

Time period	CGRP inhibitor users subcohort		CGRP inhibitor switchers subcohort		CGRP inhibitor discontinuers subcohort	
	1 year before index	1 year after index	1 year before index	1 year after index	1 year before index	1 year after index
Rescue medications dispensed during CGRP inhibitor use, n (%)						
Had ≥ 1 dispensation, n (%)	NR	2,068	174	168	662	NR
By class, n (%)						
Had ≥ 1 dispensation of nonspecific rescue medications	NR	1,271	118	104	411	NR
Had ≥ 1 dispensation of migraine-specific medications	NR	1,554	124	125	450	NR
Triptans	NR	1,526	121	124	442	NR
Ergots	NR	49	6	5	12	NR
Prophylactic medications						
Overall						
Had ≥ 1 dispensation, n (%)	2,295	1,952	189	171	852	756
Nonspecific						
Had ≥ 1 dispensation, n (%)	1,981	1,658	155	138	732	633
Number of days supplied						
Mean (SD)[a]	368.45 (292.31)	380.27 (295.20)	349.11 (278.01)	376.84 (251.44)	346.61 (280.78)	378.50 (299.31)
Median (Q1-Q3)[a]	312 (154 to 480)	350 (173.25 to 510)	317 (131 to 420)	337.5 (245.75 to 501.5)	288 (130 to 450)	338 (150 to 482)
Number of classes dispensed, n (%)						
1	1,038	1,068	94	88	424	403
2	748	483	52	39	243	179
≥ 3	195	107	9	11	65	51
By class, n (%)						
Antidepressants	1,117	845	78	68	393	306
Antiepileptics	1,161	875	85	68	413	346

Time period	CGRP inhibitor users subcohort		CGRP inhibitor switchers subcohort		CGRP inhibitor discontinuers subcohort	
	1 year before index	1 year after index	1 year before index	1 year after index	1 year before index	1 year after index
Antihypertensives	765	571	54	52	280	225
Calcium antagonist	84	66	9	11	23	39
Specific	—	—	—	—	—	—
Had ≥ 1 dispensation, n (%)	1,012	740	87	77	317	329
OnabotulinumtoxinA: Number of injections						
Mean (SD)[a]	3.20 (1.32)	3.03 (1.45)	3.24 (1.50)	3.21 (1.94)	2.90 (1.52)	3.05 (1.34)
Median (Q1-Q3)[a]	3 (2 to 4)	3 (2 to 4)	4 (2 to 4)	3 (2 to 4)	3 (2 to 4)	3 (2 to 4)
Pizotifen: Number of days supplied						
Mean (SD)[a]	< 5	< 5	0 (0)	< 5	< 5	< 5
Median (Q1-Q3)[a]	< 5	< 5	0 (0 to 0)	< 5	< 5	< 5

CGRP = calcitonin gene–related peptide; NR = not reported; NSAID = nonsteroidal anti-inflammatory drug; Q1-Q3 = first and third quartiles; SD = standard deviation.
[a]Means and medians are calculated for those with 1 or more dispensations.

Table 42: Migraine-Related Medication Use (Manitoba)

Time period	CGRP inhibitor users subcohort		CGRP inhibitor switchers subcohort		CGRP inhibitor discontinuers subcohort	
	1-year preindex	1-year postindex	1-year preindex	1-year postindex	1-year preindex	1-year postindex
Total Number of Individuals	860		58		340	
Any migraine-related medication						
Had ≥ 1 dispensation, n (%)	834	801	54	49	320	300
Acute rescue medications						
Overall						
Had ≥ 1 dispensation, n (%)	717	664	48	42	273	242
Number of days supplied						
Mean (SD)[a]	166.81 (202.58)	153.84 (193.85)	175.37 (247.70)	228.26 (356.25)	160.28 (191.43)	164.27 (188.79)

Time period	CGRP inhibitor users subcohort		CGRP inhibitor switchers subcohort		CGRP inhibitor discontinuers subcohort	
	1-year preindex	1-year postindex	1-year preindex	1-year postindex	1-year preindex	1-year postindex
Median (Q1-Q3)[a]	96 (30 to 214)	75 (24 to 210.5)	94.5 (23.5 to 199.5)	103.5 (36 to 317.25)	82 (26 to 228)	94.5 (29.25 to 245.75)
Number of classes dispensed, n (%)						
1	345	363	28	22	146	130
2	275	243	S	S	89	89
≥ 3	97	58	< 5	< 5	38	23
Nonspecific						
Had ≥ 1 dispensation, n (%)	506	453	30	27	197	178
By class, n (%)						
NSAIDs	285	218	12	8	110	90
Opioids	378	345	21	22	152	139
Migraine-specific						
Had ≥ 1 dispensation, n (%)	522	457	37	32	176	147
By class, n (%)						
Triptans	519	455	37	32	175	146
Ergots	5	5	0	< 5	< 5	< 5
Rescue medications dispensed during CGRP inhibitor use, n (%)						
Had ≥ 1 dispensation, n (%)	NR	611	39	40	211	NR
By class, n (%)						
Had ≥ 1 dispensation of nonspecific rescue medications	NR	393	22	23	139	NR
Had ≥ 1 dispensation of migraine-specific medications	NR	425	29	31	131	NR
Triptans	NR	423	29	31	130	NR
Ergots	NR	< 5	0	0	< 5	NR
Prophylactic medications						

Time period	CGRP inhibitor users subcohort		CGRP inhibitor switchers subcohort		CGRP inhibitor discontinuers subcohort	
	1-year preindex	1-year postindex	1-year preindex	1-year postindex	1-year preindex	1-year postindex
Overall						
Had ≥ 1 dispensation, n (%)	751	631	42	38	271	251
Nonspecific						
Had ≥ 1 dispensation, n (%)	703	600	40	37	257	234
Number of days supplied						
Mean (SD)[a]	425.51 (325.92)	423.96 (329.92)	389.52 (304.73)	426.62 (313.23)	421.05 (346.41)	444.32 (363.19)
Median (Q1-Q3)[a]	360 (180 to 600)	360 (179.5 to 596)	352.5 (145.5 to 603.75)	360 (157 to 687)	360 (150 to 602)	360 (210 to 615)
Number of classes dispensed, n (%)						
1	287	333	21	21	108	124
2	292	205	S	S	107	90
≥ 3	124	62	< 5	< 5	42	20
By class						
Antidepressants	389	298	18	16	142	117
Antiepileptics	443	331	24	23	155	127
Antihypertensives	272	198	11	15	95	81
Calcium antagonist	155	106	8	5	61	41
Specific						
Had ≥ 1 dispensation, n (%)	149	89	5	< 5	40	53
Botulinum toxin: Number of injections						
Mean (SD)[a]	2.40 (1.33)	2.42 (1.37)	< 5	< 5	2.15 (1.32)	2.58 (1.31)
Median (Q1-Q3)[a]	2 (1 to 3)	2 (1 to 3.5)	< 5	< 5	2 (1 to 3)	2 (1 to 4)
Pizotifen: Number of days supplied						
Mean (SD)[a]	< 5	< 5	< 5	< 5	< 5	< 5
Median (Q1-Q3)[a]	< 5	< 5	< 5	< 5	< 5	< 5

CGRP = calcitonin gene–related peptide; NR = not reported; Q1-Q3 = first and third quartiles; S = suppressed; SD = standard deviation.

[a]Means and medians are calculated for those with 1 or more dispensations.

Table 43: Migraine-Related Medication Use (Nova Scotia)

Time period	CGRP inhibitor users subcohort		CGRP inhibitor discontinuers subcohort	
	1-year preindex	1-year postindex	1-year preindex	1-year postindex
Total Number of Individuals	578		222	
Any migraine-related medication				
Had ≥ 1 dispensation, n (%)	549 (95.0)	528 (91.3)	203 (91.4)	203 (91.4)
Acute rescue medications				
Overall				
Had ≥ 1 dispensation, n (%)	447 (77.3)	420 (72.7)	148 (66.7)	148 (66.7)
Number of days supplied				
Mean (SD)[a]	156.2 (187.0)	151.2 (187.6)	166.3 (219.3)	179.1 (204.9)
Median (Q1-Q3)[a]	87.0 (30.0 to 210.0)	73.0 (30.0 to 205.5)	80.0 (24.5 to 231.0)	105.5 (30.0 to 267.5)
Number of classes dispensed, n (%)				
1	304 (68.0)	282 (67.1)	103 (69.6)	97 (65.5)
2	117 (26.2)	119 (28.3)	37 (25.0)	42 (28.4)
≥ 3	26 (5.8)	19 (4.5)	8 (5.4)	9 (6.1)
Nonspecific				
Had ≥ 1 dispensation, n (%)	225 (38.9)	225 (38.9)	86 (38.7)	98 (44.1)
By class, n (%)				
NSAIDs	137 (23.7)	134 (23.2)	47 (21.2)	50 (22.5)
Opioids	130 (22.5)	126 (21.8)	55 (24.8)	66 (29.7)
Migraine-specific				
Had ≥ 1 dispensation, n (%)	345 (59.7)	314 (54.3)	98 (44.1)	91 (41.0)
By class, n (%)				
Triptans	339 (58.7)	312 (54.0)	98 (44.1)	90 (40.5)
Ergots	10 (1.7)	5 (0.9)	< 5	< 5
Rescue medications dispensed during CGRP inhibitor use, n (%)				
Had ≥ 1 dispensation, n (%)	NR	377 (65.2)	112 (50.5)	NR
By class, n (%)				
Had ≥ 1 dispensation of nonspecific rescue medications	NR	189 (32.7)	61 (27.5)	NR
Had ≥ 1 dispensation of migraine-specific medications	NR	284 (49.1)	76 (34.2)	NR

Time period	CGRP inhibitor users subcohort		CGRP inhibitor discontinuers subcohort	
	1-year preindex	1-year postindex	1-year preindex	1-year postindex
Triptans	NR	282 (48.8)	76 (34.2)	NR
Ergots	NR	< 5	< 5	NR
Prophylactic medications				
Overall				
Had ≥ 1 dispensation, n (%)	492 (85.1)	433 (74.9)	183 (82.4)	182 (82.0)
Nonspecific				
Had ≥ 1 dispensation, n (%)	398 (68.9)	322 (55.7)	145 (65.3)	131 (59.0)
Number of days supplied				
Mean (SD)[a]	374.2 (265.4)	384.7 (269.5)	375.5 (291.4)	403.1 (297.1)
Median (Q1-Q3)[a]	340.0 (180.0 to 480.0)	360.0 (180.0 to 520.0)	330.0 (150.0 to 504.0)	360.0 (180.0 to 590.0)
Number of classes dispensed, n (%)				
1	216 (54.3)	220 (68.3)	85 (58.6)	82 (62.6)
2	150 (37.7)	86 (26.7)	50 (34.5)	43 (32.8)
≥ 3	32 (8.0)	16 (5.0)	10 (6.9)	6 (4.6)
By class				
Antidepressants	213 (36.9)	161 (27.9)	76 (34.2)	64 (28.8)
Antiepileptics	233 (40.3)	168 (29.1)	84 (37.8)	73 (32.9)
Antihypertensives	150 (26.0)	101 (17.5)	47 (21.2)	42 (18.9)
Calcium antagonist	18 (3.1)	10 (1.7)	9 (4.1)	7 (3.2)
Specific				
Had ≥ 1 dispensation, n (%)	254 (43.9)	248 (42.9)	92 (41.4)	119 (53.6)
Botulinum toxin: Number of injections				
Mean (SD)[a]	3.6 (1.3)	3.0 (1.4)	3.6 (1.3)	3.2 (1.2)
Median (Q1-Q3)[a]	4.0 (3.0 to 4.0)	3.0 (2.0 to 4.0)	4.0 (3.0 to 4.0)	3.0 (2.0 to 4.0)

CGRP = calcitonin gene–related peptide; NR = not reported; S = suppressed; Q1-Q3 = first and third quartiles; SD = standard deviation.

[a]Means and medians are calculated for those with 1 or more dispensations.

Table 44: Migraine-Related Medication Use (Quebec)

	CGRP inhibitor users subcohort		CGRP inhibitor switchers subcohort		CGRP inhibitor discontinuers subcohort	
	1-year preindex	1-year postindex	1-year preindex	1-year postindex	1-year preindex	1-year postindex
N	N = 890		N = 20		N = 44	
Any migraine-related medication						
Had ≥ 1 dispensation, n (%)	865 (97.19%)	823 (92.47%)	19 (95.00%)	16 (80.00%)	40 (90.91%)	33 (75.00%)
Acute rescue medications						
Overall						
Had ≥ 1 dispensation, n (%)	784 (88.09%)	747 (83.93%)	17 (85%)	16 (80%)	35 (79.55%)	32 (72.73%)
Number of days supplied	122,915	113,778	3195	2944	5424	3448
Mean (SD)[a]	156.78 (168.86)	152.31 (173.95)	187.94 (205.31)	184.00 (196.64)	154.97 (152.59)	107.75 (123.61)
Median (Q1-Q3)[a]	96.00 (36.75 to 223.50)	81.00 (35.00 to 210.00)	112.00 (33.00 to 308.00)	126.00 (37.75 to 246.75)	66.00 (39.00 to 252.50)	62.00 (16.50 to 150.50)
Number of classes dispensed, n (%)						
1	434 (48.76%)	427 (47.98%)	10 (50%)	10 (50%)	19 (43.18%)	22 (50.00%)
2	281 (31.57%)	247 (27.75%)	6 (30%)	< 5	15 (34.09%)	8 (18.18%)
≥ 3	69 (7.75%)	73 (8.20%)	< 5	< 5	< 5	< 5
Nonspecific						
Had ≥ 1 dispensation, n (%)	431 (48.43%)	405 (45.51%)	8 (40%)	8 (40%)	20 (45.45%)	16 (36.36%)
By class, n (%)						
NSAIDs	286 (32.13%)	258 (28.99%)	< 5	< 5	14 (31.82%)	10 (22.73%)
Opioids	231 (25.96%)	238 (26.74%)	7 (35%)	5 (25%)	7 (15.91%)	8 (18.18%)
Migraine-specific						
Had ≥ 1 dispensation, n (%)	678 (76.18%)	637 (71.57%)	16 (80%)	14 (70%)	31 (70.45%)	26 (59.09%)

	CGRP inhibitor users subcohort		CGRP inhibitor switchers subcohort		CGRP inhibitor discontinuers subcohort	
	1-year preindex	1-year postindex	1-year preindex	1-year postindex	1-year preindex	1-year postindex
N	N = 890		N = 20		N = 44	
By class, n (%)						
Triptans	674 (75.73%)	632 (71.01%)	16 (80%)	13 (65%)	31 (70.45%)	26 (59.09%)
Ergots	14 (1.57%)	16 (1.80%)	0	< 5	0	0
Rescue medications dispensed during CGRP inhibitor use, n (%)						
Had ≥ 1 dispensation	NR	724 (81.35%)	14 (70.00%)	15 (75.00%)	30 (68.18%)	NR
Had ≥ 1 dispensation of nonspecific rescue medications	NR	370 (41.57%)	5 (25.00%)	7 (35.00%)	26 (59.09%)	NR
Had ≥ 1 dispensation of migraine-specific medications	NR	626 (70.34%)	13 (65.00%)	13 (65.00%)	11 (25.00%)	NR
Triptans	NR	622 (69.89%)	13 (65.00%)	13 (65.00%)	11 (25.00%)	NR
Ergots	NR	12 (1.35%)	0	< 5	0	NR
Prophylactic medications						
Overall						
Had ≥ 1 dispensation, n (%)	720 (80.90%)	517 (58.09%)	11 (55.00%)	7 (35.00%)	17 (38.64%)	< 5
Nonspecific						
Had ≥ 1 dispensation, n (%)	699 (78.54%)	501 (56.29%)	10 (50.00%)	7 (35.00%)	16 (36.36%)	< 5
Number of days supplied	535,446	227,585	5235	4773	1,927	451
Mean (SD)[a]	766.02 (765.45)	454.26 (421.91)	523.50 (320.08)	681.86 (436.94)	120.44 (140.92)	150.33 (183.06)
Median (Q1-Q3)[a]	514.00 (255.00 to 1014.50)	352.00 (168.00 to 638.00)	487.50 (343.50 to 765.50)	540.00 (423.00 to 919.00)	55.50 (30.00 to 157.25)	60.00 (45.00 to 210.50)

	CGRP inhibitor users subcohort		CGRP inhibitor switchers subcohort		CGRP inhibitor discontinuers subcohort	
	1-year preindex	1-year postindex	1-year preindex	1-year postindex	1-year preindex	1-year postindex
N	N = 890		N = 20		N = 44	
Number of classes dispensed, n (%)						
1	321 (36.07%)	332 (37.30%)	< 5	< 5	14 (31.82%)	< 5
2	263 (29.55%)	149 (16.74%)	5 (25.00%)	5 (25.00%)	< 5	0
≥ 3	115 (12.92%)	20 (2.25%)	< 5	< 5	0	0
By class						
Antidepressants	400 (44.94%)	269 (30.22%)	5 (25.00%)	< 5	4 (9.09%)	2 (4.55%)
Antiepileptics	388 (43.60%)	206 (23.15%)	6 (30.00%)	6 (30.00%)	6 (13.64%)	1 (2.27%)
Antihypertensives	346 (38.88%)	183 (20.56%)	5 (25.00%)	< 5	7 (15.91%)	0
Calcium antagonist	64 (7.19%)	33 (3.71%)	< 5	0	< 5	0
Specific						
Had ≥ 1 dispensation, n (%)	86 (9.66%)	43 (4.83%)	< 5	0	< 5	< 5
Botulinum toxin						
Had ≥ 1 dispensation, n (%)	73 (8.20%)	40 (4.49%)	< 5	0	< 5	0
Number of injections	122	65	1	0	2	0
Mean (SD)[a]	1.67 (0.78)	1.62 (0.81)	1 (NA)	0	2.00 (NA)	0
Median (Q1-Q3)[a]	1.00 (1.00 to 2.00)	1.00 (1.00 to 2.00)	1.00 (1.00 to 1.00)	0	2.00 (2.00 to 2.00)	0
Pizotifen	—	—	—	—	—	—
Had ≥ 1 dispensation, n (%)	15 (1.69%)	< 5	< 5	0	0	< 5

CGRP = calcitonin gene–related peptide; NR = not reported; NSAID = nonsteroidal anti-inflammatory drug; Q1-Q3 = first and third quartile; SD = standard deviation.

[a]Means and medians are calculated for those with 1 or more dispensations.

Table 45: Migraine-Related Medication Use (Saskatchewan)

Time period	CGRP inhibitor users subcohort		CGRP inhibitor switchers subcohort		CGRP inhibitor discontinuers subcohort	
	1-year preindex	1-year postindex	1-year preindex	1-year postindex	1-year preindex	1-year postindex
Total number of individuals	482		10		173	
Any migraine-related medication						
Had ≥ 1 dispensation, n (%)	462	444	10	10	163	148
Acute rescue medications						
Overall						
Had ≥ 1 dispensation, n (%)	423	393	9	9	142	125
Number of days supplied						
Mean (SD)[a]	134.93 (185.64)	130.83 (179.47)	< 5	< 5	123.16 (185.18)	134.01 (183.50)
Median (Q1-Q3)[a]	66 (26 to 156)	61 (20 to 161)	< 5	< 5	60 (15 to 127.75)	60 (16 to 185)
Number of classes dispensed, n (%)						
1	233	234	5	S	82	68
2	143	128	< 5	< 5	44	50
≥ 3	47	31	< 5	0	16	7
Nonspecific						
Had ≥ 1 dispensation, n (%)	251	226	5	6	87	83
By class, n (%)						
NSAIDs	166	144	5	6	55	50
Opioids	159	140	< 5	< 5	58	50
Migraine-specific						
Had ≥ 1 dispensation, n (%)	334	298	7	6	104	89
By class, n (%)						
Triptans	333	298	7	6	104	89
Ergots	< 5	< 5	0	0	< 5	0

Time period	CGRP inhibitor users subcohort		CGRP inhibitor switchers subcohort		CGRP inhibitor discontinuers subcohort	
	1-year preindex	1-year postindex	1-year preindex	1-year postindex	1-year preindex	1-year postindex
Rescue medications dispensed during CGRP inhibitor use, n (%)						
Had ≥ 1 dispensation, n (%)	NR	355	6	8	108	NR
By class, n (%)						
Had ≥ 1 dispensation of nonspecific rescue medications	NR	186	< 5	5	59	NR
Had ≥ 1 dispensation of migraine-specific medications	NR	270	5	5	75	NR
Triptans	NR	270	5	5	75	NR
Ergots	NR	< 5	0	0	< 5	NR
Prophylactic medications						
Overall						
Had ≥ 1 dispensation, n (%)	393	333	7	7	132	124
Nonspecific						
Had ≥ 1 dispensation, n (%)	366	313	6	7	129	117
Number of days supplied						
Mean (SD)[a]	369.93 (289.24)	363.66 (286.63)	< 5	< 5	342.55 (292.61)	376.76 (299.22)
Median (Q1-Q3)[a]	319 (150 to 498)	330 (170 to 460)	< 5	< 5	298 (104 to 417)	336 (130 to 540)
Number of classes dispensed, n (%)						
1	195	202	< 5	S	77	66
2	122	89	< 5	< 5	37	37
≥ 3	49	22	0	0	15	14
By class						
Antidepressants	213	162	< 5	< 5	68	62
Antiepileptics	211	160	6	5	76	63
Antihypertensives	136	106	0	< 5	46	48
Calcium antagonist	28	19	0	0	6	10

Time period	CGRP inhibitor users subcohort		CGRP inhibitor switchers subcohort		CGRP inhibitor discontinuers subcohort	
	1-year preindex	1-year postindex	1-year preindex	1-year postindex	1-year preindex	1-year postindex
Specific						
Had ≥ 1 dispensation, n (%)	104	72	< 5	0	24	30
OnabotulinumtoxinA: Number of injections						
Mean (SD)[a]	2.73 (1.40)	2.58 (1.38)	< 5	0 (0)	2.37 (1.46)	2.83 (1.34)
Median (Q1-Q3)[a]	3 (1.75 to 4)	3 (1 to 3.25)	< 5	0 (0 to 0)	2 (1 to 3.25)	3 (2 to 4)

CGRP = calcitonin gene–related peptide; NR = not reported; NSAID = nonsteroidal anti-inflammatory drug; Q1-Q3 = first and third quartile; S = suppressed; SD = standard deviation.

[a]Means and medians are calculated for those with 1 or more dispensations.

Table 46: Migraine-Related Medication Use (US)

Time period	CGRP inhibitor users subcohort N = 55,212		CGRP inhibitor switchers subcohort N = 4,048		CGRP inhibitor discontinuers subcohort N = 7,078	
	1-year preindex	1-year postindex	1-year preindex	1-year postindex	1-year preindex	1-year postindex
Any migraine-related medication						
Had ≥ 1 dispensation, n (%)	51,435 (93.2%)	48,992 (88.7%)	3,876 (95.8%)	3,723 (92.0%)	5,580 (78.8%)	4,959 (70.1%)
Acute rescue medications						
Overall						
Had ≥ 1 dispensation, n (%)	47,614 (86.2%)	44,232 (80.1%)	3,651 (90.2%)	3,378 (83.5%)	5,265 (74.4%)	4,871 (68.8%)
Number of days supplied						
Mean (SD)[a]	162.5 (168.7)	159.0 (171.3)	187.5 (184.9)	185.3 (194.6)	125.4 (144.2)	180.5 (331.3)
Median (Q1-Q3)[a]	101 (35 to 240)	94 (30 to 240)	126 (52 to 270)	120 (36 to 276)	65 (30 to 177)	68 (20 to 220)
Number of classes dispensed, n (%)						
1	23,324 (42.2%)	23,033 (41.7%)	1,581 (39.1%)	1,590 (39.3%)	2,944 (41.6%)	2,701 (38.2%)
2	17,980 (32.6%)	15,540 (28.2%)	1,410 (34.8%)	1,173 (29.0%)	1,784 (25.2%)	1,562 (22.1%)

Time period	CGRP inhibitor users subcohort N = 55,212		CGRP inhibitor switchers subcohort N = 4,048		CGRP inhibitor discontinuers subcohort N = 7,078	
	1-year preindex	1-year postindex	1-year preindex	1-year postindex	1-year preindex	1-year postindex
≥ 3	6,310 (11.4%)	5,659 (10.3%)	660 (16.3%)	615 (15.2%)	537 (7.6%)	608 (8.6%)
Nonspecific						
Had ≥ 1 dispensation, n (%)	30,772 (55.7%)	28,970 (52.5%)	2,351 (58.1%)	2,207 (54.5%)	3,237 (45.7%)	3,463 (48.9%)
By class, n (%)						
NSAIDs	17,153 (55.7%)	15,467 (53.4%)	1,372 (58.4%)	1,239 (56.1%)	1,762 (54.4%)	1878 (54.2%)
Opioids	13,619 (44.3%)	13,503 (46.6%)	979 (41.6%)	968 (43.9%)	1,475 (45.6%)	1,585 (45.8%)
Migraine-specific						
Had ≥ 1 dispensation, n (%)	37,223 (67.4%)	32,435 (58.8%)	3,046 (75.3%)	2,606 (64.4%)	3,922 (55.4%)	3,090 (43.7%)
By class, n (%)						
Triptans	31,717 (85.2%)	25,165 (77.6%)	2,263 (74.3%)	1,698 (65.2%)	3,238 (82.6%)	2,308 (74.7%)
Ergots	292 (0.8%)	262 (0.8%)	31 (1.0%)	34 (1.3%)	21 (0.5%)	15 (0.5%)
Ditans	31 (0.1%)	124 (0.4%)	9 (0.3%)	28 (1.1%)	6 (0.2%)	10 (0.3%)
Gepants	5,183 (13.9%)	6,884 (21.2%)	743 (24.4%)	846 (32.5%)	657 (16.8%)	757 (24.5%)
Rescue medications dispensed during CGRP inhibitor use, n (%)						
Had ≥ 1 dispensation	NR	36,424 (66.0%)	3,065 (75.7%)	3,172 (78.4%)	3,574 (50.5%)	NR
By class						
Had ≥ 1 dispensation of nonspecific rescue medications	NR	14,870 (26.9%)	1,050 (25.9%)	1,217 (30.1%)	1,288 (18.2%)	NR
Had ≥ 1 dispensation of migraine-specific medications	NR	21,554 (39.0%)	2,015 (49.8%)	1,955 (48.3%)	2,286 (32.3%)	NR
Triptans	NR	16,670 (77.3%)	549 (27.3%)	1,231 (63.0%)	1,941 (84.9%)	NR
Ergots	NR	86 (0.4%)	12 (0.6%)	11 (0.6%)	8 (0.4%)	NR

Time period	CGRP inhibitor users subcohort N = 55,212		CGRP inhibitor switchers subcohort N = 4,048		CGRP inhibitor discontinuers subcohort N = 7,078	
	1-year preindex	1-year postindex	1-year preindex	1-year postindex	1-year preindex	1-year postindex
Ditans	NR	44 (0.2%)	3 (0.2%)	10 (0.5%)	6 (0.3%)	NR
Gepants	NR	4,754 (22.1%)	549 (27.3%)	703 (36.0%)	331 (14.5%)	NR
Prophylactic medications						
Overall						
Had ≥ 1 dispensation, n (%)	34,313 (62.2%)	30,151 (54.6%)	2,807 (69.3%)	2,536 (62.7%)	1,979 (28.0%)	744 (10.5%)
Nonspecific						
Had ≥ 1 dispensation, n (%)	30,976 (56.1%)	26,737 (48.4%)	2,532 (62.6%)	2,213 (54.7%)	1,811 (25.6%)	642 (9.1%)
Number of days supplied						
Mean (SD)[a]	282.1 (242.0)	306.8 (223.9)	308.5 (229.0)	342.3 (240.2)	100.1 (93.9)	240.1 (397.7)
Median (Q1-Q3)[a]	210 (90 to 400)	300 (120 to 390)	287.5 (120 to 420)	330 (150 to 450)	60 (30 to 120)	90 (30 to 240)
Number of classes dispensed, n (%)						
1	21,716 (39.3%)	19,269 (34.9%)	1,675 (41.4%)	1,473 (36.4%)	1,554 (22.0%)	476 (6.7%)
2	8,058 (14.6%)	6,625 (11.8%)	736 (18.2%)	650 (16.1%)	235 (3.3%)	133 (1.9%)
≥ 3	1202 (2.2%)	943 (1.7%)	121 (3.0%)	90 (2.2)	22 (0.3%)	33 (0.5%)
By class						
Antidepressants	8,310 (26.8%)	6,760 (25.3%)	625 (24.7%)	502 (22.7%)	618 (34.1%)	173 (27.0%)
Antiepileptics	8,864 (28.6%)	8,913 (33.3%)	743 (29.3%)	750 (33.9%)	527 (29.1%)	226 (35.2%)
Antihypertensives	13,802 (44.6%)	11.064 (41.4%)	1,164 (46.0%)	961 (43.4%)	666 (36.8%)	243 (37.9%)
Calcium antagonist	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
OnabotulinumtoxinA						
Had ≥ 1 dispensation, n (%)	8,478 (15.4%)	8,169 (14.8%)	766 (18.9%)	846 (20.9%)	242 (3.4%)	185 (2.6%)
Number of injections						

Time period	CGRP inhibitor users subcohort N = 55,212		CGRP inhibitor switchers subcohort N = 4,048		CGRP inhibitor discontinuers subcohort N = 7,078	
	1-year preindex	1-year postindex	1-year preindex	1-year postindex	1-year preindex	1-year postindex
Mean (SD)[a]	3.0 (1.3)	2.9 (1.3)	2.8 (1.4)	3.0 (1.3)	1.9 (1.0)	3.0 (2.9)
Median (Q1-Q3)[a]	3 (2 to 4)	3 (2 to 4)	3 (2 to 4)	3 (2 to 4)	2 (1 to 2)	2 (1 to 3)

CGRP = calcitonin gene–related peptide; NR = not reported; NSAID = nonsteroidal anti-inflammatory drug; Q1-Q3 = first and third quartile; SD = standard deviation.
[a]Means and medians are calculated for those with ≥ 1 dispensation.

Table 47: Migraine-Related Medication Use (US)

Initial CGRP inhibitor	Erenumab	Galcanezumab	Fremanezumab	Eptinezumab	Atogepant	Rimegepant
Rescue medications dispensed during CGRP inhibitor use, n (%)						
Had ≥ 1 dispensation	15,129 (71.6%)	11,875 (67.8%)	6,162 (68.1%)	25 (80.7%)	47 (49.5%)	3,186 (43.0%)
By class						
Had ≥ 1 dispensation of nonspecific rescue medications	6,271 (29.7%)	4,702 (26.9%)	2,562 (28.3%)	14 (45.2%)	14 (14.7%)	1,307 (17.7%)
Had ≥ 1 dispensation of migraine-specific medications	8,858 (41.9%)	7,173 (41.0%)	3,600 (39.8%)	11 (35.5%)	33 (34.7%)	1,879 (25.4%)
Triptans	7,308 (82.5%)	5,590 (77.9%)	2,838 (78.8%)	6 (54.6%)	18 (54.6%)	910 (48.4%)
Ergots	36 (0.4%)	26 (0.4%)	14 (0.4%)	0 (0.0%)	0 (0.0%)	10 (0.5%)
Ditans	16 (0.2%)	13 (0.2%)	6 (0.2%)	0 (0.0%)	1 (3.0%)	8 (0.4%)
Gepants	1,498 (16.9%)	1,544 (21.5%)	742 (20.6%)	5 (45.5%)	14 (42.4%)	951 (50.6%)
Prophylactic medications						
Overall						
Had ≥ 1 dispensation, n (%)	13,934 (64.8%)	11,150 (62.1%)	5,947 (63.6%)	28 (70.0%)	118 (65.2%)	3,136 (50.6%)
Nonspecific						
Had ≥ 1 dispensation, n (%)	12,459 (58.0%)	10,293 (57.4%)	5,360 (57.3%)	21 (52.5%)	102 (56.4%)	2,741 (44.2%)
Number of days supplied						

Initial CGRP inhibitor	Erenumab	Galcanezumab	Fremanezumab	Eptinezumab	Atogepant	Rimegepant
Mean (SD)[a]	285.4 (219.1)	276.8 (217.9)	281.9 (217.3)	271.9 (174.3)	263.7 (209.1)	258.3 (197.3)
Median (Q1-Q3)[a]	270 (90 to 390)	270 (90 to 370)	270 (90 to 390)	294 (90 to 360)	210 (90 to 360)	240 (90 to 360)
Number of classes dispensed, n (%)						
1	8,601 (40.0%)	7,181 (40.0%)	3,733 (39.9%)	15 (37.5%)	72 (39.8%)	2,114 (34.1%)
2	3,343 (15.6%)	2,716 (15.1%)	1,403 (15.0%)	5 (12.5%)	28 (15.5%)	563 (9.1%)
≥ 3	515 (2.4%)	396 (2.2%)	224 (2.4%)	1 (2.5%)	2 (1.1%)	64 (1.0%)
By class						
Antidepressants	3,199 (25.7%)	2,823 (27.4%)	1,448 (27.0%)	5 (23.8%)	29 (28.4%)	806 (29.4%)
Antiepileptics	3,557 (28.6%)	2,847 (27.7%)	1,598 (29.8%)	6 (28.6%)	37 (36.3%)	819 (29.9%)
Antihypertensives	5,703 (45.8%)	4,623 (44.9%)	2,314 (43.2%)	10 (47.6%)	36 (35.3%)	1,116 (40.7%)
Calcium antagonist	0	0	0	0	0	0
OnabotulinumtoxinA						
Had ≥ 1 dispensation, n (%)	3,906 (18.2%)	2,261 (12.6%)	1,412 (15.1%)	17 (42.5%)	38 (21.0%)	844 (13.6%)
Number of injections						
Mean (SD)[a]	3.0 (1.3)	3.0 (1.4)	3.0 (1.4)	2.9 (0.9)	3.3 (1.1)	3.3 (1.3)
Median (Q1-Q3)[a]	3 (2 to 4)	3 (2 to 4)	3 (2 to 4)	3 (3 to 3)	4 (3 to 4)	4 (2 to 4)

CGRP = calcitonin gene–related peptide; SD = standard deviation; NSAID = nonsteroidal anti-inflammatory drug; Q1-Q3 = first and third quartile.

[a]Means and medians are calculated for those with 1 or more dispensations.

Table 48: Sociodemographic and Clinical Characteristics (Alberta)

Characteristics	CGRP inhibitor users subcohort N = 3,869	CGRP inhibitor switchers subcohort N = 243	CGRP discontinuers subcohort N = 1,375
Demographic			
Age (years)			
Mean (SD)	45.6 (12.9)	46.0 (13.4)	46.2 (13.6)
Median (1st quartile – 3rd quartile)	46.0 (37.0 to 54.0)	47.0 (36.0 to 57.0)	46.0 (36.0 to 55.0)
Age (years): n (%)			
18 to 44	1,789 (46.2)	103 (42.4)	628 (45.7)
45 to 64	1,797 (46.4)	119 (49.0)	608 (44.2)
65+	283 (7.3)	21 (8.6)	139 (10.1)
Sex: n (%)			
Female	3,221 (83.3)	201 (82.7)	1,123 (81.7)
Male	648 (16.7)	42 (17.3)	252 (18.3)
Residence location: n (%)			
Urban	3,482 (90.0)	220 (90.5)	1,226 (89.2)
Rural	387 (10.0)	23 (9.5)	149 (10.8)
Socioeconomic (CIMD), n (%)			
Residential instability			
1 (most well off)	886 (22.9)	61 (25.1)	312 (22.7)
2	862 (22.3)	61 (25.1)	288 (20.9)
3	773 (20.0)	41 (16.9)	280 (20.4)
4	652 (16.9)	S	S
5 (most deprived)	684 (17.7)	41 (16.9)	253 (18.4)
Unknown	12 (0.3)	< 10	< 10
Economic dependency			
1 (most well off)	1,150 (29.7)	69 (28.4)	400 (29.1)
2	782 (20.2)	59 (24.3)	264 (19.2)
3	776 (20.1)	36 (14.8)	271 (19.7)
4	677 (17.5)	44 (18.1)	269 (19.6)
5 (most deprived)	472 (12.2)	S	S
Unknown	12 (0.3)	< 10	< 10
Situational vulnerability			
1 (most well off)	1,019 (26.3)	80 (32.9)	338 (24.6)

Characteristics	CGRP inhibitor users subcohort N = 3,869	CGRP inhibitor switchers subcohort N = 243	CGRP discontinuers subcohort N = 1,375
2	995 (25.7)	47 (19.3)	346 (25.2)
3	833 (21.5)	50 (20.6)	299 (21.7)
4	665 (17.2)	46 (18.9)	256 (18.6)
5 (most deprived)	345 (8.9)	S	S
Unknown	12 (0.3)	< 10	< 10
Ethnocultural composition			
1 (most well off)	482 (12.5)	S	S
2	688 (17.8)	44 (18.1)	254 (18.5)
3	817 (21.1)	51 (21.0)	292 (21.2)
4	854 (22.1)	60 (24.7)	291 (21.2)
5 (most deprived)	1,016 (26.3)	65 (26.7)	361 (26.3)
Unknown	12 (0.3)	< 10	< 10
Comorbidities			
Charlson Comorbidity Index			
Mean (SD)	0.2 (0.7)	0.3 (0.7)	0.3 (0.7)
Median; min, max	0.0; 0.0, 10.0	0.0; 0.0, 5.0	0.0; 0.0, 8.0
Category, n (%)			
0: no comorbid condition	3,226 (83.4)	197 (81.1)	1,147 (83.4)
1 to 2: mild comorbidity	584 (15.1)	41 (16.9)	204 (14.8)
3 to 4: moderate comorbidity	45 (1.2)	< 10	S
≥ 5: severe comorbidity	14 (0.4)	< 10	< 10
Comorbid condition, n (%)			
Cardiovascular disease	73 (1.9)	< 10	30 (2.2)
Depression	735 (19.0)	61 (25.1)	287 (20.9)
Anxiety	535 (13.8)	41 (16.9)	196 (14.3)
Asthma	76 (2.0)	< 10	< 10
Epilepsy	45 (1.2)	0 (0.0)	18 (1.3)
Hypertension	293 (7.6)	19 (7.8)	119 (8.7)
Obstructive sleep apnea	142 (3.7)	12 (4.9)	49 (3.6)

CIMD = Canadian Index of Multiple Deprivation; SD = standard deviation.

Table 49: Sociodemographic and Clinical Characteristics (British Columbia)

Characteristics	CGRP inhibitor users subcohort N = 2,877	CGRP inhibitor switchers subcohort N = 229	CGRP discontinuers subcohort N = 1,117
Demographic			
Age (years)			
Mean (SD)	46.18 (13.19)	48.29 (12.78)	46.49 (13.88)
Median (1st quartile – 3rd quartile)	46 (37 to 56)	48 (40 to 57)	47 (36 to 57)
Age (years): n (%)			
18 to 44	1,287 (44.73%)	84 (36.68%)	502 (44.94%)
45 to 64	1,345 (46.75%)	114 (49.78%)	505 (45.21%)
65+	245 (8.52%)	31 (13.54%)	110 (9.85%)
Sex: n (%)			
Female	2,336 (81.20%)	192 (83.84%)	868 (77.71%)
Male	541 (18.80%)	37 (16.16%)	249 (22.29%)
Socioeconomic, n (%)			
Residential instability			
1 (most well off)	495 (17.21%)	42 (18.34%)	176 (15.76%)
2	586 (20.37%)	45 (19.65%)	221 (19.79%)
3	552 (19.19%)	45 (19.65%)	223 (19.96%)
4	505 (17.55%)	S	200 (17.91%)
5 (most deprived)	603 (20.96%)	57 (24.89%)	231 (20.68%)
Unknown	136 (4.73%)	< 5	66 (5.91%)
Economic dependency			
1 (most well off)	104 (3.61%)	S	39 (3.49%)
2	401 (13.94%)	41 (17.90%)	158 (14.15%)
3	641 (22.28%)	60 (26.20%)	245 (21.93%)
4	836 (29.06%)	64 (27.95%)	313 (28.02%)
5 (most deprived)	759 (26.38%)	56 (24.45%)	296 (26.50%)
Unknown	136 (4.73%)	< 5	66 (5.91%)
Ethnocultural composition			
1 (most well off)	967 (33.61%)	83 (36.24%)	334 (29.90%)
2	552 (19.19%)	S	234 (20.95%)
3	445 (15.47%)	35 (15.28%)	170 (15.22%)
4	402 (13.97%)	36 (15.72%)	158 (14.15%)

Characteristics	CGRP inhibitor users subcohort N = 2,877	CGRP inhibitor switchers subcohort N = 229	CGRP discontinuers subcohort N = 1,117
5 (most deprived)	375 (13.03%)	39 (17.03%)	155 (13.88%)
Unknown	136 (4.73%)	< 5	66 (5.91%)
Residence location: n (%)			
Urban	2,550 (88.63%)	208 (90.83%)	967 (86.57%)
Rural/Remote	196 (6.81%)	S	85 (7.61%)
Missing/Invalid	131 (4.55%)	< 5	65 (5.82%)

CGRP = calcitonin gene–related peptide; Q1-Q3 = first and third quartile; Q = quintile; SD = standard deviation.

Table 50: Sociodemographic and Clinical Characteristics (Manitoba)

Characteristics	CGRP inhibitor users subcohort N = 860	CGRP inhibitor switchers subcohort N = 58	CGRP discontinuers subcohort N = 340
Demographic			
Age (years)			
Mean (SD)	45.20 (14.62)	44.55 (14.77)	46.27 (15.33)
Median (Q1-Q3)	45.5 (34 to 56)	47 (32 to 55.75)	46 (34 to 57)
Age (years): n (%)			
18 to 44	414 (48.14%)	25 (43.10%)	155 (45.59%)
45 to 64	362 (42.09%)	27 (46.55%)	146 (42.94%)
65+	84 (9.77%)	6 (10.34%)	39 (11.47%)
Sex: n (%)			
Female	705 (81.98%)	41 (70.69%)	269 (79.12%)
Male	155 (18.02%)	17 (29.31%)	71 (20.88%)
Socioeconomic, n (%)			
Residential instability			
1 (most well off)	208 (24.19%)	18 (31.03%)	86 (25.29%)
2	S	11 (18.97%)	S
3	155 (18.02%)	6 (10.34%)	58 (17.06%)
4	201 (23.37%)	14 (24.14%)	69 (20.29%)
5 (most deprived)	149 (17.33%)	9 (15.52%)	72 (21.18%)
Unknown	< 5	0 (0.00%)	< 5
Economic dependency			
1 (most well off)	114 (13.26%)	6 (10.34%)	46 (13.53%)

Characteristics	CGRP inhibitor users subcohort N = 860	CGRP inhibitor switchers subcohort N = 58	CGRP discontinuers subcohort N = 340
2	210 (24.42%)	15 (25.86%)	89 (26.18%)
3	210 (24.42%)	16 (27.59%)	69 (20.29%)
4	232 (26.98%)	11 (18.97%)	91 (26.76%)
5 (most deprived)	< 5 < 5	10 (17.24%)	S
Unknown	< 5	0 (0.00%)	< 5
Ethnocultural composition			
1 (most well off)	229 (26.63%)	18 (31.03%)	97 (28.53%)
2	195 (22.67%)	8 (13.79%)	75 (22.06%)
3	179 (20.81%)	13 (22.41%)	63 (18.53%)
4	S	7 (12.07%)	< 5 < 5
5 (most deprived)	128 (14.88%)	12 (20.69%)	58 (17.06%)
Unknown	< 5	0 (0.00%)	< 5
Residence location: n (%)			
Urban	661 (76.86%)	50 (86.21%)	255 (75.00%)
Rural/Remote	S	8 (13.79%)	S
Missing/Invalid	< 5	0 (0.00%)	< 5

CGRP = calcitonin gene–related peptide; Q = quintile; Q1-Q3 = first and third quartile; S = suppressed; SD = standard deviation.

Table 51: Sociodemographic and Clinical Characteristics (Nova Scotia)

Characteristics	CGRP inhibitor users subcohort	CGRP discontinuers subcohort
Demographic		
Age (years)		
Mean (SD)	47.9 (12.2)	49.5 (12.7)
Median (IQR)	49.0 (40.0 to 57.0)	50.0 (42.0 to 59.0)
Age (years): n (%)		
18 to 44	215 (37.2)	81 (36.5)
45 to 64	323 (55.9)	118 (53.2)
65+	40 (6.9)	23 (10.4)
Sex: n (%)		
Female	475 (82.2)	175 (78.8)
Male	103 (17.8)	47 (21.2)
Residence location: n (%)		

Characteristics	CGRP inhibitor users subcohort	CGRP discontinuers subcohort
Urban	N/A	N/A
Rural	N/A	N/A
Socioeconomic (CIMD), n (%)		
Residential instability		
1 (most well off)	186 (32.2)	72 (32.4)
2	113 (19.6)	45 (20.3)
3	116 (20.1)	41 (18.5)
4	105 (18.2)	37 (16.7)
5 (most deprived)	58 (10.0)	27 (12.2)
Unknown	0 (0.0)	0 (0.0)
Economic dependency		
1 (most well off)	39 (6.7)	16 (7.2)
2	81 (14.0)	23 (10.4)
3	117 (20.2)	41 (18.5)
4	168 (29.1)	68 (30.6)
5 (most deprived)	173 (29.9)	74 (33.3)
Unknown	0 (0.0)	0 (0.0)
Situational vulnerability		
1 (most well off)	198 (34.3)	70 (31.5)
2	119 (20.6)	43 (19.4)
3	102 (17.6)	45 (20.3)
4	79 (13.7)	35 (15.8)
5 (most deprived)	80 (13.8)	29 (13.1)
Unknown	0 (0.0)	0 (0.0)
Ethnocultural composition		
1 (most well off)	109 (18.9)	40 (18.0)
2	94 (16.3)	43 (19.4)
3	104 (18.0)	37 (16.7)
4	92 (15.9)	36 (16.2)
5 (most deprived)	179 (31.0)	66 (29.7)
Unknown	0 (0.0)	0 (0.0)
Comorbidities		
Charlson Comorbidity Index		

Characteristics	CGRP inhibitor users subcohort	CGRP discontinuers subcohort
Mean (SD)	0.2 (0.5)	0.1 (0.3)
Median; min, max	0.0; 0.0, 5.0	0.0; 0.0, 2.0
Category, n (%)		
0: no comorbid condition	509 (88.1)	207 (93.2)
1 to 2: mild comorbidity	65 (11.2)	15 (6.8)
3 to 4: moderate comorbidity	< 5	0 (0.0)
≥ 5: severe comorbidity	< 5	0 (0.0)
Comorbid condition, n (%)		
Cardiovascular disease	71 (12.3)	17 (7.7)
Depression	48 (8.3)	6 (2.7)
Anxiety	76 (13.1)	21 (9.5)
Asthma	5 (0.9)	< 5
Epilepsy	< 5	0 (0.0)
Hypertension	36 (6.2)	6 (2.7)
Obstructive sleep apnea	15 (2.6)	< 5

Table 52: Sociodemographic and Clinical Characteristics (Quebec)

Characteristics	CGRP inhibitor users subcohort N = 890	CGRP inhibitor switchers subcohort N = 20	CGRP discontinuers subcohort N = 44
Demographic			
Age (years)			
Mean (SD)	53.78(14.68)	59.1 (14.57)	49.73 (17.88)
Median (Q1-Q3)	56 (43 to 66)	61.5 (55 to 68)	52 (31.75 to 66)
Age (years): n (%)			
18 to 44	238 (26.74%)	< 5	16 (36.36%)
45 to 64	405 (45.51%)	S	15 (34.09%)
65+	247 (27.75%)	9 (45%)	13 (29.55%)
Sex: n (%)			
Female	742 (83.37%)	S	35 (79.55%)
Male	148 (16.63%)	< 5	5 (11.36%)
Residence location: n (%)			
Urban	694 (77.98%)	S	35 (81.63%)

Characteristics	CGRP inhibitor users subcohort N = 890	CGRP inhibitor switchers subcohort N = 20	CGRP discontinuers subcohort N = 44
Rural	196 (22.02%)	< 5	9 (20.45%)
Socioeconomic, n (%)			
Material deprivation			
1 (most well off)	146 (16.40%)	< 5	8 (18.18%)
2	165 (18.54%)	8 (40.00%)	S
3	168 (18.88%)	< 5	8 (18.18%)
4	185 (20.79%)	< 5	13 (29.55%)
5 (most deprived)	181 (20.34%)	7 (35.00%)	8 (18.18%)
Unknown	45 (5.06%)	0	< 5
Social deprivation			
1 (most well off)	161 (18.09%)	< 5	S
2	180 (20.22%)	< 5	10 (22.73%)
3	162 (18.20%)	8 (40.00%)	10 (22.73%)
4	173 (19.44%)	< 5	S
5 (most deprived)	169 (18.99%)	< 5	10 (20.41%)
Unknown	45 (5.06%)	0	< 5
Comorbidities			
Charlson Comorbidity Index			
Mean (SD)	0.35 (1.04)	0.65 (1.56)	0.18 (0.58)
Median; min, max	0;0,9	0;0;0	0; 0;3
Category, n (%)			
0: no comorbid condition	716 (80.45%)	S	37 (84.09%)
1 to 2: mild comorbidity	162 (18.20%)	< 5	7 (15.90%)
3 to 4: moderate comorbidity	12 (1.35%)	0	0
≥ 5: severe comorbidity	0 (0%)	0	0
Comorbid condition, n (%)			
Cardiovascular disease	24 (2.70%)	0	< 5
Depression	27 (3.03%)	0	< 5
Anxiety	65 (7.30%)	0	6 (13.64%)
Asthma	27 (3.03%)	0	0
Epilepsy	10 (1.12%)	0	0
Hypertension	37 (4.16%)	0	0

Characteristics	CGRP inhibitor users subcohort N = 890	CGRP inhibitor switchers subcohort N = 20	CGRP discontinuers subcohort N = 44
Obstructive sleep apnea	12 (1.35%)	0	0

CGRP = calcitonin gene–related peptide; Q = quintile; Q1-3 = first and third quartile; S = suppressed; SD = standard deviation.

Table 53: Sociodemographic and Clinical Characteristics (Saskatchewan)

Characteristics	CGRP inhibitor users subcohort N = 482	CGRP inhibitor switchers subcohort N = 10	CGRP discontinuers subcohort N = 173
Demographic			
Age (years)			
Mean (SD)	43.59 (12.61)	< 5	43.15 (12.97)
Median (Q1-Q3)	43 (35 to 52.75)	< 5	42 (34 to 52)
Age (years): n (%)			
18 to 44	265 (54.98%)	7 (70.00%)	101 (58.38%)
45 to 64	S	< 5	65 (37.57%)
65+	< 5	< 5	7 (4.05%)
Sex: n (%)			
Female	396 (82.16%)	S	145 (83.82%)
Male	86 (17.84%)	< 5	28 (16.18%)
Socioeconomic, n (%)			
Residential instability			
Q1	111 (23.03%)	< 5	35 (20.23%)
Q2	90 (18.67%)	< 5	37 (21.39%)
Q3	95 (19.71%)	< 5	40 (23.12%)
Q4	121 (25.10%)	< 5	34 (19.65%)
Q5	58 (12.03%)	< 5	S
Missing/Invalid	7 (1.45%)	0 (0.00%)	< 5
Economic dependency			
Q1	141 (29.25%)	< 5	48 (27.75%)
Q2	75 (15.56%)	0 (0.00%)	29 (16.76%)
Q3	92 (19.09%)	< 5	32 (18.50%)
Q4	130 (26.97%)	< 5	47 (27.17%)
Q5	37 (7.68%)	< 5	S
Missing/Invalid	7 (1.45%)	0 (0.00%)	< 5

Characteristics	CGRP inhibitor users subcohort N = 482	CGRP inhibitor switchers subcohort N = 10	CGRP discontinuers subcohort N = 173
Ethnocultural composition			
Q1	172 (35.68%)	< 5	58 (33.53%)
Q2	109 (22.61%)	< 5	39 (22.54%)
Q3	92 (19.09%)	< 5	33 (19.08%)
Q4	50 (10.37%)	< 5	21 (12.14%)
Q5	52 (10.79%)	< 5	S
Missing/Invalid	7 (1.45%)	0 (0.00%)	< 5
Residence location: n (%)			
Urban	371 (76.97%)	S	128 (73.99%)
Rural/Remote	S	< 5	S
Missing/Invalid	< 5	0 (0.00%)	< 5

CGRP = calcitonin gene–related peptide; Q = quintile; Q1-Q3 = first and third quartile; S = suppressed; SD = standard deviation.

Table 54: Sociodemographic and Clinical Characteristics (US)

Characteristics	CGRP inhibitor users subcohort N = 55,212	CGRP inhibitor switchers subcohort N = 4,048	CGRP discontinuers subcohort N = 7,078
Demographic			
Age (years)			
Mean (SD)	43.9 (11.8)	43.9 (11.5)	42.1 (12.2)
Median (Q1-Q3)	45 (36 to 52)	45 (37 to 52)	43 (33 to 51)
Age (years): n (%)			
18 to 44	27,064 (49.0%)	2,012 (49.7%)	3,887 (54.9%)
45 to 64	27,242 (49.3%)	1,980 (48.9%)	3,090 (43.7%)
65+	906 (1.6%)	56 (1.4%)	101 (1.4%)
Sex: n (%)			
Female	47,412 (85.9%)	3,490 (86.2%)	5,854 (82.7%)
Male	7,800 (14.1%)	558 (13.8%)	1,224 (17.3%)
Residence location: n (%)			
Urban	48,096 (87.1%)	3,556 (87.9%)	6,089 (86.0%)
Rural	7,116 (12.9%)	492 (12.2%)	989 (14.0%)
Comorbidities			
Charlson Comorbidity Index			

Characteristics	CGRP inhibitor users subcohort N = 55,212	CGRP inhibitor switchers subcohort N = 4,048	CGRP discontinuers subcohort N = 7,078
Mean (SD)	0.6 (1.3)	0.6 (1.3)	0.5 (1.2)
Median; min, max	0 (0 to 1)	0 (0 to 1)	0 (0 to 1)
Category, n (%)			
0: no comorbid condition	38,469 (69.7%)	2,742 (67.7%)	5,192 (73.4%)
1 to 2: mild comorbidity	12,079 (21.9%)	959 (23.7%)	1,376 (19.4%)
3 to 4: moderate comorbidity	3,409 (6.2%)	266 (6.6%)	378 (5.3%)
≥ 5: severe comorbidity	1,255 (2.3%)	81 (2.0%)	132 (1.9%)
Comorbid condition, n (%)			
Cardiovascular disease	2,324 (4.2%)	173 (4.3%)	275 (3.9%)
Depression	13,527 (24.5%)	1,094 (27.0%)	1,345 (19.0%)
Anxiety	16,833 (30.5%)	1,343 (33.2%)	1,797 (25.4%)
Asthma	5,556 (10.1%)	453 (11.2%)	586 (8.3%)
Epilepsy	1,542 (2.8%)	111 (2.7%)	147 (2.1%)
Hypertension	13,112 (23.8%)	916 (22.6%)	1,449 (20.5%)
Obstructive sleep apnea	6,320 (11.5%)	504 (12.5%)	617 (8.7%)

CGRP = calcitonin gene–related peptide; Q1-Q3 = first and third quartile; SD = standard deviation.

Table 55: Premigraine and Postmigraine-Related Health Care Encounters (Alberta)

	CGRP inhibitor users subcohort		CGRP inhibitor switchers subcohort		CGRP inhibitor discontinuers subcohort	
	1 year before index	1 year after index	1 year before index	1 year after index	1 year before index	1 year after index
N	3,869		243		1,375	
Any migraine-related health care encounter						
Had ≥ 1 visit, n (%)	3,696 (95.5)	3,570 (92.3)	239 (98.4)	231 (95.1)	1,295 (94.2)	1,163 (84.6)
Number of visits						
Mean (SD)[a]	9.6 (10.1)	8.0 (8.8)	11.0 (10.9)	9.0 (10.7)	9.2 (9.0)	8.4 (7.5)
Median (Q1-Q3)[a]	8.0 (4.0 to 12.0)	6.0 (3.0 to 10.0)	8.0 (5.0 to 12.0)	7.0 (4.0 to 10.0)	7.0 (4.0 to 11.0)	7.0 (3.0 to 11.0)
Migraine-related hospitalizations						
Had ≥ 1 visit, n (%)	23 (0.6)	17 (0.4)	< 10	0 (0.0)	< 10	< 10
Length of hospital stay (day)						

	CGRP inhibitor users subcohort		CGRP inhibitor switchers subcohort		CGRP inhibitor discontinuers subcohort	
	1 year before index	1 year after index	1 year before index	1 year after index	1 year before index	1 year after index
N	**3,869**		**243**		**1,375**	
Mean (SD)[a]	6.1 (7.6)	4.4 (4.8)	3.3 (2.1)	0.0 (0.0)	2.3 (1.5)	2.0 (0.0)
Median (Q1-Q3)[a]	4.0 (1.0 to 8.0)	3.0 (2.0 to 4.0)	4.0 (1.0 to 5.0)	0.0 (0.0 to 0.0)	2.0 (1.0 to 3.0)	2.0 (2.0 to 2.0)
Migraine-related ED visits						
Had ≥ 1 visit, n (%)	520 (13.4)	330 (8.5)	23 (9.5)	12 (4.9)	168 (12.2)	98 (7.1)
Number of visits						
Mean (SD)[a]	3.1 (6.6)	3.3 (6.6)	2.0 (2.4)	1.9 (1.7)	3.2 (7.1)	2.9 (4.1)
Median (Q1-Q3)[a]	1.0 (1.0 to 2.0)	1.0 (1.0 to 2.0)	1.0 (1.0 to 2.0)	1.0 (1.0 to 2.0)	1.0 (1.0 to 2.0)	1.0 (1.0 to 2.0)
Migraine-related ambulatory care visits						
Had ≥ 1 visit, n (%)	610 (15.8)	529 (13.7)	43 (17.7)	40 (16.5)	214 (15.6)	174 (12.7)
Number of visits						
Mean (SD)[a]	3.1 (2.6)	3.4 (2.6)	4.3 (3.5)	4.5 (2.8)	3.3 (2.7)	3.5 (2.9)
Median (Q1-Q3)[a]	2.0 (1.0 to 4.0)	3.0 (2.0 to 4.0)	3.0 (2.0 to 6.0)	4.0 (2.0 to 6.5)	3.0 (2.0 to 4.0)	3.0 (1.0 to 5.0)
Migraine-related physician visits						
Had ≥ 1 visit, n (%)	3,682 (95.2)	3,546 (91.7)	237 (97.5)	229 (94.2)	1,290 (93.8)	1,150 (83.6)
Number of visits						
Mean (SD)[a]	8.7 (8.0)	7.2 (7.2)	10.1 (10.0)	8.2 (9.8)	8.2 (7.2)	7.8 (6.6)
Median (Q1-Q3)[a]	7.0 (4.0 to 11.0)	6.0 (3.0 to 9.0)	8.0 (5.0 to 11.0)	6.0 (3.0 to 9.0)	7.0 (4.0 to 10.0)	7.0 (3.0 to 10.0)

CGRP = calcitonin gene–related peptide; ED = emergency department; Q = quintile; Q1-Q3 = first and third quartile; SD = standard deviation.

[a]Mean and median are calculated for those with 1 or more visits.

Table 56: Premigraine and Postmigraine-Related Health Care Encounters in CGRP Inhibitor Users (US)

Health care encounter	CGRP inhibitor users subcohort N = 55,212		CGRP inhibitor switchers subcohort N = 4,048		CGRP inhibitor discontinuers subcohort N = 7,078	
	1 year before index	1 year after index	1 year before index	1 year after index	1 year before index	1 year after index
Any migraine-related health care encounter						
Had ≥ 1 visit, n (%)	44,701 (81.0%)	37,662 (68.2%)	3,505 (86.6%)	2,919 (72.1%)	4,754 (67.2%)	3,539 (50.0%)
Number of visits						
Mean (SD)[a]	3.5 (3.7)	3.3 (3.8)	4.5 (4.6)	3.8 (4.5)	3.0 (2.8)	3.3 (4.2)
Median (Q1-Q3)[a]	3 (1 to 4)	2 (1 to 4)	3 (2 to 6)	3 (1 to 5)	2 (1 to 4)	2 (1 to 4)
Migraine-related hospitalizations						
Had ≥ 1 visit, n (%)	301 (0.6%)	213 (0.4%)	36 (0.9%)	22 (0.5%)	29 (0.4%)	20 (0.3%)
Length of hospital stay (day)						
Mean (SD)[a]	4.6 (4.5)	4.8 (4.2)	4.7 (6.1)	5.0 (3.5)	4.5 (3.8)	3.0 (2.1)
Median (Q1-Q3)[a]	3 (2 to 6)	3 (2 to 6)	3.5 (1 to 4.5)	3.5 (3 to 8)	3 (2 to 6)	2 (2 to 3)
Migraine-related ED visits						
Had ≥ 1 visit, n (%)	4,582 (8.3%)	3,077 (5.6%)	387 (9.6%)	284 (7.0%)	416 (5.9%)	362 (5.1%)
Number of visits						
Mean (SD)[a]	1.7 (2.6)	1.8 (3.0)	1.9 (3.1)	2.2 (3.7)	1.6 (1.4)	1.6 (1.9)
Median (Q1-Q3)[a]	1 (1 to 2)	1 (1 to 2)	1 (1 to 2)	1 (1 to 2)	1 (1 to 2)	1 (1 to 2)
Migraine-related ambulatory care visits						
Had ≥ 1 visit, n (%)	11,383 (20.6%)	9,540 (17.3%)	1,085 (26.8%)	898 (22.2%)	1,103 (15.6%)	891 (12.6%)
Number of visits						
Mean (SD)[a]	2.2 (3.2)	2.2 (3.3)	2.6 (3.8)	2.6 (3.8)	1.8 (1.6)	2.0 (2.5)
Median (Q1-Q3)[a]	1 (1 to 2)	1 (1 to 2)	1 (1 to 3)	1 (1 to 3)	1 (1 to 2)	1 (1 to 2)
Migraine-related physician visits						
Had ≥ 1 visit, n (%)	42,573 (77.1%)	35,001 (63.4%)	3,324 (82.1%)	2,684 (66.3%)	4,503 (63.6%)	3,241 (45.8%)

Health care encounter	CGRP inhibitor users subcohort N = 55,212		CGRP inhibitor switchers subcohort N = 4,048		CGRP inhibitor discontinuers subcohort N = 7,078	
	1 year before index	1 year after index	1 year before index	1 year after index	1 year before index	1 year after index
Number of visits						
Mean (SD)[a]	3.0 (2.5)	2.8 (2.6)	3.7 (2.9)	3.0 (2.8)	2.6 (2.3)	2.9 (3.3)
Median (Q1-Q3)[a]	2 (1 to 4)	2 (1 to 3)	3 (2 to 5)	2 (1 to 4)	2 (1 to 3)	2 (1 to 3)

CGRP = calcitonin gene–related peptide; ED = emergency department; SD = standard deviation; Q1-Q3 = first and third quartile.

[a]Mean and median are calculated for those with 1 or more visits.

Table 57: Postmigraine-Related Health Care Encounters (US)

Health care encounter	Initial CGRP inhibitor					
	Erenumab	Galcanezumab	Fremanezumab	Eptinezumab	Atogepant	Rimegepant
Any migraine-related health care encounter						
Had ≥ 1 visit, n (%)	15,747 (73.3%)	11,938 (66.5%)	6,656 (71.2%)	34 (85.0%)	102 56.4%)	3,185 (51.4%)
Number of visits						
Mean (SD)[a]	3.5 (4.5)	3.1 (3.2)	3.4 (3.5)	4.1 (2.4)	2.4 (1.7)	2.6 (2.4)
Median (Q1-Q3)[a]	2 (1 to 4)	2 (1 to 4)	2 (1 to 4)	3 (3 to 5)	2 (1 to 3)	2 (1 to 3)
Migraine-related hospitalizations						
Had ≥ 1 visit, n (%)	114 (0.5%)	56 (0.3%)	36 (0.4%)	1 (2.5%)	0 (0)	6 (0.1%)
Hospital stay (days)						
Mean (SD)[a]	4.8 (3.9)	3.7 (3.5)	6.3 (5.8)	11 (0)	0 (0)	3.8 (1.7)
Median (Q1-Q3)[a]	3 (2 to 6)	3 (2 to 4)	5 (2 to 8)	11 (11 to 11)	0 (0)	3.5 (3 to 4)
Migraine-related ED visits						
Had ≥ 1 visit, n (%)	1,341 (6.2%)	988 (5.5%)	531 (5.7%)	4 (10.0%)	8 (4.4%)	205 (3.3%)
Number of visits						
Mean (SD)[a]	1.97 (3.9)	1.63 (2.1)	1.69 (1.9)	1.75 (1.0)	1.25 (0.5)	1.62 (1.2)
Median (Q1-Q3)[a]	1 (1 to 2)	1 (1 to 2)	1 (1 to 2)	1.5 (1 to 2.5)	1 (1 to 1.5)	1 (1 to 2)
Migraine-related ambulatory care visits						
Had ≥ 1 visit, n (%)	4,034 (18.8%)	3, 171 (17.7%)	1,554 (16.6%)	15 (37.5%)	21 (11.6%)	745 (12.0%)

Health care encounter	Initial CGRP inhibitor					
	Erenumab	Galcanezumab	Fremanezumab	Eptinezumab	Atogepant	Rimegepant
Number of visits						
Mean (SD)[a]	2.4 (3.9)	2.1 (2.7)	2.2 (3.1)	2.3 (1.4)	1.1 (0.4)	2.0 (2.1)
Median (Q1-Q3)[a]	1 (1 to 3)	1 (1 to 2)	1 (1 to 2)	2 (1 to 4)	1 (1 to 1)	1 (1 to 2)
Migraine-related physician visits						
Had ≥ 1 visit, n (%)	14,744 (68.6%)	10,950 (61.0%)	6,299 (67.3%)	31 (77.5%)	92 (50.8%)	2,885 (46.6%)
Number of visits						
Mean (SD)[a]	2.9 (3.0)	2.6 (2.3)	2.9 (2.5)	3.1 (2.4)	2.3 (1.6)	2.2 (1.8)
Median (Q1-Q3)[a]	2 (1 to 4)	2 (1 to 3)	2 (1 to 4)	3 (1 to 4)	2 (1 to 3)	2 (1 to 3)

CGRP = calcitonin gene–related peptide; ED = emergency department; Q1-Q3 = first and third quartile; SD = standard deviation.

[a]Mean and median are calculated for those with 1 or more visits.

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This work was conducted by the Alberta Drug and Technology Evaluation Consortium (ADTEC), the CAnadian Network for Advanced Interdisciplinary Methods for comparative effectiveness research (CAN-AIM), and the Institut national d'excellence en santé et en services sociaux (INESSS) through the Post-Market Drug Evaluation CoLab Network. It was supported by Canada's Drug Agency (CDA-AMC) and its Post-Market Drug Evaluation Program through funding provided by Health Canada.

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