CADTH

CADTH Health Technology Review

Analysis of FPT Formulary Harmonization: Specialty Care Medications

Service Line: CADTH Health Technology Review
Publication Date: May 2021
Report Length: 41 Pages

CADTH

Authors: Peter Dyrda and Mina Tadrous

Cite as: *Analysis of FPT Formulary Management for Specialty Drugs*. Ottawa: CADTH; 2021 May. (CADTH health technology review).

Acknowledgments: Christine Perras, Tarry Ahuja, Nevzeta Bosnic, Jeffrey Menzies, and Tanya Potashnik

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

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

CADTH

Table of Contents

CADTH

Tables

Figures

CADTH

Abbreviations

ATC	Anatomical Therapeutic Chemical
CIHI	Canadian Institute for Health Information
CML	chronic myeloid leukemia
DME	diabetic macular edema
FPT	federal, provincial, and territorial governments
NIHB	Non-Insured Health Benefits
NPDUIS	National Prescription Drug Utilization Information System
pCPA	Pan-Canadian Pharmaceutical Alliance
PMPRB	Patented Medicines Prices Review Board
PsO	plaque psoriasis
RA	rheumatoid arthritis
RRMS	relapsing-remitting multiple sclerosis
TNF	tumour necrosis factor
UC	ulcerative colitis
wAMD	wet age-related macular degeneration

Definitions

Administrative criteria	Evidence or tests required to be completed by a physician or patient to submit to the federal, provincial, and territorial governments for reimbursement
Clinical criteria	Disease severity measurement or patient eligibility requirements for reimbursement by the federal, provincial, and territorial governments
Formulary	A list of medications reimbursed by the payer
Harmonization	Agreement or comparability of formularies among the federal, provincial, and territorial governments, particularly for listing status and reimbursement criteria of individual drugs
Listing rate	The proportion of reimbursed versus not reimbursed medications
Listing status	The type of benefit for a medication on the formulary, which could be unrestricted, restricted, or not reimbursed
Prior authorization	A process to seek approval of the reimbursement of a medication by the payer for a patient before beginning treatment, usually requiring a review of patient eligibility versus reimbursement criteria, and often required for restricted benefit status drugs
Reimbursement criteria	A set of requirements that must be met for reimbursement to be approved by the payer, which can be administrative or clinical
Restricted benefit	A listing status for drugs that require patients meet a set of reimbursement criteria, usually through the process of prior authorization
Specialty care medication	Medications reimbursed within specialized programs (e.g., cancer agencies), prescribed by specialists (e.g., neurologists), or dispensed in specialty pharmacies
Unrestricted benefit	A listing status for drugs that do not require a patient to meet reimbursement criteria

Executive Summary

As policy-makers consider the implementation of a national pharmacare program, the potential challenges associated with formulary harmonization will need to be addressed. A previous study demonstrated a high degree of similarity in listing status for primary care drugs across Canada but excluded drugs for specialty care. Assessing formulary harmonization for specialty care medications is critical given that these medications represent a high proportion of overall drug spending and are often reimbursed using a restricted benefit status that requires prior authorization approval based on reimbursement criteria. This analysis sought to evaluate formulary harmonization for specialty care medications by assessing listing status and reimbursement criteria for a select sample of drugs.

There was a high degree of similarity of listing rates for specialty care medications, which was also comparable (81.5%) to primary care medications (79%); and listing rates for oncology medications were much higher (mean = 91%; range = 77% to 95%) than non-oncology medications (mean = 71%; range = 60% to 78%). On average, two-thirds of reimbursed specialty care medications had a restricted benefit status; thus, reimbursement criteria would have a significant role in formulary management for these medications. Listing status was consistent for federal, provincial, and territorial governments (FPTs) across therapeutic classes, and were highest within antineoplastics, oncology, and nervous system medications. Only 18% of medications were listed by less than half of the FPTs, which signifies a high degree of consensus in listing status among FPTs. Overall, listing status rates for specialty care medications were found to be comparable (thus harmonized) as drugs in primary care with approximately 80% agreement across FPTs.

An assessment of a sample of 12 medications representing $4.1 billion in Canadian expenditure (approximately 12% of total drug spending in Canada) in 2019 found that reimbursement criteria were largely comparable. Importantly, variations in reimbursement criteria were noted for all except 1 drug despite having a similar listing status (i.e., restricted benefit). Variations of reimbursement criteria arose in 2 forms: administrative (e.g., requirements for tests) and clinical (e.g., patient eligibility). Each FPT also demonstrated varying levels of restriction with reimbursement criteria by therapeutic subgroup (e.g., Saskatchewan was less restrictive for anti–tumour necrosis factor [TNF] drugs and more restrictive for anti-neovascularization agents), and each medication saw varying levels of restriction across different FPTs. Alberta, Saskatchewan, Manitoba, Nova Scotia, Non-Insured Health Benefits (NIHB), and Yukon appear to be generally less restrictive compared with British Columbia, Ontario, New Brunswick, Prince Edward Island, and Newfoundland and Labrador.

This analysis provided insight into how FPTs may prefer to manage their drug plans using listing status versus reimbursement criteria. For example, New Brunswick had the highest listing rates, but among the most restrictive reimbursement criteria. Conversely, NIHB did not use unrestricted benefit listings for specialized care medications but had the least restrictive criteria. British Columbia used supply-side policies to curb spending at the prescription level by mandating switching to biosimilars or incentivizing physicians to prescribe less costly off-label products. Ontario used relatively less restrictive criteria when prior authorization was not required, which may be due to non-transparent agreements with manufacturers providing budget certainty.

As policy-makers consider formulary harmonization in the context of national pharmacare, 2 key insights should be noted. First, although FPTs work together for drug negotiations, variance in listing status and reimbursement criteria demonstrate different strategies employed for formulary management and the influence of local decision-making. Second, if harmonization of formularies was pursued, variation in administrative and clinical criteria could create budgetary and clinical practice challenges given the differences in access to care and patient populations that are eligible for treatment across FPTs. It will be critical to have expert feedback when harmonizing criteria to ensure optimal care with each medication in the context of its therapeutic alternatives. Changes to patient eligibility may also have meaningful impacts on budgets, which will also require future economic analyses to measure the effects of harmonization.

Background

The reimbursement of prescription drugs in Canada is managed by the federal, provincial, and territorial (FPT) governments for their respective beneficiaries. Differences in decision-making frameworks and drug program designs (e.g., patient eligibility for public reimbursement) have resulted in incongruity across Canadian FPT formularies and reimbursement policies. Initiatives such as CADTH and the pan-Canadian Pharmaceutical Alliance (pCPA) have sought to improve consistency in formulary decisions for newly reimbursed medications. However, jurisdictional differences remain because many medications pre-date the pCPA and because of variations in clinical practice and decision-making frameworks across jurisdictions.

In the context of implementing a potential national pharmacare program, it is important for policy-makers to identify the degree of variation and overlap of formularies (i.e., harmonization) to understand the potential operational and administrative challenges in drug coverage, which may have incremental budgetary impacts or unintended clinical implications for FPTs. In 2017, the Patented Medicine Prices Review Board (PMPRB) published a report based on 2015 data from the National Prescription Drug Utilization Information System (NPDUIS) that assessed the degree of alignment of listing status among public formularies.[1] Of the 1,456 publicly reimbursed drugs captured by the NPDUIS data, 729 were included in the analysis; these comprised 262 single-source brand-name products and 467 multi-source products. The PMPRB found that there was a high degree of alignment among public drug plans in listing status, with an average of 79% of the 729 selected drugs reimbursed by FPTs (which increased to 95% when weighted by relative expenditure). However, this analysis did not include drugs covered under specialized programs, such as oral cancer treatments, age-related macular degeneration treatments, and diagnostic agents (note that PMPRB included approximately 50% of drugs available on formularies from the NPDUIS data sample in 2015).

Policy Issue

As policy-makers consider the implementation of a national pharmacare program, the potential challenges associated with formulary harmonization will need to be addressed. This work began with an analysis of the differences of listing status for primary care drugs by the PMPRB in 2017, although there were key limitations that warranted further study; namely, formulary harmonization of specialty care drugs is unknown.

There are 2 major reasons to prioritize the analysis of formulary harmonization for specialty care medications, defined as drugs used within specialized programs (e.g., cancer

agencies), prescribed by specialists, or dispensed by specialty pharmacies. First, specialty care medications are associated with significantly higher costs versus primary care. There has been a shift toward increased use of higher-cost medications and the share of total sales of patented medicines that represent high-cost medicines saw a sharp increase from 5% in 2006 to 42% in 2018, despite less than 1% of the population using these medicines.[2] Second, these medications often have complex reimbursement criteria that can comprise different administrative or clinical requirements for funding, which may also differ between FPTs.

There is a need for policy-makers to better understand formulary harmonization for specialty care medications in the context of a national pharmacare program. For these medications, the assessment of formulary harmonization should expand beyond simply comparing differences in listing status across FPTs, but by also comparing differences in reimbursement criteria because most of these medications will be reimbursed in a restricted manner (i.e., a similar benefit status across all FPTs). Although assessing differences in reimbursement criteria can be an onerous qualitative exercise, a representative sample of highly utilized medications may provide insight into the degree of harmonization.

Policy Question

PQ1: What are the similarities and differences in formulary harmonization (listing status and reimbursement criteria) for specialty care medications for FPTs (provinces, NIHB, and Yukon)?

Research Questions

RQ1: What proportion of specialty care medications are reimbursed on average by FPTs as of 2020?

RQ2: How many specialty care medications fall within a restricted benefit, unrestricted benefit, or not reimbursed listing status by each FPT?

RQ3: How many specialty care medications are reimbursed on average by FPTs by therapeutic area?

RQ4: How many specialty care medications are reimbursed by all FPT plans versus by more than or less than half of FPT plans?

RQ5: How do reimbursement criteria compare across FPTs (except Quebec) for a representative sample of specialty care medications that are frequently used?

Methods

This analysis evaluated the degree of harmonization between FPT formularies for specialty care medications in 2020, including oncology programs (for both hospital-administered and “take-home” medications). Formulary harmonization was measured by 2 characteristics: listing status and reimbursement criteria. Listing status refers to the way a drug is funded (or reimbursed) by the FPT, which can include a restricted benefit listing on the formulary, unrestricted benefit listing on the formulary, or not being reimbursed on the formulary. The difference between restricted and unrestricted listings was the requirement for special authorization (i.e., a review of eligibility for reimbursement based on criteria) before reimbursement approval for a patient. Reimbursement criteria refers to the set of

requirements, both administrative and clinical, that are applied to a reimbursement decision for an individual patient. Administrative criteria were defined as evidence or tests required to be completed by a physician or patient to submit to FPTs for reimbursement, and clinical criteria were defined as disease severity measurements or patient eligibility requirements for reimbursement by FPTs.

FPT formulary lists include publicly reimbursed medications classified by their active ingredient, manufacturer, product name, strength, dosage form, and route of administration. The drugs analyzed in this study were grouped by active ingredient at level 5 of the Anatomical Therapeutic Chemical (ATC) Classification System as reported by the Canadian Institute for Health Information (CIHI). Listing status information was collected from NPDUIS datasets, and reimbursement criteria were collected directly from FPT websites (as of February 2021).

This analysis was conducted in 2 phases: an assessment of the listing status of specialty care medications across FPTs and an assessment of the reimbursement criteria for 12 selected specialty care medications for FPTs. These 2 phases included different payers and time frames due to differences in the availability of data. Phase 1 aimed to address RQ1 to RQ4; phase 2 addressed RQ5.

The selected list of medications was sourced from an unpublished CADTH report[3] describing a clinical expert panel that was convened in 2018 to create a prototype formulary for a potential national pharmacare program. A list of 1,594 medications from the NPDUIS database were assessed (up to July 1, 2018). Medications were split into 3 categories: those used in a primary care setting (category 1), those prescribed by specialists (category 2), and those dispensed at specialty pharmacies (category 3). The resulting formulary included a prototype list of 1,033 medications from 14 ATC groups comprising 89 therapeutic subgroups. This prototype formulary was based on expert opinion to sufficiently provide therapeutics for the Canadian population, and thus acted as a starting point for drug selection for this analysis.

Phase 1: An Assessment of Listing Status of Specialty Care Medications Across FPTs

Drug Selection

Of the initial formulary of 1,033 medications,[3] the list was narrowed to focus on 9 ATC therapeutic classes (N = 398 medications) with significantly more specialty medications (categories 2 and 3 versus category 1): alimentary tract and metabolism, blood and blood forming organs, cardiovascular system, systemic hormonal preparations, anti-infectives for systemic use, antineoplastics, antiparasitic products, nervous system, and sensory organs. Within these 9 ATC therapeutic classes, all category 1 (primary care setting) medications were eliminated, which resulted in a final list of 285 drugs. Of note, these medications included both hospital-administered and take-home or community oncology medications.

Outcome Measures

For oncology medications, the outcome was binary and denoted either as *reimbursed* or *not reimbursed* by drug and, when available, by indication. Nine public drug plans were included: Alberta, British Columbia, New Brunswick, Newfoundland and Labrador, Nova Scotia, Ontario, Prince Edward Island, Quebec, and Saskatchewan. No information on listing status for territorial or federal drug plans was available for oncology medications.

Listing statuses were collected as of March 31, 2020, for hospital-administered oncology medications and as of June 30, 2020, for take-home oncology medications (based on availability of data). For non-oncology medications, the outcomes were denoted as either *unrestricted benefit* (for a listing that does not require prior authorization), *restricted benefit* (requires prior authorization), or *not reimbursed*. The same public drug plans were included as for oncology medications with the addition of the NIHB program and Yukon. Listing statuses were collected as of June 30, 2020, except for Quebec which was collected as of May 27, 2020.

Phase 2: An Assessment of the Reimbursement Criteria for 12 Selected Specialty Care Medications for FPTs

Drug Selection

Investigators sought to assess relevant medications for reimbursement criteria assessment based on highest utilization (i.e., specialty care medications with the highest annual expenditures). Of the initial formulary of 1,033 medications,[3] the list was narrowed to focus on the top 5 therapeutic subgroups based on a CIHI report of public drug plan spending in 2019,[4] which included (from highest expenditure to lowest): anti-TNF drugs, anti-neovascularization agents, antivirals for hepatitis C, oral protein kinase inhibitors, and selective immunosuppressants. Medications from the original list (N = 1,033) that were within these therapeutic subgroups were compared in terms of 2019 total Canadian expenditures (all payers), and the top 2 to 3 medications (based on expenditure) for each of the 5 subgroups were selected for analysis. These medications included infliximab, adalimumab, ranibizumab, aflibercept, elbasvir + grazoprevir, sofosbuvir + velpatasvir, dasatinib, ruxolitinib, palbociclib, fingolimod, teriflunomide, and vedolizumab. These 12 medications accounted for $4.1 billion in total expenditure by all Canadian payers (i.e., public and private) in 2019, representing an approximate share of 12% of total expenditure on medications.[4] For each medication, the branded version was used in the analysis when a generic or biosimilar version was available. The rationale for using the branded version was that it was expected to represent the most common representation of reimbursement criteria for all drugs within the class and would capture any biosimilar policies (e.g., switching). Additionally, only 1 approved indication was analyzed per medication at the discretion of the investigators (where applicable), which included chronic myeloid leukemia (CML), diabetic macular edema (DME), plaque psoriasis (PsO), rheumatoid arthritis (RA), relapsing-remitting multiple sclerosis (RRMS), ulcerative colitis (UC), and wet age-related macular degeneration (wAMD).

Outcome Measures

Listing status and reimbursement criteria as of January 2021 were collected for each of the 12 included drugs for the following FPT plans: British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador, Yukon, and NIHB. The definition of listing status was expanded from phase I and was categorized as 1 of the following: requires prior authorization (i.e., restricted benefit listing), does not require prior authorization (i.e., unrestricted benefit listing), reimbursement at the physician's discretion (i.e., a form of restricted benefit listing that does not require special authorization for the prescriber), initial treatment or switch of existing treatment with a less costly drug mandated (i.e., a form of restricted benefit listing), or not reimbursed. Criteria for each medication were compared between FPTs for that specific indication for both administrative (evidence or tests required to be completed to submit for

reimbursement) and clinical (disease severity or patient eligibility criteria) differences and rated on a 3-point scale from least restrictive to most restrictive reimbursement criteria. Not reimbursed drugs and those with more than 1 listing status were not assigned a relative value for reimbursement criteria. If no differences in criteria were detected between payers, a *no variance* rating was assigned. Two reviewers (MT and PD) independently studied the listing status and reimbursement criteria and provided ratings using their own discretion; disagreements were resolved through discussion.

Findings

Phase 1: An Assessment of Listing Status of Speciality Care Medications Across FPTs

Of the sample of n = 285, there were 174 non-oncology and 86 oncology medications for which the listing status data were available (n = 260); data were unavailable for 25 medications that were hospital-administered IV oncology medications. The average listing rate (the proportion of reimbursed versus not reimbursed medications) for the 260 drugs was 81.5% (65% to 85%), which was higher for oncology medications at 91% (77% to 95%), and differed by payers (Table 1). For non-oncology medications, the FPTs with the highest listing rates were New Brunswick, Alberta, and Quebec, whereas FPTs with the lowest listing rates were Prince Edward Island, Nova Scotia, and Newfoundland and Labrador. For oncology medications, Nova Scotia had the highest listing rate, whereas Newfoundland and Labrador and Prince Edward Island had the lowest listing rate. There was no statistical analysis planned to measure significance; however, there was a trend of lower listing rates for Prince Edward Island and Newfoundland and Labrador.

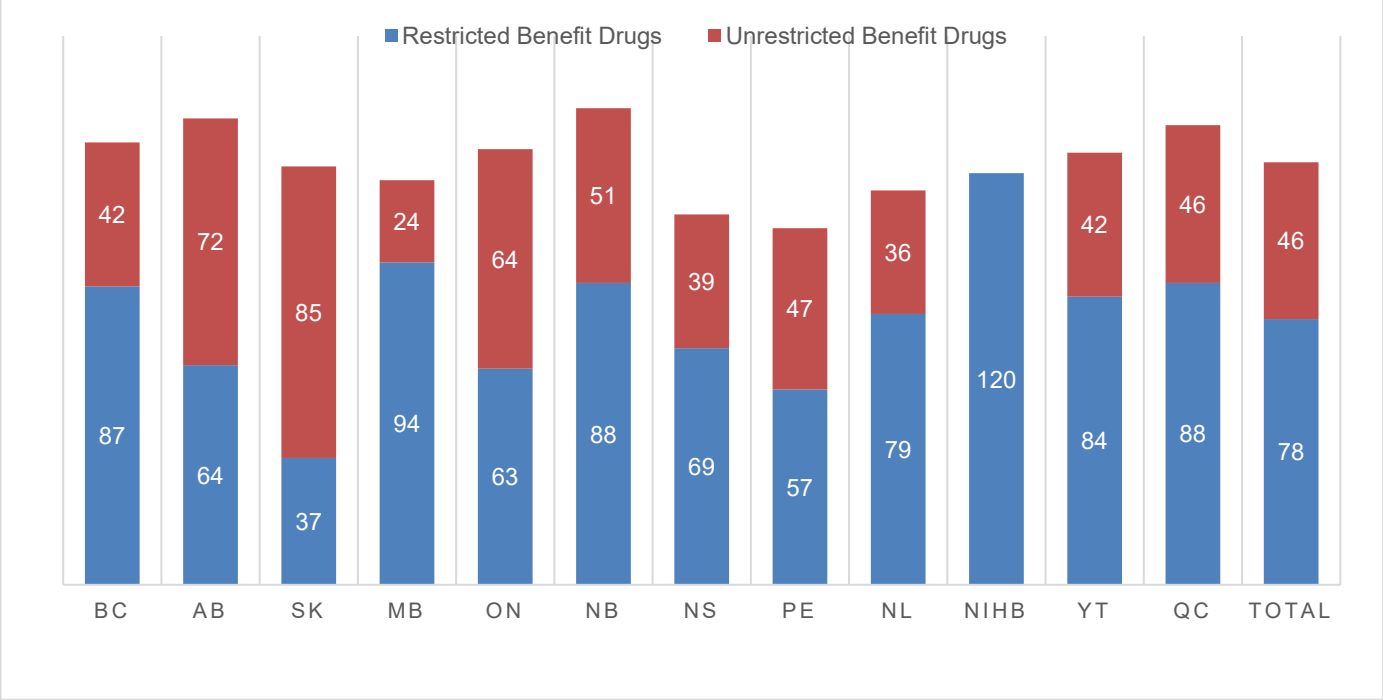
The listing status for non-oncology medications was assessed to compare the difference in restricted versus unrestricted benefits for drugs (Figure 1). Of the 174 non-oncology medications, the mean number of unrestricted benefit and restricted benefit drugs was 46 (37% of reimbursed drugs) and 78 (67% of reimbursed drugs), respectively. Of these, Saskatchewan, Ontario, and Prince Edward Island had the fewest number of unrestricted benefit drugs, whereas NIHB had none. The FPTs with the most restricted benefit medications were NIHB, Manitoba, and New Brunswick. Listing rates were consistent across therapeutic areas. Discrepancies (i.e., wide variance between the maximum and minimum values) in listing rates were found in therapeutic areas with older medications that some provinces did not reimburse any within the class (e.g., Newfoundland and Labrador did not reimburse any of the antiparasitic drugs) and for classes with smaller sample sizes (e.g., systemic hormonal preparations, n = 4). The highest levels of consistency were observed within antineoplastics, oncology, and nervous system medications (Figure 2).

Table 1: Formulary Listing Rates for Specialty Care Medications by FPT as of 2020

FPT	Formulary listing rates, %	
	Non-oncology medications (n = 174)	Oncology medications (n = 86)
British Columbia	74.1	94.2
Alberta	78.2	90.7
Saskatchewan	70.1	94.2
Manitoba	67.8	93.0
Ontario	73.0	95.3
New Brunswick	79.9	94.2
Nova Scotia	62.1	95.3
Prince Edward Island	59.8	86.0
Newfoundland and Labrador	66.1	76.7
NIHB	69.0	—
Yukon	72.4	—
Quebec	77.0	—

FPT = federal, provincial, and territorial governments; NIHB = Non-Insured Health Benefits.

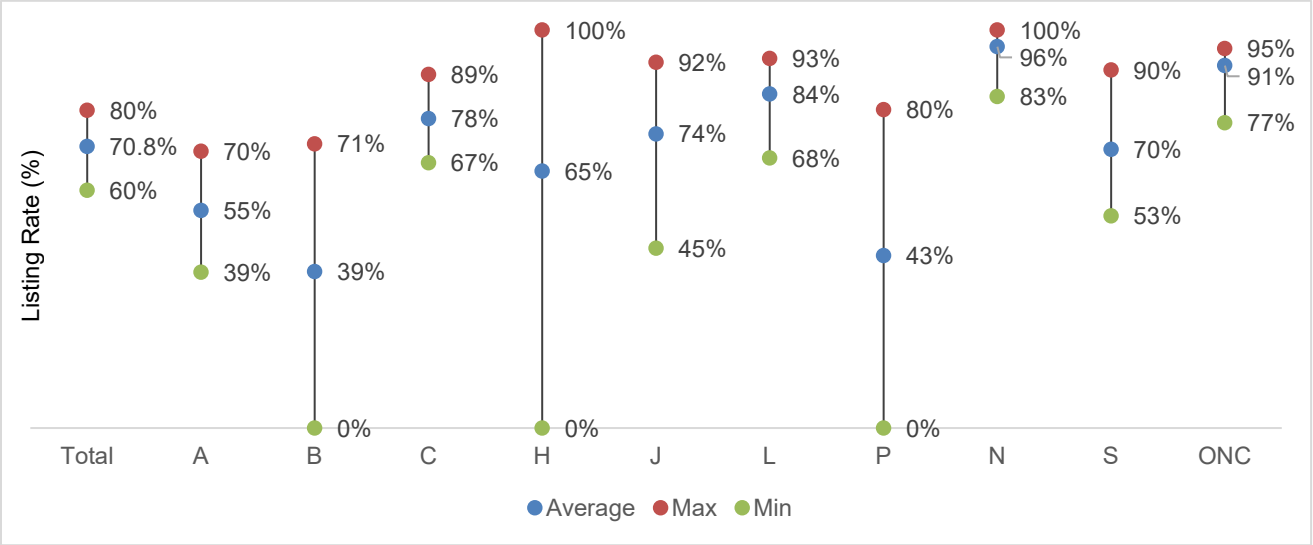
Figure 1: Listing Status (Restricted Versus Unrestricted Benefit) for Non-Oncology Drugs by FPTs as of 2020 (n = 174)



AB = Alberta; BC = British Columbia; NB = New Brunswick; NL = Newfoundland & Labrador; NIHB = Non-Insured Health Benefits; NS = Nova Scotia; ON = Ontario; PE = Prince Edward Island; QC = Quebec; SK = Saskatchewan; YT = Yukon.

Note: Restricted benefit refers to requiring prior authorization and unrestricted benefit refers to not requiring prior authorization.

Figure 2: Listing Rates by Therapeutic Class for FPTs as of 2020 (n = 260)

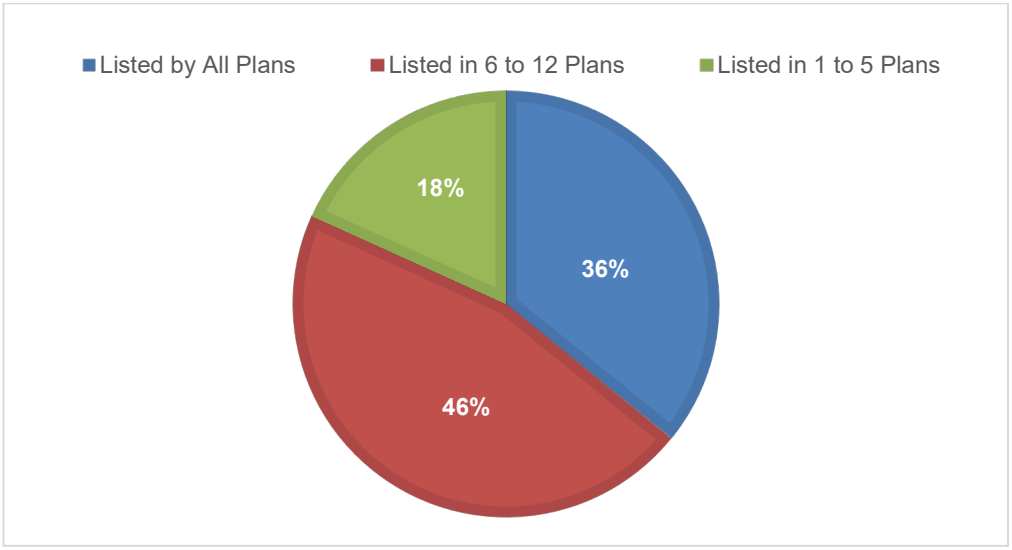


A = alimentary tract and metabolism (n = 23); B = blood and blood forming organs (n = 7); C =cardiovascular system (n = 9); H = systemic hormonal preparations (n = 4); J = anti-infectives for systemic use (n = 62); L = antineoplastics (n = 28); P = antiparasitic products (n = 5); N = nervous system (n = 6); S = sensory organs (n = 30); ONC = oncology (n = 86).

Note: Total includes all non-oncology medications. Minimum was the FPT with the least number of medications reimbursed, whereas maximum was the FPT with the greatest number of medications reimbursed (as a percentage of the total within the class in the sample).

Listing status was grouped by the number of FPT plans that listed drugs (listed in all plans, in 1 to 5 plans, or in 6 to 12 plans), and Figure 3 demonstrates that there is a significant level of consensus for reimbursement: 82% of drugs are listed in 6 to 12 plans or all plans. This means that approximately 1 in 5 of these selected medications would have an inconsistent listing status in which reimbursement was available in less than half of the FPTs.

Figure 3: Drugs Listed by FPTs by Number of Plans as of 2020



Phase 2: An Assessment of the Reimbursement Criteria for 12 Selected Speciality Care Medications for FPTs

Table 2 provides the reimbursement criteria comparisons across FPTs as of 2021.

Most of the selected medications required some form of prior authorization; however, Ontario specifically utilized a less restricted benefit status of *limited use*, which included reimbursement criteria but reimbursement was not reviewed a priori. Instead, pharmacies could be audited for compliance after dispensing. This form of benefit means that FPTs do not approve or reject a patient's claim for reimbursement but reimburses all claims and checks that the reimbursement criteria were adhered to after the fact. For phase I of this analysis, *limited use* was considered a restricted benefit; however, in phase 2, it was categorized as an unrestricted benefit because it was fairly aligned with unrestricted benefit listings in New Brunswick and Prince Edward Island.

Several FTPs used the discretion of the physician rather than publishing any reimbursement criteria, such as British Columbia, Manitoba, Nova Scotia, and Yukon for anti-neovascularization agents. Prince Edward Island and New Brunswick also did not require prior authorization for specialists such as oncologists and neurologists, respectively, although criteria were provided for their guidance. Several FPTs mandated the use of less costly medications, such as British Columbia and Alberta for biologics in RA and British Columbia and Newfoundland and Labrador for anti-neovascularization agents for wAMD and DME. Variation in the implementation of listings was most evident with biologics, particularly with anti-TNF drugs and anti-neovascularization agents, which were the top 2 most costly therapeutic subgroups for FPTs.

Table 2: Reimbursement Criteria Comparison Across FPTs as of 2021

Therapeutic subgroup	Chemical name	Indication	BC	AB	SK	MB	ON	NB	NS	PE	NL	NIHB	YT
Anti-TNF drugs	Infliximab	RA	+	+++	+	++	+	++	++	++	+	++	++
	Adalimumab	PsO	+++	++	+	+	+++	++	++	+	++	++	++
Anti-neo-vascularization agents	Ranibizumab	wAMD		++	+++	+	+	+++	+	+++	+++	+++	+
	Aflibercept	DME		++	+++		+	+++	+	+++	++	+	+
Antivirals for treatment of hepatitis C infections	Elbasvir and grazoprevir	Hepatitis C (genotypes 1, 3, and 4)	++	++	+	++	+++	++	++		++	++	++
	Sofosbuvir and velpatasvir	Hepatitis C	++	++	+	++	+++	++	++		++	++	++
Oral PKIs	Dasatinib	CML	+++	+	++	+	+++	+++	+++	+++	+++		+
	Ruxolitinib	Myelofibrosis	No variance										
	Palbociclib	Breast cancer	+++	+	+	+++	+	++	+	+++	+++	+	+++
Selective immuno-suppressants	Fingolimod	RRMS (second line)	+++	++	++	++	+++	+++	+++	++	+++	+	++
	Teriflunomide	RRMS (first line)	+	+	++	++	+++	+	++	+	++	++	+
	Vedolizumab	UC	++	++	+	+	+++	++	++	++	++	++	+++

AB = Alberta; BC = British Columbia; CML = chronic myeloid leukemia; DME: diabetic macular edema; MB = Manitoba; ON = Ontario; NB = New Brunswick; NIHB = Non-Insured Health Benefits; NL = Newfoundland and Labrador; NS = Nova Scotia; PE = Prince Edward Island; PKI = protein kinase inhibitor; PsO = plaque psoriasis; RA = rheumatoid arthritis; RRMS = relapsing-remitting multiple sclerosis; SK = Saskatchewan; TNF = tumour necrosis factor; UC = ulcerative colitis; wAMD = wet age-related macular degeneration; YT = Yukon.

Legend: orange denotes prior authorization required (i.e., restricted benefit), purple denotes not requiring prior authorization (i.e., unrestricted benefit), blue denotes reimbursement at the physician's discretion, yellow denotes initial treatment or switch existing treatment with a cheaper agent, green denotes switch plus physician discretion, and red denotes not reimbursed. **+** denotes least restrictive and **+++** is most restrictive within an individual drug and indication across FPTs.

Generally, reimbursement criteria differed slightly across FPTs for each medication. Administrative requirements (i.e., defined as evidence or tests required to be completed by a physician or patient to submit for reimbursement) were consistent across FPTs, except for hepatitis C drugs in which there were different requirements for the timing of virology tests and inclusion of the fibrosis stage of the disease, for RRMS in which some FPTs required a neurology examination within 90 days of applying for reimbursement, and for UC in which some payers required endoscopy for approval. Of the 12 medications, only 1 (ruxolitinib for myelofibrosis) had harmonized criteria across all FPTs; the rest varied in their reimbursement criteria including clinical definitions and patient eligibility. Differences between FPTs often existed for disease threshold to define severity, prior treatments, and eligibility. Differences in the definition of threshold of disease severity were found in PsO, DME (hemoglobin A1C levels), and RRMS (disability level). For RA, criteria varied on the number of lines of therapy of conventional medications required to fail before being approved for infliximab. Finally, oncology medications varied based on the population that was eligible for coverage (i.e., where the medication was approved for use) in CML (chronic versus blast phase) and for metastatic breast cancer (use with fulvestrant after progression).

Each FPT demonstrated varying levels of restriction with its reimbursement criteria by therapeutic subgroup (e.g., Saskatchewan was less restrictive for anti-TNF drugs and more restrictive for anti-neovascularization agents), and each medication saw varying levels of restriction across different FPTs. However, in general, there appeared to be 2 tiers of behaviour by FPTs within this sample of 12 medications. Alberta, Saskatchewan, Manitoba, Nova Scotia, NIHB, and Yukon appeared to be generally less restrictive compared with

British Columbia, Ontario, New Brunswick, Prince Edward Island, and Newfoundland and Labrador. British Columbia also seemed to manage expenditures more proactively by mandating less costly medications for biologics (switching to biosimilars for infliximab and off-label use of Avastin versus Lucentis or Eylea).

Conclusions and Implications for Decision- or Policy-Making

The listing rates for the selected specialty care medications (81.5%) were comparable to the listing rates of primary care medications from the PMPRB report in 2017 (79%). The listing rates for oncology were high, with a mean of 91%, whereas non-oncology was lower at 71%. Differences in listing rates between these 2 broad classes of medications could be due to differences in health technology assessment recommendations or differences in jurisdictional decision-making for reimbursement between oncology and non-oncology medications. One-third of specialized care medications were considered unrestricted benefit; thus, the majority required special authorization in which the reimbursement criteria would impact reimbursement eligibility. Listing rates for non-oncology medications across FPTs were consistent, from 60% (Prince Edward Island) to 78% (Alberta), and even more so for oncology medications, from 77% (Newfoundland and Labrador) to 95% (Nova Scotia and Ontario). Most notably, only 18% of medications were listed by 5 or fewer FPTs, which signifies a high degree of consensus in listing status among FPTs. Overall, specialty care medications were found to have comparable listing rates (and thus harmonization) to drugs in primary care, with approximately 80% agreement across public programs.

A qualitative assessment of a sample of 12 medications representing $4.1 billion in Canadian expenditure (approximately 12% of total drug spending in Canada) in 2019 found that reimbursement criteria were largely comparable. Importantly, variations in reimbursement criteria were noted despite having similar listing status (i.e., restricted benefit). This is important context when assessing harmonization because listings are not necessarily equivalent and would have impact on which patients would have access to some treatments.

In this sample, variations of reimbursement criteria arose in 2 forms: administrative and clinical. If harmonization of formularies was pursued within a national pharmacare platform, differences in administrative criteria could create challenges given that access to specialists and diagnostics may differ across Canada. If the most restrictive of these administrative criteria were chosen as a baseline for harmonization, this may increase the demand for diagnostics and specialists visits and potentially lead to delays in treatment if capacity cannot meet the new demand. Differences in clinical practice between jurisdictions or patient eligibility may prove to have bigger impacts on harmonization. If reimbursement criteria are harmonized with the most restrictive version of clinical criteria, it is possible that patients with less severe disease may lose access and/or may be required to try therapeutic alternatives. The opposite is also true — if the criteria become less restrictive, access may increase. Changes in eligibility would likely impact the number of treated patients and thus would impact expenditure. However, this analysis did not account for alternative therapeutic options which may fill gaps in access presented for these 12 medications and may have comparable criteria and/or costs. If reimbursement criteria were to be harmonized across FPTs within a national pharmacare platform, it may warrant an expert panel of clinicians to provide this context alongside an economic analysis (cost-effectiveness and/or budgetary impact).

This analysis provided insight into how FPTs may prefer to manage their drug plans using listing status versus reimbursement criteria. For example, New Brunswick had the highest listing rates, but had among the most restrictive reimbursement criteria. Conversely, although NIHB did not use unrestricted benefit listings for specialized care medications, the least restrictive criteria were used. British Columbia used supply-side policies to curb spending at the prescription level by mandating switching to biosimilars or incentivizing physicians to prescribe less costly off-label products. However, Ontario used relatively less restrictive criteria when prior authorization was not required, which may be due to non-transparent agreements with manufacturers providing budget certainty. Harmonization across FPTs will need to carefully consider these different formulary management strategies. Surprisingly, only 1 of the 12 medications had no variance in reimbursement criteria despite many of these medications having undergone negotiations through pCPA. This may be evidence that although FPTs work together for negotiations, listing status and reimbursement criteria are heavily influenced by local decision-makers.

Limitations of this study should be considered when interpreting policy implications. For phase I, the sample used did not capture all drugs used for specialty care. Rather, the therapeutic ATC classes which were most likely to include specialized care medications were identified. To align with the previous PMPRB report, the definition of restricted benefit was maintained as any listing status that required prior authorization. However, it could be argued that there are varying levels of restriction that are important for consideration within restricted benefit listings (e.g., limited use in Ontario). Furthermore, listing rates in this analysis were not weighted based on expenditure because of challenges in collecting cost data for specialized program medications, especially for oncology. For phase 2, the qualitative exercise of assessing restriction of reimbursement criteria may be subjective. Furthermore, it was challenging to quantify the clinical impact of these differences without input from clinical experts, especially because each medication should also have reimbursement criteria assessed in comparison with each FPT's therapeutic alternatives (e.g., if a FPT had restricted criteria for 1 medication, did it have less stringent criteria for an alternative medication that was not assessed?).

In summary, the results of this analysis have revealed that specialty care medications have comparable listing rates to primary care medications previously studied. However, even when harmonization in listing status exists, there is potential for administrative and clinical differences within reimbursement criteria. This analysis also revealed that drug plans implement different strategies for formulary management through supply-side policies (e.g., special programs for reimbursement of a therapeutic class), restriction within reimbursement criteria, reliance on the discretion of prescribers, and/or listing agreements that provide budget certainty within unrestricted benefit listings. As policy-makers work toward harmonization of formularies, all these insights should be considered in the context of national pharmacare.

References

1. Alignment among public formularies in Canada – Part 1: General overview. *(NPDUIS Reports & Trends)*. Ottawa (ON): Patented Medicine Prices Review Board; 2017: http://www.pmprb-cepmb.gc.ca/CMFiles/NPDUIS/NPDUIS_formulary_report_part_1_en.pdf. Accessed 2021 Jan.
2. Annual report: 2018. Ottawa (ON): Patented Medicine Prices Review Board; 2020: https://www.canada.ca/content/dam/pmprb-cepmb/documents/reports-and-studies/annual-report/2018/PMPRB-annual-report-2018-en.pdf. Accessed 2021 Jan.
3. Report of CADTH's Ad Hoc Primary Care Committee on three formulary options [CONFIDENTIAL internal report]. Ottawa (ON): CADTH; 2018.
4. Prescribed drug spending in Canada, 2020: A focus on public drug programs. Ottawa (ON): Canadian Institute for Health Information; 2020: https://www.cihi.ca/sites/default/files/document/prescribed-drug-spending-in-canada-2020-report-en.pdf. Accessed 2021 Jan.

Appendix 1: Summary of Reimbursement Criteria for British Columbia, Alberta, Saskatchewan, Manitoba, and Ontario as of 2021

Table 3: Summary of Reimbursement Criteria for British Columbia, Alberta, Saskatchewan, Manitoba, and Ontario as of 2021

		British Columbia		Alberta		Saskatchewan		Manitoba		Ontario	
Brand name	Indication	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes
Remicade	RA	• MTX + ≥ 1 of the following (not including HCQ): LEF, SSZ, azathioprine, tacrolimus, cyclosporine, gold, doxycycline, OR • ≥ 1 DMARD combination	> 8 weeks trial of MTX (parenteral) ≥ 25 mg/week (≥ 15 mg/week if patient is ≥ 65 years of age); > 10 weeks trial of LEF, 20 mg/day; > 3 months trial of SSZ, > 2 gm/day; > 3 months trial of azathioprine, 2 to 3 mg/kg/day DMARD combination: > 4 months trial MTX + HCQ + SSZ (O'Dell protocol), > 10 weeks trial MTX + LEF Mandatory switching policy effective for all Remicade patients to a biosimilar version	• MTX AND • MTX + other DMARDs, AND • LEF	> 12 weeks trial of MTX ≥ 20 mg/week (p.o., SC or IM) (≥ 15 mg/week if patient is ≥ 65 years of age) > 4 months trial of MTX + other DMARDs (e.g., MTX + HCQ or MTX + SSZ) > 10 weeks trial of LEF 20 mg/day Mandatory switching policy effective for all Mandatory switching policy effective for all Remicade patients to a biosimilar version	• MTX AND • LEF	New patients have the option to be treated with brand and biosimilar versions of IFX	• ≥ 3 DMARDs (1 of which is MTX and/or LEF), AND • 1 combination of DMARDs	Unless intolerance or contraindications to these agents is documented	• MTX AND • LEF AND • ≥ 1 DMARD combination OR • MTX AND • MTX + LEF OR • MTX, SSZ, and HCQ	> 3 months trial of each therapy. MTX (20 mg/week), LEF (20 mg/day), SSZ (2 gm/day) and HCQ (400 mg/day, based by weight up to 400 mg per day)
Humira	PsO	Definition of severe disease: BSA ≥ 10%, involvement of sensitive areas (e.g., hands), baseline PASI > 12; prior treatments: patient has failed to respond or experienced a specific intolerance to BOTH MTX and ciclosporin, and/or is unable to access UV phototherapy	MTX 20 mg weekly for 3 months and cyclosporine 4 mg/kg daily for 3 months	PASI >10 and DLQI > 10 OR involvement of sensitive areas (e.g., hands, face, genitals) AND refractory or intolerant to conventional therapies	Conventional therapies: MTX at 20 mg (p.o., SC, or IM) or greater total weekly dosage (≥ 15 mg if patient ≥ 65 years of age) for > 12 weeks OR • Cyclosporine (6 weeks treatment); AND • Phototherapy (unless restricted by geographic location)	Failure to respond to, or intolerant of, MTX and cyclosporine; AND failure to respond to, intolerant to, or unable to access phototherapy	—	For treatment of adult patients with severe PsO presently with 1 or more of the following: • PASI ≥ 10 • BSA > 10% • Significant involvement of the face, hands feet or genital region • DLQI > 10 AND • Failure to respond to, contraindications to, intolerant of, or unable to access MTX, cyclosporine, and/or phototherapy	—	Definition of severe PsO: BSA involvement ≥ 10%, or involvement of the face, hands, feet, or genital regions, AND PASI score ≥ 10 AND DLQI score ≥ 10	6-month trial ≥ 3 topical agents including vitamin D analogues and steroids 12-week trial of phototherapy (unless not accessible) 6-month trial ≥ 2 systemic, oral agents used alone or in combination

Brand name	Indication	British Columbia		Alberta		Saskatchewan		Manitoba		Ontario	
		Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes
Lucentis	wAMD	Provincial Retinal Diseases Program provides drug treatment therapy for BC patients. The 29 retinal specialists participating in the Provincial Retinal Diseases Treatment Program, collaborate with PHSA and the Ministry of Health to ensure the planning, coordination, accessibility, quality, efficiency, and effectiveness of the provincial program	There are 3 drugs used for the retinal program. The approximate percentage of Avastin usage is 85%, Eylea 14%, and Lucentis is 1%	Anti-VEGF treatment-naive patients if all of the following apply to the eye to be treated: • The BCVA is between 6/12 (20/40) and 6/96 (20/320); • There is active disease activity (and no permanent structural damage to the central fovea; • There is evidence of recent (< 3 months) presumed disease progression	Coverage will not be provided for patients who have failed to respond to a previous anti-VEGF agent No concurrent verteporfin PDT treatment Blood vessel growth, as indicated by fluorescein angiography, OCT, or recent visual acuity changes	If all of the following circumstances apply to the eye to be treated: • The BCVA is between 6/12 and 6/96 • The lesion size is ≤ 12 disc areas in greatest linear dimension • There is evidence of recent (< 3 months) presumed disease progression	Coverage will not be provided for patients: (a) With permanent structural damage to the central fovea or no active disease (b) Receiving concurrent verteporfin PDT treatment Disease progression as blood vessel growth, as indicated by fluorescein angiography, OCT, or recent visual acuity changes	Funded by Manitoba with requests being assessed through a special provincial eye care program.	—	If there is clinical or diagnostic evidence of disease activity, such as a loss > 5 letters in visual acuity (ETDRS chart or 1 Snellen line equivalent), Lucentis may be administered	Patients receiving concurrent administration of verteporfin PDT (Visudyne) or aflibercept (Eylea) are not eligible for reimbursement. For clarity, coverage will be provided for patients responding to therapy with Eylea who switch to Lucentis. Coverage will NOT be provided for patients who have failed to respond to Eylea
Eylea	DME	Provincial Retinal Diseases Program provides drug treatment therapy for BC patients. The 29 retinal specialists participating in the Provincial Retinal Diseases Treatment Program, collaborate with PHSA and the Ministry of Health to ensure the planning, coordination, accessibility, quality, efficiency, and effectiveness of the provincial program	There are 3 drugs used for the retinal program. The approximate percentage of Avastin usage is 85%, Eylea 14%, and Lucentis is 1%	BCVA (using the Early Treatment Diabetic Retinopathy Study visual acuity test) of 78 to 24 letters and a central retinal thickness ≥ 300 µm meeting all of the following criteria: • clinically significant DME for whom laser photocoagulation is also indicated, and • hemoglobin A1C ≤ 12%	Coverage will not be provided to patients who have failed to respond to a previous anti-VEGF agent	(i) Diffuse DME involving the central fovea with central fovea thickness of 300 microns or greater on OCT and vision < 20/32 (ii) Patients with focal macular edema for which laser photocoagulation is indicated should be treated with laser, except in situations where focal laser therapy treatment can not be safely performed due to the proximity of microaneurysms to the fovea (iii) hemoglobin A1C < 11%	FA should be considered prior to initiation of treatment to assess perfusion and characterize the leakage and should also be considered if the patient is not responding to treatment as expected	Not reimbursed	—	For the treatment of patients with clinically significant DME for whom laser photocoagulation is also indicated; and a hemoglobin A1C < 12%	For clarity, coverage will be provided for patients responding to therapy with Lucentis who switch to Eylea. Coverage will NOT be provided for patients who have failed to respond to Lucentis
Zepatier	Hepatitis C genotypes 1, 3, and 4	For the treatment of treatment-naive or treatment-experienced adult patients with CHC genotype 1 or 4 infection who meet **all** the following criteria: A. Fibrosis stage of F0 or greater (Metavir scale or equivalent);	—	For treatment-naive or treatment-experienced (1) adult patients with CHC infection who meet all of the following criteria: I) Prescribed by or in consultation with a hepatologist,	Exclusion criteria: • Patients currently being treated with another HCV antiviral agent • Re-treatment for failure or re-infection in patients who have received an adequate prior	For use as monotherapy or combination therapy with ribavirin for treatment-naive or treatment-experienced (1) adult patients with CHC infection according to the following criteria: (i) Treatment is prescribed by a hepatologist, gastroenterologist, an	—	For treatment-naive or treatment-experienced adult patients with chronic hepatitis C gen 1 or 4 infection who meet all of the following: I. Treatment is prescribed by a	Combo therapy with Sovaldi will not be considered for funding for any genotypes	For treatment-naive or treatment-experienced adult patients with CHC infection who meet all the following criteria: (i) Treatment is prescribed by a hepatologist, gastroenterologist, infectious disease specialist or other prescriber experienced in treating CHC; AND (ii) Laboratory-confirmed	—

Brand name	Indication	British Columbia		Alberta		Saskatchewan		Manitoba		Ontario	
		Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes
		AND B. Treatment is prescribed by a hepatologist, a gastroenterologist, an infectious disease specialist or other prescriber experienced with treating hepatitis C; AND C. Laboratory-confirmed hepatitis C genotype 1 or 4; AND D. Laboratory-confirmed quantitative HCV RNA test must be done within the previous 12 months; AND E. Patient is NOT currently being treated with another hepatitis C direct-acting antiviral drug		gastroenterologist or infectious disease specialist (except on a case-by-case basis, in geographic areas where access to these specialties is not available); AND II) Laboratory-confirmed hepatitis C genotype 1 or genotype 4; AND III) Laboratory-confirmed quantitative HCV RNA value within the last 6 months; AND IV) Fibrosis (2) stage of F0 or greater (Metavir scale or equivalent)	course of an HCV direct-acting antiviral drug regimen may be considered on an exceptional case-by-case basis • Combination therapy with sofosbuvir will not be considered for any genotypes Note: As approved by Health Canada, 8 weeks may be considered in treatment-naive genotype 1b patients without significant fibrosis or cirrhosis, as determined by liver biopsy (i.e., Metavir F0-F2) or by non-invasive tests	infectious disease specialist or other prescriber experienced in treating hepatitis C as determined by the Drug Plan; AND (ii) Laboratory-confirmed hepatitis C genotype 1 or 4; AND (iii) Laboratory-confirmed quantitative HCV RNA value within the last 12 months		hepatologist, gastroenterologist, or infectious disease specialist AND II. Laboratory-confirmed hep C gen 1 or gen 4 AND III. Patient has a quant HCV RNA value within the last 6 months		hepatitis C genotype 1 or genotype 4; AND (iii) Two laboratory-confirmed quantitative HCV RNA values taken at least 6 months apart as demonstration of chronicity of infection. 1 level must be within the last 6 months while the first level may be at the time of the initial diagnosis	
Epclusa	Hepatitis C	The treatment of treatment-naive or treatment-experienced1 adult patients with CHC genotype 1, 2, 3, 4, 5, 6 or mixed genotype infection who meet **all** of the following criteria: A. Fibrosis stage of F0 or greater (Metavir scale or equivalent); AND B. Treatment is prescribed by a hepatologist, a gastroenterologist, an infectious disease specialist, or other prescriber experienced with treating hepatitis C; AND C. Laboratory-confirmed hepatitis C genotype 1, 2, 3, 4, 5	1. Treatment-experienced is defined as patients who have been previously treated with pegIFN/RBV regimen, including regimens containing HCV protease inhibitors (for genotype 1) and who have relapsed or not responded. 2. Special Authority requests for patients must include the most recent genotyping test report and HCV RNA test performed in the last 12 months	For treatment-naive or treatment-experienced (1) adult patients with CHC infection who meet all of the following criteria: I) Prescribed by or in consultation with a hepatologist, gastroenterologist or infectious disease specialist (except on a case-by-case basis, in geographic areas where access to these specialties is not available); AND II) Laboratory-confirmed hepatitis C genotype (2) 1, 2, 3, 4, 5, 6 or mixed genotypes; AND III) Laboratory-	Exclusion criteria: • Patients currently being treated with another HCV antiviral agent • Re-treatment for failure or re-infection in patients who have received an adequate prior course of an HCV direct-acting antiviral drug regimen may be considered on an exceptional case-by-case basis Notes: Treatment-experienced is defined as those who failed prior therapy with an interferon-based regimen, including regimens containing	For use as monotherapy or as combination therapy with ribavirin for treatment-naive or treatment-experienced adult patients with CHC infection according to the following criteria: (i) Treatment is prescribed by a hepatologist, gastroenterologist, an infectious disease specialist or other prescriber experienced in treating hepatitis C as determined by the drug plan; AND (ii) Laboratory-confirmed hepatitis C genotype 1, 2, 3, 4, 5, 6, or mixed genotypes; AND (iii) Laboratory-confirmed quantitative HCV RNA value within the last 12 months	—	For treatment-naive or treatment-experienced adult patients with CHC genotype 1, 2,3,4,5,6 or mixed genotypes infection who meet **all** of the following: (i) Treatment is prescribed by a hepatologist, gastroenterologist, or infectious disease specialist AND (ii) Laboratory-confirmed hepatitis C genotype 1, 2, 3, 4, 5, 6 or mixed genotypes AND (iii) Patient has a quantitative HCV RNA value within the last 6 months	Re-treatment for failure or re-infection in patients who have received an adequate prior course of direct-acting antiviral will be considered on a case-by-case basis	For treatment-naive or treatment-experienced (1) adult patients with CHC infection who meet all the following criteria: (i) Treatment is prescribed by a hepatologist, gastroenterologist, infectious disease specialist or other prescriber experienced in treating CHC; AND (ii) Laboratory-confirmed hepatitis C genotype 1, 2, 3, 4, 5, 6 or mixed genotypes; AND (iii) Two laboratory-confirmed quantitative HCV RNA values taken at least 6 months apart as demonstration of chronicity of infection. 1 level must be within the last 6 months while the first level may be at the time of the initial diagnosis	Re-treatment is not funded. Re-treatment for failure or re-infection in patients who have received an adequate prior course of direct-acting antiviral will be considered on a case-by-case basis through the Exceptional Access Program

Brand name	Indication	British Columbia		Alberta		Saskatchewan		Manitoba		Ontario	
		Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes
		or 6; AND D. Laboratory-confirmed quantitative HCV RNA test must be done within the previous 12 months; AND E. Patient is NOT currently being treated with another hepatitis C direct-acting antiviral drug		confirmed quantitative HCV RNA value within the last 6 months; AND IV) Fibrosis (3) stage of F0 or greater (Metavir scale or equivalent)	an HCV protease inhibitor						
Sprycel	CML	• Patients with chronic phase CML, who are resistant to imatinib: ° No CHR after 3 months of imatinib ° Lack of any cytogenetic response after 3, 6, and 12 months of imatinib ° Cytogenetic relapse on imatinib (loss of CCR/< 2 log or MCR/< 1 log or any Ph+ increase ≥ 30%) • Patients with accelerated/blast phase CML, including Ph+ ALL patients, who are resistant to imatinib: o Lack of response following ≥ 4 weeks of treatment with imatinib ≥ 600 mg p.o. once daily o No CHR in accelerated phase after 3 months of imatinib use o Incomplete response with no further improvement in blast phase/Ph+ ALL after 1 month o Cytogenetic relapse (loss of CCR/< 2 log or MCR/< 1 log or any Ph+ increase ≥ 30%) o Loss of CHR	imatinib ≥ 600 mg p.o. once daily; • May be used in combination with busulfan, dexamethasone, hydroxyurea, interferon, melphalan or prednisone; Note: sequential use between dasatinib and nilotinib for disease progression is not allowed unless a specific kinase domain mutation is demonstrated mediating resistance to 1 second generation TKI but has demonstrated sensitivity to the other TKI	• Dasatinib as first-line treatment of Ph+ CML in chronic phase • For the treatment of patients with chronic, accelerated or blast phase Ph+ CML who have resistance or intolerance to prior TKI therapy • For adult patients with Ph+ ALL whose disease is resistant to imatinib containing chemotherapy (patient must have tried 600 mg/day) or have experienced grade 3 non-hematologic toxicity, or grade 4 hematologic toxicity persisting for more than 7 days to Imatinib	—	• Second-line treatment in chronic phase, accelerated phase or blast crisis with primary or acquired resistance to Imatinib • First-line treatment "switch" in patients with chronic phase, accelerated phase or blast crisis who were initiated on Imatinib, but are experiencing a suboptimal response by not meeting established therapeutic milestones according to the Canadian Hematology Society or European LeukemiaNet guidelines, or who are experiencing unacceptable toxicity to Imatinib • Subsequent line of treatment in patients who are resistant to or experiencing toxicity to other second generation TKI therapies (e.g., Nilotinib or Bosutinib) • First-line treatment in patients with accelerated phase or blast crisis	Second generation TKI's (Dasatinib, Nilotinib, Bosutinib) are not funded as options after Ponatinib	For the treatment of patients: • With CML (chronic phase, accelerated phase, blast phase) AND • With resistant disease despite imatinib therapy OR • With intolerance to imatinib and/or nilotinib	Patients should be treated with an imatinib dose of ≥ 600 mg daily for at least 4 weeks unless intolerant to imatinib Exclusion criteria: • Resistant disease to both imatinib and nilotinib	For the treatment of patients with accelerated phase or blast phase (Ph+ CML with documented resistance or intolerance to imatinib therapy) Imatinib resistance is defined as primary or acquired resistance to imatinib at doses ≥ 600 mg/day or through a mutational analysis report	Intolerance to imatinib (at any dose) is defined as persistent grade 3 or grade 4 toxicity requiring discontinuation of therapy

Brand name	Indication	British Columbia		Alberta		Saskatchewan		Manitoba		Ontario	
		Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes
		○ Progression of accelerated phase to blast phase or recurrent blast phase/Ph+ ALL • Patients with chronic/accelerated/blast phase CML, including Ph+ ALL patients, who are intolerant to imatinib, including patients with: ○ ≥ Grade 3 non-hematologic toxicity, not responding to symptomatic treatment or dose adjustments to imatinib 300 mg p.o. once daily ○ Grade 4 hematologic toxicity lasting > 7 days ○ Sustained, highly symptomatic Grade 2 non-hematologic toxicity ○ Patients with intolerance to nilotinib (grade 3 or 4 non-hematologic toxicity) for chronic/accelerated phase CML treatment									
Jakavi	Myelofibrosis	Primary myelofibrosis, post-essential thrombocythemia myelofibrosis and post-polycythemia vera myelofibrosis; DIPSS score Intermediate-1, intermediate-2 or high risk, OR low risk with symptomatic splenomegaly; ECOG 0 to 3	BCCA Compassionate Access Program request must be approved	For patients with intermediate- to high-risk symptomatic myelofibrosis as assessed using DIPSS Plus for patients with symptomatic splenomegaly. Patients whose ECOG performance status ≤ 3 and be either previously untreated or refractory to other treatment	—	For the treatment of patients with intermediate to high-risk symptomatic myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis and post-essential thrombocythemia myelofibrosis, as assessed using the Dynamic International Prognostic Scoring System-Plus (DIPSS Plus) or symptomatic splenomegaly who have an ECOG performance status of ≤ 3 and who are either untreated or refractory to previous therapies	Completion of the SCA Treatment Evaluation Program request form for each patient is required for treatment approval	For patients with intermediate- to high-risk myelofibrosis as assessed using the DIPSS Plus or patients with symptomatic splenomegaly. Patients should have ECOG performance status ≤3 and be either previously untreated or refractory to other treatment.	—	For the treatment of intermediate to high-risk symptomatic myelofibrosis in patients meeting the following criteria: i) myelofibrosis is assessed using the DIPSS Plus; or the patient has symptomatic splenomegaly ii) Patient has an ECOG performance status ≤ 3 iii) Patient is previously untreated or refractory to other treatment	—

Brand name	Indication	British Columbia		Alberta		Saskatchewan		Manitoba		Ontario	
		Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes
Ibrance	Breast cancer	Post-menopausal women and men with ER-positive, HER2-negative advanced breast cancer with no prior systemic treatment for metastatic disease (including women with chemically induced menopause with LHRH agonists). • Patients should not be resistant to prior (neo)adjuvant aromatase inhibitor therapy (patients must be a minimum of 12 months from last adjuvant aromatase inhibitor), nor have active or uncontrolled metastases to the central nervous system. • Good performance status	Patients are eligible to receive palbociclib plus letrozole/ anastrozole (Ubravpalai) or ribociclib plus letrozole/anastrozole (Ubravribai) or everolimus plus exemestane (Bravevex), but not sequential use of these combination regimens. For patients recently diagnosed with metastatic breast cancer, and who have initiated anastrozole or letrozole monotherapy within the past 6 months, palbociclib can be added if the rest of the above criteria are met	In combination with an aromatase inhibitor as a first-line treatment of post-menopausal women with ER-positive HER2 negative advanced or metastatic breast cancer (de novo stage IV or prior earlier stage and disease-free for at least 12 months following completion of (neo)adjuvant nonsteroidal aromatase inhibitor). Physicians may choose only 1 of the following combinations: palbociclib + AI first line, ribociclib + AI first line, or everolimus + exemestane second line for an individual patient. The following groups would be included: pre-menopausal patients with chemically induced menopause, patients with bone-only metastases, patients that are HER2 equivocal by FISH testing, or male patients. • Palbociclib in combination with fulvestrant for the treatment of patients with HR-positive, HER2 negative, advanced or metastatic breast cancer whose disease has progressed after prior	Not to be used after fulvestrant	In combination with an AI, for the treatment of post-menopausal women or men with ER-positive, HER2-negative advanced breast cancer who have not received any prior endocrine treatment for metastatic disease. Patients should have a good performance status and not be resistant to prior (neo)adjuvant aromatase inhibitor therapy, nor have active or uncontrolled metastases to the central nervous system. Notes (with AI): • anastrozole or letrozole are the approved aromatase inhibitors for use in combination with palbociclib; other endocrine therapies (e.g., Tamoxifen, Exemestane) are not approved • Good performance status for palbociclib eligibility is interpreted as ECOG ≤2 • For patients who received anastrozole or letrozole in the (neo)adjuvant setting, a minimum disease-free interval of 12 months after stopping therapy is required for palbociclib eligibility; there is no time restriction for patients who relapse after receiving Tamoxifen or Exemestane in the (neo)adjuvant setting • Patients will be eligible for EITHER palbociclib or ribociclib with anastrozole or letrozole in the first-line setting OR Everolimus with Exemestane as a subsequent line of therapy, not both therapies • In combination with fulvestrant for treatment of hormone receptor–positive, HER2-negative advanced or metastatic breast cancer either as initial therapy, or following disease progression in	• Good performance status is usually interpreted as ECOG 0-2 • Patients who have received prior neo/adjuvant endocrine therapy are eligible for palbociclib plus fulvestrant, including those w ho progress to metastatic disease < 12 months from completion • More than 1 hormone treatment can be given for advanced disease before utilizing palbociclib plus fulvestrant, excluding patients w ho experienced disease progression on a prior CDK 4/6 inhibitor or fulvestrant • Patients w ho received chemotherapy as initial treatment for advanced breast cancer are eligible for Palbociclib plus fulvestrant • Only 1 of a CDK 4/6 inhibitor plus AI or fulvestrant, or Everolimus plus Exemestane are funded for each patient	Palbociclib in combination with an aromatase inhibitor: For the treatment of post-menopausal women with ER-positive, HER2-negative advanced breast cancer who have not received any prior treatment for metastatic disease. Patients should have good performance status. Patients cannot be resistant to prior (neo)adjuvant AI therapy, nor have active or uncontrolled central nervous system metastases.	—	For the treatment of patients with ER-positive, human epidermal growth factor receptor 2 (HER 2)-negative; unresectable locally advanced breast cancer or metastatic breast cancer in patients who meet the following criteria; 1. Palbociclib is being used as combination therapy in 1 of the following treatment regimens; i) As first-line therapy in combination with an AI (i.e., letrozole, anastrozole, or exemestane) or fulvestrant in a patient who has not progressed on a prior systemic treatment (i.e., chemotherapy, immunotherapy, or endocrine therapy) for their unresectable locally advanced or metastatic disease; OR ii) As second-line therapy in combination with an AI (i.e., letrozole, anastrozole, or exemestane) or fulvestrant after progression on a chemotherapy for unresectable locally advanced or metastatic disease; OR iii) As a second or subsequent line therapy in combination with fulvestrant after progression on any number of endocrine monotherapies with the exception of progression during prior fulvestrant therapy	EAP funding will be considered for only 1 CDK 4/6 inhibitor regimen (i.e., palbociclib or ribociclib) OR Everolimus based regimen for the treatment of unresectable locally advanced or metastatic disease. No funding for sequential treatment regimens involving palbociclib or ribociclib or everolimus will be considered. AND Patients who received anastrozole or letrozole in the neo-adjuvant or adjuvant setting, must demonstrate a minimum disease-free interval of 12 months after stopping therapy to qualify for funding of palbociclib in combination with anastrozole or letrozole. Patient has good performance status defined as an ECOG score of 0 to 2; Patient does not have active or uncontrolled metastases to the central nervous system; AND in the case of a Patient who is pre-menopausal or

Brand name	Indication	British Columbia		Alberta		Saskatchewan		Manitoba		Ontario	
		Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes
				endocrine therapy including progression on adjuvant/ neoadjuvant endocrine therapy, progression within 12 months of completing adjuvant endocrine therapy, and progression on/after endocrine therapy for advanced/ metastatic breast cancer. There is no limit to the number of prior endocrine therapies received in the advanced/metastatic setting. Having received 1 prior line of chemotherapy for advanced/ metastatic disease is permitted. Eligible patients are CDK 4/6 inhibitor naive and include post-menopausal women, pre- or peri-menopausal women who are on a gonadotropin releasing hormone agonist, and men		previously treated patients • Eligible patients include men and women independent of their menopausal status; pre and peri-menopausal women must be rendered post-menopausal, either chemically or surgically, and should be treated with a LHRH agonist or bilateral salpingo-oophorectomy • Patients should have good performance status and not have active or uncontrolled metastases to the central nervous system					peri-menopausal, the Patient is receiving a LHRH agonist to achieve chemically induced menopause. The Patient has not experienced disease progression on any of the following regimens for locally advanced or metastatic breast cancer: (i) a palbociclib or ribociclib regimen; (ii) an everolimus regimen; or (iii) another CDK 4/6 regimen that has been publicly funded. Patients meeting the following criteria will not be funded. i) Patient is using palbociclib as re-treatment after disease progression on a prior palbociclib-based regimen. ii) Patient is using palbociclib with other drugs. iii) Patient is using palbociclib in combination with letrozole or anastrozole and experienced progression in the neoadjuvant or adjuvant setting within 12 months of treatment with letrozole or anastrozole; iv) Patient is pre- or peri-menopausal

Brand name	Indication	British Columbia		Alberta		Saskatchewan		Manitoba		Ontario	
		Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes
											who is not being treated with a LHRH agonist. v) Patient who is intending to use palbociclib with fulvestrant who has progressed on prior fulvestrant used as monotherapy or as part of another regimen. vi) Patient whose disease has progressed during treatment with a ribociclib regimen, an everolimus regimen, or another CDK 4/6 inhibitor regimen used for advanced, metastatic breast cancer, unless that use was through a clinical trial. vii) Patient who has active or uncontrolled CNS metastases. viii) Patient is requesting Ibrance for use with fulvestrant and has extensive, symptomatic, potentially life-threatening visceral metastases
Gilenya	RRMS - second line	As second-line monotherapy for the treatment of RRMS which is diagnosed according to the current clinical criteria and magnetic resonance imaging (MRI) evidence. Combination therapy is not covered.	Must be prescribed by a neurologist experienced in the management of RRMS and the request is received within 90 days of a recent neurological examination	Special authorization coverage may be provided for the treatment of RRMS to reduce the frequency of clinical relapses and to delay the progression of physical disability in adult patients (18 years of age or older)	A relapse is defined as the appearance of new symptoms or worsening of old symptoms, lasting at least 48 hours in the absence of fever, not associated with withdrawal from steroids. Onset of clinical relapses	For the treatment of patients with RRMS who meet all of the following criteria: • Have failed to respond to an adequate course* (i.e., at least 6 months) ≥ 1 DMT listed on the SK Formulary listed as initial therapy, OR has contraindications/intolerance to at least 2 DMTs listed on the SK Formulary as initial therapy;	Exclusion Criteria: • Patients on combination therapy of Gilenya with other DMTs. • Patients with EDSS > 5.5 • Patients who have had a heart attack or stroke in	For the treatment of patients with RRMS who meet all the following criteria: • After failure on at least 1 (1) Manitoba Provincial Drug Plan (PDP) approved first-line	Exclusion criteria: • In combination neither with other DMTs (e.g., Avonex, Betaseron, Copaxone, Extavia, Tysabri not in combination with Fampyra).	• The patient's physician provides documentation setting out the details of the patient's most recent neurological examination within ninety (90) days of the submitted request. This must include a description of any recent attack(s), the date(s) of the attack(s), and the neurological findings; AND • Failure to respond to full and	Exclusion criteria (Patients meeting any of the following exclusion criteria will not be funded): • Patient's receiving combination therapy of Gilenya with other DMTs (e.g., Aubagio,

Brand name	Indication	British Columbia		Alberta		Saskatchewan		Manitoba		Ontario	
		Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes
		This drug is for the treatment of patients 18 years of age and older who meet ALL of the following criteria: Patient has failed to respond to full and adequate courses of treatment with at least 1 first-line MS disease-modifying drug therapy OR has documented intolerance to at least 2 of these therapies AND Evidence that patient has had a significant increase in T2 lesion load compared to a previous MRI scan OR at least 1 gadolinium-enhancing lesion AND Patient has had 1 or more disabling attack/ relapses in the previous year AND Patient has not experienced a heart attack or stroke in the last 6 months and does not have a history of sick sinus syndrome, atrioventricular block, significant QT prolongation, bradycardia, ischemic heart disease, or congestive heart failures AND Patient has a recent EDSS score ≤ 5.5		who are refractory or intolerant to at least 1 of the first line agent: • When the above MS DMTs are taken at the recommended doses for a full and adequate course of treatment, within a consecutive 12-month period while the patient was on the MS DMT, the patient has: 1) Been adherent to the MS DMT (> 80% of approved doses have been administered); 2) Experienced at least 2 relapses of MS confirmed by the presence of neurologic deficits on examination. i. The first qualifying clinical relapse must have begun at least 1 month after treatment initiation. ii. Both qualifying relapses must be classified with a relapse severity of moderate, severe or very severe	must be separated by a period ≥ 1 month. At least 1 new T2 lesion or definite gadolinium-enhancing T1 MRI lesion (not questionable faint enhancement) obtained at least 90 days after initiation of the DMT and at least 90 days before or after a relapse may substitute for 1 clinical relapse. 1) The registered MS neurologist must confirm a diagnosis of RRMS; 2) The patient must have active disease which is defined as at least 2 relapses of MS during the previous 2 years or in the 2 years prior to starting an MS DMT. In most cases this will be satisfied by the refractory to treatment criterion but if a patient failed an MS DMT more than 1 year earlier, ongoing active disease must be confirmed. 3) The patient must be ambulatory with or without aid (The registered MS neurologist must provide a current updated EDSS score ≤ 6.5). Coverage will not be approved when any MS DMT or other immunosuppressive therapy is to be used	AND • 1 or more clinically disabling relapses in the previous year • Significant increase in T2 lesion load compared with that from a previous MRI scan (i.e., 3 or more new lesions) or at least 1 gadolinium-enhancing lesion • Requested and followed by a neurologist experienced in the management of RRMS • Recent EDSS score	the last 6 months of funding request, history of sick sinus syndrome, atrioventricular block, significant QT prolongation, bradycardia, ischemic heart disease or congestive heart failure • Patients taking class IA or III anti-arrhythmic drugs, immune-compromised due to immune-suppressant or cancer or AIDS, severe hepatic impairment, concurrent malignancies, pregnancy/ anticipated pregnancy/breast feeding or active infectious disease such as TB or hepatitis. • Patients < 18 years of age • Skin reactions at the site of injection do NOT qualify as a contraindication to injectable DMT	therapies OR documented intolerance to at least 2 Manitoba PDP approved first-line therapies • 1 or more clinically disabling relapses in the previous year. • Significant increase in T2 lesion load compared with that from a previous MRI scan or at least 1 gadolinium-enhancing lesion. • Requested and followed by a neurologist experienced in the management of RRMS • Recent EDSS score	• In patients with and EDSS > 5.5 • In patients who have had a heart attack or stroke in the last 6 months, or in a patient with a history of sick sinus syndrome, atrioventricular block, significant QT prolongation, bradycardia, ischemic heart disease or congestive heart failure • In patients < 18 years of age • In patients with a needle phobia or preference for oral therapy over injections in patients without clinical contraindication to interferon or glatiramer therapy	adequate courses1 ≥ 1 of interferon OR glatiramer acetate OR dimethyl fumarate; OR teriflunomide OR ocrelizumab OR documented intolerance or contraindication to 2 of the above listed therapies; AND • Experienced 1 or more clinically disabling relapses in the previous year; AND • Has had a significant increase in T2 lesion load compared with that from a previous MRI scan (i.e., 3 or more new lesions) OR at least 1 gadolinium-enhancing lesion. • Has a current EDSS of ≤ 5.5 (i.e., patients must be able to ambulate at least 100 m without assistance)	Avonex, Betaseron, Copaxone/Glatect, Extavia, Rebif, Extavia, Ocrevus, Tysabri, and Tecfidera). • Patients with EDSS > 5.5 • Patients who have had a heart attack or stroke in the last 6 months of the funding request, history of sick sinus syndrome, atrioventricular block, significant QT prolongation, bradycardia, ischemic heart disease, or congestive heart failure. • Patients younger than 18 years of age. • Patients requesting Gilenya due to needle phobia or preference for oral therapy over injection who do not have a clinical contraindication to interferon or glatiramer therapy. • Skin reactions at the site of injection do NOT qualify as a contraindication to interferon or glatiramer therapy

Brand name	Indication	British Columbia		Alberta		Saskatchewan		Manitoba		Ontario	
		Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes
					in combination with fingolimod. Coverage of fingolimod will not be approved if the patient was deemed to be refractory to fingolimod in the past						
Aubagio	RRMS - first line	As first-line monotherapy for the treatment of RRMS diagnosed according to the current McDonaldi clinical criteria and MRI evidence, when prescribed by a neurologist from a designated MS clinic, for patients who meet ALL of the following criteria: Patient has had at least 2 disabling attacks of MS in the previous 2 years, AND Patient is ambulatory with or without aid (EDSS of 6.5 or less), AND Patient is 18 years of age or older	The McDonald clinical criteria for the diagnosis of MS are current as of October 26, 2010 An attack is defined as the appearance of new symptoms or worsening of old symptoms, lasting at least 24 hours in the absence of fever, and preceded by stability for at least 1 month	Special authorization coverage may be provided for the reduction of the frequency and severity of clinical relapses and reduction of the number and volume of active brain lesions, identified on MRI scans, in ambulatory patients with RRMS. 1) The registered MS neurologist must confirm a diagnosis of RRMS; 2) The patient must have active disease which is defined as at least 2 relapses of MS during the previous 2 years or in the 2 years prior to starting an MS DMT. 3) The patient must be ambulatory with or without aid (The registered MS neurologist must provide a current updated EDSS score ≤ 6.5)	*A relapse is defined as the appearance of new symptoms or worsening of old symptoms, lasting at least 48 hours in the absence of fever, not associated with withdrawal from steroids. Onset of clinical relapses must be separated by a period ≥ 1 month. At least 1 new T2 lesion or definite gadolinium-enhancing T1 MRI lesion (not questionable faint enhancement) obtained at least 90 days after initiation of the DMT and at least 90 days before or after a relapse may substitute for 1 clinical relapse	Approval for coverage will be given to patients who are assessed and meet the following criteria: • have clinical definite RRMS, as defined by the 2017 McDonald diagnostic criteria; and • have had a clinical relapse1 and/or new MRI activity in the last 2 years; and • are fully ambulatory for 100 m without aids (canes, walkers, or wheelchairs) – EDSS of 5.5 or less; and • are age 18 or older	1 A clinical relapse is defined as the appearance of new symptoms or worsening of old symptoms, lasting at least 24 hours in the absence of fever, preceded by stability for at least 1 month. 2 MRI activity is defined as any new multiple sclerosis lesion/s, expanding lesion/s, and/or enhancing lesion/s. Physicians should also forward the following information: • attacks, date of onset, date of diagnosis; • neurological findings, EDSS; • MRI reports or other significant information; and • list of current medications	For the treatment of patients who have RRMS when prescribed by a neurologist from the Manitoba MS Clinic and: • Patients must have met diagnostic criteria for MS, as per the revised McDonald criteria. • The patient must be 18 years or older. • The course of disease must include at least 1 recent clinical attack in the year prior to therapy or 2 attacks in the previous 2 years. • The patient must still be ambulatory (with aids, if necessary).	—	i) The physician making the request on behalf of the patient is a neurologist who is experienced in the management of RRMS; AND ii) The physician provides documentation of the patient's most recent neurological examination which must have been conducted within ninety (90) days preceding the submission of the EAP request. This must include a description and dates of any recent attacks and other pertinent neurological findings; AND iii) The patient's diagnosis is confirmed to be RRMS; AND iv) The patient has experienced 1 or more clinical attacks/relapses in the year preceding the request; AND v) The patient has a recent EDSS score that is equal to or < 5.0 prior to starting therapy with teriflunomide	—
Entyvio	UC	For the treatment of moderate to severe UC when prescribed by a gastroenterologist. Mayo score must ≥ 4, with a rectal bleeding subscore ≥ 2. Patients	—	Special authorization coverage may be provided for the reduction in signs and symptoms and induction and maintenance of clinical remission of	Immuno-suppressive therapy as follows may also be initiated if in the clinician's judgment a trial is warranted: i) Azathioprine: minimum of 2	For treatment of UC in patients unresponsive to high dose steroids	—	For the treatment of patients > 18 years of age with moderate to severely active UC who have had inadequate response,	—	Moderate disease a. Mayo score between 6 and 10 (inclusive) AND b. Endoscopic subscore of 2 AND c. Failed 2 weeks of oral prednisone at daily doses ≥ 40 mg and 3 months of AZA/6MP	—

Brand name	Indication	British Columbia		Alberta		Saskatchewan		Manitoba		Ontario	
		Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes
		must have trialled 5-ASA for a minimum of 4 weeks and oral prednisone 40 mg or more daily for ≥ 14 days		UC in adult patients (18 years of age or older) with active disease (characterized by a partial Mayo score > 4 prior to initiation of biologic therapy) and who are refractory or intolerant to: • mesalamine: minimum of 4 g/day for a minimum of 4 weeks AND • steroids (failure to respond to prednisone 40 mg daily for 2 weeks, or; steroid dependent (i.e., failure to taper off steroids without recurrence of disease or disease requiring a second dose of steroids within 12 months of previous dose)	mg/kg/day for a minimum of 2 months; OR ii) 6-MP: minimum of 1 mg/kg/day for a minimum of 2 months			intolerance or contraindications to conventional therapy including 5-ASA compounds AND corticosteroids		OR Stabilized with 2 weeks of oral prednisone at daily dose ≥ 40 mg Severe disease a. Mayo score >10 AND b. Endoscopic* subscore of ≥ 2 AND c. Failed 2 weeks of oral prednisone at daily dose ≥ 40 mg OR Stabilized with 2 weeks oral prednisone ≥ 40 mg but the prednisone dose cannot be tapered despite 3 months of AZA/6MP	

6MP = 6-mercaptopurine; ALL = acute lymphoblastic leukemia; AZA = azathioprine; BCVA = best corrected visual acuity; BSA = body surface area; CHC = chronic hepatitis C; CHR = complete hematological response; CML = chronic myeloid leukemia; DIPSS = Dynamic International Prognostic Scoring System; DLQI = Dermatology Life Quality Index; DMARD = disease-modifying antirheumatic drug; DME = diabetic macular edema; DMT = disease-modifying therapy; EDSS = Expanded Disability Status Scale; ECOG = Eastern Cooperative Oncology Group; ETDRS = Early Treatment Diabetic Retinopathy Score; ER = estrogen receptor FA = fluorescein angiography; HCQ = hydroxychloroquine; HCV = hepatitis C virus; HER2 = human epidermal growth factor receptor 2; IM = intramuscular; LEF = leflunomide; LHRH = luteinizing hormone-releasing hormone; MTX = methotrexate; OCT = optical occurrence tomography; PDT = photodynamic therapy; RRMS = relapsing-remitting multiple sclerosis; PASI = Psoriasis Area Severity Index; Ph+ = Philadelphia chromosome positive; PHSA = Provincial Health Services Authority; p.o. = orally; PsO = plaque psoriasis; RA = rheumatoid arthritis; RRMS = relapsing-remitting multiple sclerosis; SC = subcutaneous; SSZ = sulfasalazine; UC = ulcerative colitis; UV = ultraviolet; VEGF = vascular endothelial growth factor; wAMD = wet age-related macular degeneration.

Appendix 2: Summary of Reimbursement Criteria for New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador, NIHB, and Yukon as of 2021

Table 4: Summary of Reimbursement Criteria for New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador, NIHB, and Yukon as of 2021

Brand name	Indication	New Brunswick		Nova Scotia		Prince Edward Island		Newfoundland and Labrador		NIHB		Yukon	
		Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes
Remicade	RA	• MTX or MTX + DMARD, AND • MTX + ≥ 2 DMARDs	> 12 weeks trial of MTX ≥ 20 mg/week (p.o., SC, or IM) (≥ 15 mg if patient is ≥ 65 years of age). > 3 months trial of MTX + other DMARDs e.g., MTX with HCQ and SSZ Optimal treatment response to DMARDs may take up to 24 weeks, however coverage of a biologic therapy can be considered if no improvement is seen after 12 weeks of triple DMARD use. If patient factors (e.g., intolerance) prevent the use of triple DMARD therapy, these must be described and dual therapy with DMARDs must be tried	• MTX or MTX + DMARD, AND • MTX + ≥ 2 DMARDs	> 12 weeks trial of MTX ≥ 20 mg/week (≥ 15 mg if patient is ≥ 65 years of age). >3 months trial of MTX + other DMARDs Optimal treatment response to DMARDs may take up to 24 weeks, however coverage of a biologic therapy can be considered if no improvement is seen after 12 weeks of triple DMARD use	• MTX or MTX + DMARD, AND • MTX + ≥ 2 DMARDs	>12 weeks trial of MTX ≥ 20 mg/week (≥ 15 mg if patient is ≥ 65 years of age). >3 months trial of MTX + other DMARDs Optimal treatment response to DMARDs may take up to 24 weeks, however coverage of a biologic therapy can be considered if no improvement is seen after 12 weeks of triple DMARD use. New patients have the option to be treated with brand and biosimilar versions of IFX.	• MTX AND • MTX + ≥ 2 DMARDs, OR • MTX + ≥ 2 DMARDs	12 weeks trial of MTX ≥ 20 mg/week (≥ 15 mg if patient is ≥ 65 years of age). >3 months trial of MTX + other DMARDs Optimal treatment response to DMARDs may take up to 24 weeks, however coverage of a biologic therapy can be considered if no improvement is seen after 12 weeks of triple DMARD use.	• MTX, AND • MTX + ≥ 2 DMARDs (SSZ and HCQ) OR • ≥ 2 DMARDs combination (SSZ, HCQ, azathioprine, LEF, cyclosporine); if the patient has a contraindication, failure, or intolerance to MTX	> 12 weeks trial for each course of therapy. MTX ≥ 20 mg/week (p.o., SC, or IM) (≥ 15 mg if patient is ≥ 65 years of age). FOR abatacept IV ONLY: Must have failed (FOR IV FORMULATION ONLY): >12 weeks trial of etanercept SC or adalimumab SC or golimumab SC or certolizumab pegol SC or abatacept SC or tocilizumab or tofacitinib p.o. or infliximab biosimilars	• Parenteral MTX, AND • ≥ 2 of the following: LEF, SSZ, azathioprine; AND, • ≥ 1 DMARD combination	>12 weeks trial for each course of therapy. DMARD combination e.g., MTX with cyclosporine, MTX with HCQ and SSZ, MTX with LEF FOR abatacept ONLY: Must have failed adequate trial of an anti-TNF agent
Humira	PsO	For the treatment of patients with chronic moderate to severe PsO who meet all of the following criteria: PASI > 10 and DLQI > 10, or major involvement of visible areas, scalp, genitals, or nails • Refractory, intolerant or unable to access	• MTX (oral or parenteral) at a dose of ≥ 20 mg weekly (greater than or equal to 15 mg if patient is ≥ 65 years of age) for a minimum of 12 weeks • CCO for a minimum of 6 weeks	For patients with severe, debilitating chronic PsO who meet all of the following: o BSA involvement of > 10% and/or significant involvement of the face, hands, feet or genitals; o Failure to, contraindicatio	—	For treatment of adult patients with severe debilitating PsO who meet all of the following criteria: o failure to respond to, contraindications to, or intolerant of MTX and cyclosporine; AND failure to respond to, intolerant to or unable to access phototherapy	—	For patients with severe, debilitating psoriasis who meet all of the following criteria: • BSA involvement of > 10% and/or significant involvement of the face, hands, feet or genital region; • Failure to respond to, contraindication	—	For the treatment of patients with moderate to severe psoriasis who meet all of the following criteria: • BSA involvement > 10% and/or significant involvement of the face, hands, feet or genital region; and • intolerance or lack of	MTX (weekly oral or parenteral) at 20 mg or greater (15 mg or greater if patient is > 65 years of age) for more than 8 weeks	For patients with body surface involvement BSA > 10%, OR significant involvement of face, hands, feet or genitals, AND have a PASI > 12. For patients who are refractory or intolerant to a 12 week trial of parenteral methotrexate AND a 12 week	—

Brand name	Indication	New Brunswick		Nova Scotia		Prince Edward Island		Newfoundland and Labrador		NIHB		Yukon	
		Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes
		phototherapy • Refractory, intolerant or have contraindications to 1 of the following: methotrexate or cyclosporine		n to or intolerant of MTX and cyclosporine; o Failure to, intolerant of or unable to access phototherapy				s to, or intolerant of MTX and cyclosporine; • Failure to respond to, intolerant to, or unable to access phototherapy		response or inability to access phototherapy; and • intolerance, lack of response, or contraindication to MTX and cyclosporine		trial of cyclosporine	
Lucentis	wAMD	BCVA is between 6/12 and 6/96 The lesion size is ≤ 12 disc areas in greatest linear dimension There is evidence of recent (< 3 months) presumed disease progression (blood vessel growth, as indicated by fluorescein angiography, or OCT)	Coverage will not be approved for patients: With permanent retinal damage as defined by the Royal College guidelines Receiving concurrent treatment with verteporfin	No criteria - coverage at the discretion of a retinal specialist	—	The following must apply to the eye to be treated: (i) The BCVA is between 6/12 and 6/96 (ii) The lesion size is ≤ 12 disc areas in greatest linear dimension (iii) There is evidence of recent (< 3 months) presumed disease progression (blood vessel growth, as indicated by fluorescein angiography, OCT or recent visual acuity changes)	Coverage will not be approved for patients: • With permanent retinal damage as defined by the Royal College guidelines • Receiving concurrent treatment with verteporfin	• A diagnosis of neovascular wAMD; • Evidence of recent (< 3 months) disease progression (e.g., blood vessel growth, as indicated by either fluorescein angiography, OCT or recent visual acuity changes); • A corrected Visual acuity between 6/12 and 6/96; • A lesion whose size is ≤ 12 disc areas in its greatest linear dimension; • When there is no permanent structural damage to the central fovea. Criteria for Exclusion: Patients who have "permanent retinal damage," as defined by the Royal	o OCT is recognized by the NLPDP as a relevant diagnostic test for wAMD. Effective December 12, 2019, intravitreal bevacizumab will be the preferred therapy for: • treatment-naive patients, • NLPDP beneficiaries who did not have a paid claim for Lucentis/ Eylea under NLPDP between December 13, 2018, and December 12, 2019, and • beneficiaries currently receiving Avastin	Initial coverage for the treatment of neovascular wAMD where all of the following apply to the eye to be treated: • BCVA is between 6/12 and 6/96 • the lesion size is ≤ 12 disc areas in greatest linear dimension • there is evidence of recent (< 3 months) presumed disease progression (blood vessel growth, as indicated by fluorescein angiography, or OCT)	Note: Coverage will not be approved for patients: • with permanent retinal damage as defined by the Royal guidelines. • receiving concurrent treatment with verteporfin	On recommendation of a specialist for treatment of age-related macular degeneration, or visual impairment due to macular edema secondary to central vein occlusion	—

Brand name	Indication	New Brunswick		Nova Scotia		Prince Edward Island		Newfoundland and Labrador		NIHB		Yukon	
		Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes
								guidelines, including any future amendments					
Eylea	DME	For the treatment of visual impairment due to DME in patients who meet all the following criteria: • clinically significant centre-involving macular edema for whom laser photocoagulation is also indicated • hemoglobin A1c test in the past 6 months with a value ≤ 11% • BCVA of 20/32 to 20/400 • central retinal thickness ≥ 250 micron	—	No criteria - coverage at the discretion of a retinal specialist	—	For the treatment of visual impairment due to DME for patients meeting all of the following: (i.) Diffuse DME involving the central fovea with central fovea thickness of 300 microns or greater on OCT and vision < 20/32. (ii.) Patients with focal macular edema for which laser photocoagulation is indicated should be treated with laser, except in situations where focal laser therapy treatment cannot be safely performed due to the proximity of microaneurysms to the fovea. (iii.) hemoglobin A1C < 11%	Fluorescein angiography should be considered prior to initiation of treatment to assess perfusion and characterize the leakage and should also be considered if the patient is not responding to treatment as expected.	For the treatment of visual impairment due to DME meeting all of the following criteria: • clinically significant DME for whom laser photocoagulation is also indicated, and • hemoglobin A1C < 11%	Effective December 12, 2019, intravitreal bevacizumab will be the preferred therapy for: • treatment-naive patients, • NLPDP beneficiaries who did not have a paid claim for Lucentis/ Eylea under NLPDP between December 13, 2018 and December 12, 2019. Patients who have failed to respond to 3 injections of Avastin, have contraindications to the use of Avastin or are unable to tolerate Avastin will require a written request from their ophthalmologist detailing their contraindication (s)	For the treatment of DME for patients who meet the following: • clinically significant diabetic macular edema for whom laser photocoagulation is also indicated; and • have a hemoglobin A1C < 12%	—	On recommendation of a specialist	—
Zepatier	Hepatitis C genotypes 1,3,4	For treatment-naive or treatment-experienced adult patients with chronic HCV without cirrhosis or with compensated	The following information is also required: • Laboratory-confirmed hepatitis C genotype 1 or 4 • Quantitative HCV RNA value within	Genotype 1 ▪ Treatment-naive ▪ Treatment-experienced prior relapsers ▪ 12 weeks (8 weeks considered in	• Quantitative HCV RNA value within the last 6 months • Fibrosis stage must be provided	Not reimbursed	Not reimbursed	• Laboratory-confirmed hepatitis C genotype 1 or 4 • Quantitative HCV RNA value within the last 6 months Genotype 1	Exclusion criteria: • Patients currently being treated with another HCV antiviral agent. • Re-treatment for failure or re-	For adult patients with CHC infection at any fibrosis stage (F0-F4) who meet all of the following criteria:	Re-treatment for failure or re-infection in patients who have received an adequate prior course of direct-acting antivirals will be considered on a case-by-case basis	For treatment-naive or treatment-experienced adult patients with CHC infection at any fibrosis stage (F0-F4) who	All exception requests must include: Laboratory-confirmed hepatitis C genotype Quantitative HCV RNA value

Brand name	Indication	New Brunswick		Nova Scotia		Prince Edward Island		Newfoundland and Labrador		NIHB		Yukon	
		Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes
		cirrhosis who meet the following criteria: Genotype 1 • Treatment-naive • Treatment-experienced prior relapsers 12 weeks (8 weeks may be considered in treatment-naive genotype 1b patients without significant fibrosis or cirrhosis) Genotype 1b • Treatment-experienced on-treatment virologic failures 12 weeks Genotype 4 • Treatment-naive • Treatment-experienced prior relapsers 12 weeks Approval Period and Regimen	the last 6 months • Fibrosis stage	treatment-naive genotype 1b patients without significant fibrosis) Genotype 1b ▪ Treatment-experienced on-treatment virologic failures ▪ 12 weeks Genotype 4 ▪ Treatment-naive ▪ Treatment-experienced prior relapsers ▪ 12 weeks Genotype 1a ▪ Treatment-experienced on-treatment virologic failures ▪ 16 weeks in combination with ribavirin Genotype 4 ▪ Treatment-experienced on-treatment virologic failures ▪ 16 weeks in combination with ribavirin o Laboratory-confirmed CHC genotype 1 or 4;				• Treatment-naive • Treatment-experienced prior relapsers 12 weeks (8 weeks considered in treatment-naive genotype 1b patients without significant fibrosis) Genotype 1b • Treatment-experienced on-treatment virologic failures 12 weeks Genotype 1a • Treatment-experienced on-treatment virologic failures 16 weeks in combination with ribavirin Genotype 4 • Treatment-naive • Treatment-experienced prior relapsers 12 weeks Genotype 4 • Treatment-experienced on-treatment virologic failures 16 weeks in combination with ribavirin	infection in patients who have received an adequate prior course of an HCV direct-acting antiviral drug regimen may be considered on a case-by-case basis. Clinical notes: • Special Authorization requests must include the most recent HCV RNA test performed in the last 6 months	• treatment is prescribed by hepatologist, gastroentero-logist, or infectious disease specialist (or other prescriber experienced in treating patients with chronic hepatitis C); and • laboratory-confirmed quantitative HCV RNA level taken in the last 12 months		meet the following criteria: Treatment is prescribed by hepatologist, infectious disease specialist or gastroenterologist (specialist's consult to be provided); AND Laboratory-confirmed hepatitis C genotype 1,2,3,4,5,6 or mixed genotype; AND Laboratory-confirmed quantitative HCV RNA level taken in the last 12 months. Re-treatment for failure or re-infection in patients who have received an adequate prior course of direct-acting antivirals considered on a case-by-case basis	within the last 12 months Treatment-experienced is defined as those patients who have been previously treated with a pegIFN/RBV regimen (including regimens containing an HCV protease inhibitor) and have not experienced an adequate response
Epclusa	Hepatitis C	For treatment-naive or treatment-experienced adult patients with chronic HCV who meet the following criteria: Genotypes 1, 2, 3, 4, 5, 6 or	The following information is also required: 1. Laboratory-confirmed hepatitis C genotype 1, 2, 3, 4, 5, 6 or mixed genotypes 2. HCV RNA value within the last 6	• For treatment-naive or treatment-experienced adult patients with chronic HCV who meet the	• Must be prescribed by hepatologist, gastroentero-logist, or infectious disease specialist (or other physician experienced in	Not reimbursed	Not reimbursed	For treatment-naive or treatment-experienced adult patients with chronic HCV who meet the following criteria: • Prescribed by	Claim notes: • Special Authorization requests must include the genotype report from the latest post-treatment course. • Special	Limited use benefit (prior approval required). For adult patients with CHC infection at any fibrosis stage (F0-F4) who meet all of	Re-treatment for failure or re-infection in patients who have received an adequate prior course of direct-acting antivirals will be considered on a case-by-case basis	For treatment-naive or treatment-experienced adult patients with CHC infection at any fibrosis stage (F0-F4) who meet the	Re-treatment for failure or re-infection in patients who have received an adequate prior course of direct-acting antivirals will be considered on a

Brand name	Indication	New Brunswick		Nova Scotia		Prince Edward Island		Newfoundland and Labrador		NIHB		Yukon	
		Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes
		mixed genotypes: Patients with compensated cirrhosis or without cirrhosis: 12 weeks Genotypes 1, 2, 3, 4, 5, 6 or mixed genotypes: Patients with decompensated cirrhosis 12 weeks in combination with ribavirin	months 3. Fibrosis stage	following criteria: Genotypes 1, 2, 3, 4, 5, 6 or mixed genotypes: Patients with compensated cirrhosis or without cirrhosis : 12 weeks Genotypes 1, 2, 3, 4, 5, 6 or mixed genotypes : Patients with decomp-ensated cirrhosis :12 weeks in combination with ribavirin	treating a patient with hepatitis C infection) • Laboratory-confirmed hepatitis C genotype 1, 2, 3, 4, 5, 6 or mixed genotypes • Quantitative HCV RNA value within the last 6 months • Fibrosis stage must be provided Re-treatment for direct-acting antiviral failures will be considered on a case-by-case basis			a hepatologist, gastroentero-logist, or infectious disease specialist (or other physician experienced in treating a patient with hepatitis C infection). • Laboratory-confirmed hepatitis C genotype 1, 2, 3, 4, 5, 6 or mixed genotypes • Quantitative HCV RNA value within the last 6 months Exclusion criteria: • Patients currently being treated with another HCV antiviral agent • Re-treatment for failure or re-infection in patients who have received an adequate prior course of an HCV direct-acting antiviral drug regimen may be considered	Authorization requests must include the most recent HCV RNA test performed in the last 6 months	the following criteria: • treatment is prescribed by hepatologist, gastroentero-logist, or infectious disease specialist (or other prescriber experienced in treating patients with chronic hepatitis C); and • laboratory-confirmed quantitative HCV RNA level taken in the last 12 months		following criteria: Treatment is prescribed by hepatologist, infectious disease specialist or gastroentero-logist (specialist's consult to be provided); AND Laboratory-confirmed hepatitis C genotype 1,2,3,4,5,6 or mixed genotype; AND Laboratory-confirmed quantitative HCV RNA level taken in the last 12 months	case-by-case basis under the formulary exception process
Sprycel	CML	For adult patients with chronic phase CML • with primary or acquired resistance to imatinib 600 mg per day. • who progress to accelerated	—	As a single agent for the treatment of adults with chronic, accelerated or blast phase CML and Ph+ acute lymphoblastic	—	For use as a single agent for the treatment of adults with chronic, accelerated or blast phase CML and Ph+ acute lymphoblastic leukemia (Ph+ ALL) with	Prescriptions written by PEI oncologists do not require Special Authorization.	• For adult patients with chronic phase CML with primary or acquired resistance to imatinib (600 mg/day)	—	Not reimbursed	—	On recommendation of oncologist and all criteria established by cancer agency must be followed	—

Brand name	Indication	New Brunswick		Nova Scotia		Prince Edward Island		Newfoundland and Labrador		NIHB		Yukon	
		Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes
		phase on imatinib 600 mg per day. • who have blast crisis while on imatinib 600 mg per day. • who have intolerance to imatinib or have experienced grade 3 or higher toxicities to imatinib		leukemia with resistance or intolerance to prior therapy including imatinib		resistance or intolerance to prior therapy including Imatinib.		• For adult patients with chronic phase CML who progress to accelerated phase on imatinib 600 mg per day. • For adult patients with chronic phase CML who has blast crisis while on imatinib 600 mg per day. • For adult patients with CML who have intolerance to imatinib or have experienced grade 3 or higher toxicities to imatinib					
Jakavi	Myelo-fibrosis	For the treatment of patients with intermediate to high-risk symptomatic myelofibrosis as assessed using the DIPSS Plus or patients with symptomatic splenomegaly. Patients should have ECOG performance status ≤ 3 and be either previously untreated or refractory to other treatment	—	As a single agent in patients with intermediate or high-risk symptomatic myelofibrosis using the DIPSS Plus or symptomatic splenomegaly with an ECOG performance status ≤ 3 as first line therapy or refractory to other treatments	Ongoing monitoring and follow up of therapy will be required	For patients with intermediate to high-risk symptomatic myelofibrosis as assessed using the DIPSS Plus or patients with symptomatic splenomegaly. Patients should have ECOG performance status of ≤3 and be either previously untreated or refractory to other treatment.	—	For patients with intermediate to high-risk symptomatic myelofibrosis as assessed using the DIPSS Plus or patients with symptomatic splenomegaly. Patients should have ECOG performance status ≤3 and be either previously untreated or refractory to other treatment	—	For the treatment of myelofibrosis: • intermediate to high-risk symptomatic myelofibrosis as assessed using the DIPSS Plus; or • patient has symptomatic splenomegaly and • patient has an ECOG performance status of 0 to 3; and • patient previously untreated or refractory to other treatment.	—	For patients with intermediate to high-risk symptomatic myelofibrosis as assessed using the DIPSS Plus or patients with symptomatic splenomegaly. Patients should have ECOG performance status ≤ 3 and be either previously untreated or refractory to other treatment	—
Ibrance	Breast cancer	1. In combination with an AI for the treatment of patients with	1. For patients who received (neo)adjuvant NSAI therapy, a minimum	ER-positive, HER2-negative advanced	• Patients should have a good performance status and not be	In combination with an AI for the treatment of ER-positive, HER2-	• Patients must have a good performance status • Resistance is	In combination with an AI (e.g., letrozole) for the treatment of	1. Patients must have a good performance status.	For the treatment of post-menopausal	—	Patients are eligible to receive palbociclib in	Note: Patients are eligible to receive palbociclib plus

Brand name	Indication	New Brunswick		Nova Scotia		Prince Edward Island		Newfoundland and Labrador		NIHB		Yukon	
		Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes
		hormone receptor–positive, HER2-negative advanced or metastatic breast cancer who: • have not received prior endocrine therapy for advanced or metastatic disease, and • are not resistant to prior (neo)adjuvant NSAI therapy, and • do not have active or uncontrolled metastases to the CNS. 2. In combination with fulvestrant for the treatment of patients with hormone receptor–positive, HER2 negative advanced or metastatic breast cancer who: • have not received prior endocrine therapy or have experienced disease progression on endocrine therapy, and • have received up to 1 prior chemotherapy for advanced or metastatic disease, and • do not have active or uncontrolled metastases to the CNS	disease-free interval of 12 months after stopping therapy is required. 2. Pre- and peri-menopausal patients must be treated with a luteinizing hormone-releasing hormone agonist. 3. Patients must have a good performance status. 4. Treatment should be discontinued upon disease progression or unacceptable toxicity. · Requests will not be considered for patients who experience disease progression on a CDK4/6 inhibitor, fulvestrant or everolimus	breast cancer in combo with an aroma-tase inhibitor (AI) • In combination with an aromatase inhibitor (AI) (i.e., letrozole, anastrozole or exemestane) for the treatment of post-menopausal women with ER-positive, human epidermal growth factor receptor 2 (HER 2) negative advanced breast cancer who have not received any prior endocrine-based treatment for metastatic disease. Patients may have received up to 1 prior line of chemotherapy for advanced disease. HR-positive, HER2-negative advanced or metastatic breast cancer in combination with fulvestrant • In combination with	resistant to prior (neo) adjuvant AI therapy (i.e., have the potential to benefit from first-line endocrine-based therapy), without active or uncontrolled metastases to the CNS. • Patients will be eligible for either palbociclib plus an AI in the first-line setting or everolimus plus exemestane as a subsequent line of therapy, but not both therapies. Patients eligible include: • Pre and peri-menopausal patients (should be treated with a LHRH agonist) • Males • Patients with bone-only metastases • Patients who are HER2 equivocal by FISH testing (these patients are HER2 negative) • Patients currently receiving first-line AI monotherapy for ER-positive, HER2-negative metastatic breast cancer may have palbociclib added provided the above criteria is met.	negative advanced breast cancer in post-menopausal women who: • have not received prior therapy for metastatic disease and • are not resistant to (neo) adjuvant NSAI therapy and • do not have active or uncontrolled metastases to the CNS	defined as disease progression occurring during or within 12 months following NSAI therapy • Treatment should be discontinued up on disease progression or unacceptable toxicity	ER-positive, HER2-negative advanced breast cancer in post-menopausal women who: • have not received prior therapy for metastatic disease, and • are not resistant to (neo)adjuvant NSAI therapy, and • do not have active or uncontrolled metastases to the CNS	2. Resistance is defined as disease progression occurring during or within 12 months following (neo)-adjuvant NSAI therapy. • Sequential use of palbociclib and everolimus will not be reimbursed	clients with ER-positive, HER2-negative advanced breast cancer; and • the patient has not received any prior treatment for metastatic disease (first-line treatment); and • palbociclib will be used in combination with an AI; and • patient has an ECOG performance status of 0 to 2; and • patient is not resistant to prior (neo)adjuvant AI therapy; and • patient does not have active or uncontrolled metastases to the CNS. For in combination with fulvestrant, for the treatment of patients with HR-positive, HER2-negative locally advanced or metastatic breast cancer whose disease has progressed after prior endocrine therapy. • patient has an ECOG performance status of 0 to		combination with an AI (letrozole or anastrozole) for the treatment of: • Post-menopausal women and men with ER-positive, HER2-negative advanced breast cancer with no prior systemic treatment (including chemotherapy) for metastatic disease (including women with chemically induced menopause with LHRH agonists • Patients should not be resistant to prior (neo)adjuvant AI therapy (patients must be a minimum of 12 months from last adjuvant aromatase inhibitor), nor have active or uncontrolled metastases to the CNS • Good performance status EXCLUSION: • Advanced symptomatic and life-threatening visceral metastases • Pregnant women • Palbociclib monotherapy	letrozole/anastrozole or everolimus plus exemestane, but not sequential use of these combination regimens. Note: For patients recently diagnosed with metastatic breast cancer, and who have initiated anastrozole or letrozole monotherapy within the past 6 months, palbociclib can be added if the rest of the above criteria are met. • BC Cancer Compassionate Access Program approval is required

Brand name	Indication	New Brunswick		Nova Scotia		Prince Edward Island		Newfoundland and Labrador		NIHB		Yukon	
		Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes
				fulvestrant for the treatment of patients with hormone receptor (HR) positive, HER 2 negative advanced or metastatic breast cancer, as initial endocrine-based therapy or following disease progression on endocrine therapy. Patients may have also received up to 1 prior line of chemotherapy for advanced disease. Patients should have a good performance status, without active or uncontrolled metastases to the CNS and can be of any menopausal status (peri-menopausal and pre-menopausal women must be treated with an LHRH agonist)	• Patients who progress ≤ 12 months from (neo) adjuvant therapy are eligible for treatment with palbociclib plus fulvestrant. • Patients who experience disease progression on prior CDK 4/6 inhibitor therapy, fulvestrant or everolimus are not eligible for treatment with palbociclib with fulvestrant. • Patients currently receiving fulvestrant monotherapy, and who have not progressed may have palbociclib added, provided they are CDK 4/6 inhibitor naive and otherwise meet funding criteria. • Patients who previously received everolimus plus exemestane will be eligible for funding of palbociclib plus fulvestrant on progression, provided that treatment was started prior to funding of CDK 4/6 + fulvestrant, patient must be CDK 4/6 naive and otherwise					For in combination with fulvestrant, for the treatment of patients with HR-positive, HER2-negative locally advanced or metastatic breast cancer whose disease has progressed after prior endocrine therapy. • patient has an ECOG performance status of 0 to 2			

Brand name	Indication	New Brunswick		Nova Scotia		Prince Edward Island		Newfoundland and Labrador		NIHB		Yukon	
		Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes
					meet funding criteria								
Gilenya	RRMS - second line	For the treatment of patients with RRMS who meet all of the following criteria: • Failure to respond to full and adequate courses1 ≥ 1 interferon OR glatiramer acetate; OR documented intolerance2 to both therapies • Have experienced 1 or more clinically disabling relapses in the previous year • Demonstrate a significant increase in T2 lesion load compared with that from a previous MRI scan (i.e., 3 or more new lesions) OR have at least 1 gadolinium-enhancing lesion • Request is being made by and followed by a neurologist experienced in the management of RRMS • Patient has a recent EDSS score ≤ 5.5 (i.e., patients must be able to ambulate at least 100 m without assistance)	Exclusion Criteria: • Combination therapy of fingolimod with other disease-modifying therapies will not be funded. • Combination therapy of fingolimod with Fampyra will not be funded. • Patients with EDSS > 5.5 will not be funded • Patients who have experienced a heart attack or stroke within the 6 months prior to the funding request will not be considered. • Patients with a history of sick sinus syndrome, atrioventricular block, significant QT prolongation, bradycardia, ischemic heart disease, or congestive heart failure will not be considered. • Patients younger than 18 years of age will not be considered. • Patients with needle phobia or those having a preference for an oral therapy over an injection and who do not have 1 or more clinical contraindications to interferon or glatiramer therapy will not be funded.	For the treatment of patients with RRMS who meet all of the following criteria: • have failed to respond to a full and adequate course ≥ 1 DMT publicly insured in Nova Scotia as an initial therapy, or has contraindications/ intolerance to at least 2 initial therapies; • 1 or more clinically disabling relapses in the previous year; • significant increase in T2 lesion load compared with that from a previous MRI scan (i.e., 3 or more new lesions) or at least 1 gadolinium-enhancing lesion; • requested and followed by a neurologist experienced in the management of RRMS;	Exclusions: • not funded with ther DMTs; • not funded in patients with an EDSS > 5.5; • not funded in patients who have had a heart attack or stroke in the last 6 months of funding request, patients with a history of sick sinus syndrome, atrioventricular block, significant QT prolongation, bradycardia, ischemic heart disease, or congestive heart failure; • not funded in patients < 18 years of age; • not funded due to needle phobia or preference for oral therapy over injection in patients without clinical contraindications to interferon or glatiramer therapy. Note: • Skin reactions at the site of injection do not qualify as contraindications to interferon or glatiramer therapy.	For the treatment of patients with RRMS who meet all of the following criteria: a) Failure to respond to full and adequate courses ≥ 1 DMT publicly insured under PEI Pharmacare as an initial therapy, or has intolerance to at least 2 initial publicly funded therapies. b) 1 or more clinically disabling relapses in the previous year. c) Significant increase in T2 lesion load compared with that from a previous MRI scan (i.e., 3 or more new lesions) or at least 1 gadolinium-enhancing lesion. d) Requested and followed by a neurologist experienced in the management of RRMS. e) Recent EDSS score of ≤ 5.5 (i.e., patients must be able to ambulate at least 100 m without assistance)	Exclusion Criteria: a) Do not fund combination therapy of Gilenya with other DMTs (e.g., Avonex, Betaseron, Copaxone, Rebif, Extavia, Tysabri) nor in combination with Fampyra. b) Do not fund in patients with EDSS > 5.5 c) Do not fund in patients who have had a heart attack or stroke in the last 6 months of funding request, history of sick sinus syndrome, atrioventricular block, significant QT prolongation, bradycardia, ischemic heart disease, or congestive heart failure d) Patients < 18 years of age e) Needle phobia or preference for oral therapy over injection in patients without clinical contraindication to interferon or glatiramer therapy f) Skin reactions at the site of injection do NOT qualify as a contraindication to interferon or glatiramer therapy Renewal: a) Date and details of the most recent neurological examination and EDSS scores must be provided (examination must	For the treatment of patients with RRMS who meet all of the following criteria: • Failure to respond to full and adequate courses ≥ 1 at least 1 DMT publicly listed on the NLPDP Formulary ; OR documented intolerance to at least 2 therapies • Have experienced 1 or more clinically disabling relapses in the previous year • Demonstrated significant increase in T2 lesion load compared with that from a previous MRI scan OR have at least 1 gadolinium-enhancing lesion • Request is being made by and followed by a neurologist experienced in the management of RRMS • Patient has a recent EDSS score ≤ 5.5 (i.e., patients must be able to	Exclusion criteria: • Combo fingolimod with other DMTs (e.g., Avonex, Betaseron, Copaxone, Rebif, Extavia, Tysabri, Aubagio, Tecfidera) will not be funded. • Combo therapy of fingolimod with Fampyra will not be funded. • Patients with EDSS > 5.5 will not be funded • Patients who have experience-ed a heart attack or stroke within the 6 months prior to the funding request will not be considered. • Patients with a history of sick sinus syndrome, atrioventricular block, significant QT prolongation, bradycardia, ischemic heart disease, or congestive heart failure will not be considered. • Patients younger than 18 years of age will not be considered	For the treatment of patients with RRMS who meet all of the following criteria: • failure to respond to full and adequate courses ≥ 1 initial DMT (an interferon, glatiramer acetate, dimethyl fumarate, ocrelizumab or teriflunomide) or documented intolerance to at least 2 therapies; and • 1 or more clinically disabling relapses in the previous year; and • significant increase in T2 lesion load compared with that from a previous MRI scan or at least 1 gadolinium-enhancing lesion; and • requested and followed by a neurologist experienced in the management of RRMS; and • recent EDSS score	—	For treatment of RRMS in patients who meet all the following criteria: • Failure to respond to adequate courses (at least 6 months) of any 1 therapy listed on the Yukon formulary OR documented intolerance to 2 therapies listed in the formulary. Intolerance does NOT include: needle phobia, skin reactions at injection site or patient preference for oral form • 1 or more clinical relapse in the previous year; the appearance of new symptoms or worsening of symptoms, lasting at least 24 hours in the absence of fever, & preceded by stability for at least 1 month • Significant increase in T2 lesion load (3 or more new lesions) or at least 1 gadolinium-enhancing lesion	NB -will not be funded in combination with any other disease-modifying agent; in patients with EDSS > 5.5; in patients with heart conditions; or in patients under age 18 Failure to respond to full & adequate courses: defined as a trial ≥ 6 months of 1 therapy listed in the Yukon formulary AND experienced at least 1 disabling relapse while on that therapy. Intolerance is defined as: documented serious adverse effects or contraindications that are incompatible with further use of that class of drug. Recently EDSS score ≤ 5.5 (patients must be able to ambulate at least 100 m without assistance)

Brand name	Indication	New Brunswick		Nova Scotia		Prince Edward Island		Newfoundland and Labrador		NIHB		Yukon	
		Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes
			• Skin reactions at the site of the injection do NOT qualify as a contraindication to interferon or glatiramer therapy. Requirements for Initial Requests: • The patient's physician must set out the details of the patient's most recent neurological examination within ninety (90) days of the submitted request. This must include a description of any recent attacks, the dates, and the neurological findings. • Date and details of the most recent neurological examination and EDSS scores must be provided (examination must occur within last 90 days)	• recent EDSS score of 5.5 or less (i.e., patients must be able to ambulate at least 100 m without assistance)	Renewal: • EDSS score ≤ 5.5 (i.e., patients must be able to ambulate at least 100 m without assistance). Date and details of the most recent neurological examination and EDSS scores must be provided (examination must have occurred within that last 90 days); AND • Patients must be stable or have experienced no more than 1 disabling attack/relapse in the past year		have occurred within that last 90 days). b) Patients must be stable or have experienced no more than 1 disabling attack/relapse in the past year; AND c) Recent EDSS score of ≤ 5.5 (i.e., patients must be able to ambulate at least 100 m without assistance)	ambulate at least 100 m without assistance) Requirements for Initial Requests: • The patient's physician must set out the details of the patient's most recent neurological examination within ninety (90) days of the submitted request. This must include a description of any recent attacks, the dates, and neurological findings				• Requested and followed by a neurologist experienced with RRMS. Specialists consult to be provided. • Recently expanded EDSS score (EDSS ≤ 5.5)	
Aubagio	RRMS - first line	For the treatment of adult patients with RRMS who meet all of the following criteria: • Confirmed diagnosis based on McDonald criteria • Experienced 1 or more disabling relapses or new MRI activity in the past 2 years • Ambulatory with or without aid (i.e., has a recent EDSS score of ≤ 6.5)	• Treatment should be discontinued for patients with an EDSS score of ≥ 7. • Prescriptions written by neurologists licensed by the College of Physicians and Surgeons of New Brunswick do not require special authorization • Combined use with other disease-modifying therapies to treat RRMS will not be reimbursed	• For the treatment of patients with RRMS who meet all of the following criteria: o requested and followed by a neurologist experienced in the management of RRMS; and o recent EDSS score of 5.5 or less (i.e., patients must be able to	• Exclusions: o not funded in combo with other DMTs; o not funded in patients with an EDSS > 5.5	For the treatment of patients 18 years of age or older, diagnosed with RRMS (if applicable), who have had 2 attacks within the past 2 years, and have an EDSS score of 6.5 or less.	—	For the treatment of patients with RRMS who meet all of the following criteria: • requested and followed by a neurologist experienced in the management of RRMS, and • recent EDSS score of 5.5 or less (i.e., patients must be able to ambulate at	Exclusions: • not funded in combination with other disease-modifying therapies • not funded in patients with an EDSS > 5.5	As a first-line therapy for the treatment of RRMS diagnosed according to the 2017 McDonald clinical criteria and magnetic resonance imaging (MRI) evidence, when prescribed by a neurologist experienced in the management of RRMS. And for patients who meet all of	—	As first or second-line monotherapy for the treatment of RRMS when prescribed by an MS neurologist. Specialist's consult to be provided. For patients who meet all of the following criteria: -patient has had at least 2 (2) clinical relapses in the previous 2 (2) years AND -patient is ambulatory with	—

Brand name	Indication	New Brunswick		Nova Scotia		Prince Edward Island		Newfoundland and Labrador		NIHB		Yukon	
		Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes
				ambulate at least 100 m without assistance)				least 100 m without assistance)		the following criteria: • patient has had a clinical relapse and/or new MRI activity in the last 2 years; and • patient is fully ambulatory for 100 m without aids; and • patient is ≥ 18 years of age		or without aid (EDSS of ≤ 6.5),	
Entyvio	UC	For the treatment of adult patients with moderately to severely active UC who have a partial Mayo score > 4, and a rectal bleeding subscore ≥ 2 and are: • refractory or intolerant to conventional therapy (i.e., ASAs for a minimum of 4 weeks, and prednisone ≥ 40 mg daily for 2 weeks or IV equivalent for 1 week); or • corticosteroid dependent (i.e., cannot be tapered from corticosteroid without disease recurrence; or have relapsed within 3 months of stopping corticosteroid or require 2 or more courses of corticosteroid within 1 year)	Consideration will be given for patients who have not received a 4 week trial of ASAs if disease is severe (partial Mayo score > 6)	• For the treatment of adult patients with moderately to severely active UC who have a partial Mayo score > 4, and a rectal bleeding subscore ≥ 2 and are: o refractory or intolerant to conventional therapy (i.e., 5-ASA for a minimum of 4 weeks, and prednisone ≥ 40 mg daily for 2 weeks or IV equivalent for 1 week); or o cortico-steroid dependent (i.e., cannot be tapered from corticosteroid without disease recurrence; or have relapsed within 3 months of	—	For the treatment of adult patients with moderately to severely active UC who have a partial Mayo score > 4, and a rectal bleeding subscore ≥ 2 and are: • Refractory or intolerant to conventional therapy (i.e., ASAs for a minimum of 4 weeks AND prednisone ≥ 40 mg daily for 2 weeks or IV equivalent for 1 week) OR • Corticosteroid dependent (i.e., cannot be tapered from corticosteroids without disease recurrence; or have relapsed within 3 months of stopping corticosteroids; or require 2 or more courses of corticosteroid within 1 year)	—	For the treatment of adult patients with moderately to severely active UC who have a partial Mayo score > 4, and a rectal bleeding subscore ≥ 2 and are: • refractory or intolerant to conventional therapy (i.e., 5-ASA for a minimum of 4 weeks, and prednisone ≥ 40 mg daily for 2 weeks or IV equivalent for 1 week); or • corticosteroid dependent (i.e., cannot be tapered from corticosteroids without disease recurrence; or have relapsed within 3 months of stopping corticosteroids; or require 2 or more courses of	—	For the treatment of adult patients with moderately to severely active UC who meet the following: • partial Mayo score > 4; and • inadequate response to conventional therapies: • 5-ASA 4 g/day for 6 weeks; plus • glucocor-ticoids equivalent to prednisone 40 mg/day for a minimum of 2 weeks or treatment discontinued due to intolerance or contraindication	—	For patients with a Mayo score > 6 AND an endoscopic subscore ≥ 2 (within last 12 months) AND failed 2 weeks of oral prednisone ≥ 40 mg (or 1 week IV equivalent) AND 3 months of azathioprine or 6-MP OR stabilized on prednisone as above but the prednisone dose cannot be tapered despite 3 months of DMARDS	—

Brand name	Indication	New Brunswick		Nova Scotia		Prince Edward Island		Newfoundland and Labrador		NIHB		Yukon	
		Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes	Summary	Notes
				stopping corticosteroid; or require 2 or more courses of corticosteroid within 1 year)				corticosteroid within 1 year)					

ALL = acute lymphoblastic leukemia; BCVA = best corrected visual acuity; BSA = body surface area; CHC = chronic hepatitis C; CML = chronic myeloid leukemia; DIPSS = Dynamic International Prognostic Scoring System; DLQI = Dermatology Life Quality Index; DMARD = disease-modifying antirheumatic drug; DME = diabetic macular edema; DMT = disease-modifying therapy; EDSS = Expanded Disability Status Scale; ECOG = Eastern Cooperative Oncology Group; ER = estrogen receptor; HCQ = hydroxychloroquine; HCV = hepatitis C virus; HER2 = human epidermal growth factor receptor 2; IM = intramuscular; LEF = leflunomide; LHRH = luteinizing hormone-releasing hormone; MTX = methotrexate; NLPDP = Newfoundland and Labrador Prescription Drug Program; NSAI = nonsteroidal AI; OCT = optical occurrence tomography; RRMS = relapsing-remitting multiple sclerosis; PASI = Psoriasis Area Severity Index; Ph+ = Philadelphia chromosome positive; p.o. = orally; PsO = plaque psoriasis; RA = rheumatoid arthritis; RRMS = relapsing-remitting multiple sclerosis; SC = subcutaneous; SSZ = sulfasalazine; TNF = tumour necrosis factor; UC = ulcerative colitis; wAMD = wet age-related macular degeneration.