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Restrictions for reimbursement of direct-acting antiviral treatment for hepatitis C virus infection in Canada

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Abstract

Background: Interferon-free, direct-acting antiviral (DAA) HCV regimens are highly effective, achieving sustained virologic response (SVR) rates above 90%. However, because the list price for these therapies is prohibitive in Canada, universal drug coverage presents immense challenges. The aim of this study was to appraise HCV DAA reimbursement criteria in Canada for simeprevir, sofosbuvir, ledipasvir-sofosbuvir, and paritaprevir-ritonavir-ombitasvir plus dasabuvir. **Methods:** Reimbursement criteria for these HCV DAA therapies were collected for ten provinces and three territories in Canada from April 22, 2015 to January 5, 2016. The following information was extracted from health ministerial websites: 1) minimum fibrosis stage required; 2) drug and alcohol use restrictions; 3) HIV co-infection restrictions; and 4) prescriber type restrictions. Two investigators collected all data and then cross-checked responses. **Results:** Depending on the HCV DAA therapy, 82-92% of provinces/territories limit access to persons with moderate fibrosis (≥F2 METAVIR or equivalent). There are no drug and alcohol use restrictions. However, several criteria are left to the discretion of the physician. Quebec does not reimburse simeprevir and sofosbuvir for HIV co-infected persons, with no restrictions found in the remaining jurisdictions. Up to half (50%) of provinces/territories restrict prescriber type to specialists only. **Interpretation:** This first review of HCV DAA reimbursement criteria in Canada showed substantial heterogeneity by jurisdiction, which could be minimized through the development and adoption of a national HCV strategy that follows evidence-based guidelines for HCV management. Additionally, accessing criteria was challenging, supporting the need for greater information transparency.

Background

In Canada, an estimated 220,000 persons have chronic hepatitis C virus (HCV) infection [1]. By 2035, it is estimated that nearly one quarter of HCV-chronically infected Canadians will develop cirrhosis with associated healthcare costs rising from ~$161 million to ~$258 million [2]. Interferon-free, direct-acting antiviral (DAA) HCV regimens are highly effective, achieving sustained virologic response (SVR) rates above 90% even in patients with compensated cirrhosis [3-10]. SVR is associated with lowered risk of liver transplantation, liver-related mortality, all-cause mortality [11, 12], and improved quality-of-life outcomes [13, 14]. Shorter therapy duration and fewer adverse events have further reduced patient-level barriers to care [15-18]. Given these benefits, broadening access to HCV therapy is essential. However, the list price for HCV DAAs in Canada is ~$60,000 for a 12 week course, presenting immense challenges for funding all persons with HCV.

A study of sofosbuvir reimbursement criteria in the United States (US) identified considerable variability across Medicaid committees [19]. Of 42 states with available data, most states (74%) requested evidence of advanced fibrosis (Meta-Analysis of Histologic Data in Viral Hepatitis [METAVIR] stage F3) or cirrhosis (F4). The majority of states (88%) had drug and alcohol use restrictions of which half (50%) required abstinence prior to commencing treatment. In nearly one-quarter (24%) of states, HIV co-infected populations had to be treated with antiretroviral therapy (ART) or demonstrate suppressed HIV viral loads. Further, one-third of states (33%) limited prescriber type to specialists. These restrictions do not align with published and accepted clinical guidelines from the American Association for the Study of Liver Diseases-Infectious Diseases Society of America (AASLD-IDSA), the Canadian Association for the Study of the Liver (CASL), and the European Association for the Study of the Liver (EASL) [20-22].

In contrast to the US, since 2010, the pan-Canadian Pharmaceutical Alliance (pCPA) – made up of provincial/territorial health minister representatives – has negotiated drug prices with manufacturers [23]. For this reason, it was hypothesized that Canada would have greater reimbursement consistency by jurisdiction. Nonetheless, drug coverage criteria are ultimately set by provinces/territories and thus, considerable inter-jurisdiction heterogeneity is still possible.

The aim of this study was to appraise reimbursement criteria in Canada for the currently approved HCV DAAs: simeprevir, sofosbuvir, ledipasvir-sofosbuvir, and paritaprevir-ritonavir-ombitasvir plus dasabuvir. Criteria for Aboriginal persons and the incarcerated were also reviewed as these populations are disproportionately affected by HCV and receive drug coverage through federal plans [24-27].

Methods

Data Collection

Reimbursement criteria for simeprevir (with peginterferon plus ribavirin), sofosbuvir (with peginterferon and/or ribavirin), ledipasvir-sofosbuvir, and paritaprevir-ritonavir-ombitasvir plus dasabuvir (with or without ribavirin) were collected for all ten provinces and three territories in Canada as well as from the Non-Insured Health Benefits (NIHB) Program and the Correctional Service Canada (CSC) National Formulary during April 22, 2015 to January 5, 2016. The health ministry in each province/territory sets its own reimbursement criteria and hence, information was primarily collected from ministerial websites (Table 1).

Data were extracted from online, publically available reimbursement information including special authorization request forms, drug formularies, amendments to formularies, and drug benefit lists. If information was not available online, the study authors contacted the ministry directly. Healthcare practitioners (co-authors) were also contacted to facilitate access to documentation from ministries or pharmaceutical industry. When information could not be retrieved or was not available (e.g. the HCV therapy was not reimbursed), the data were labelled as 'n.a.' (i.e. not available). If a restriction (e.g. drug and alcohol use) was not listed with the criteria, these data were labelled as 'None listed'. The latter categorization does not necessarily indicate that no restriction exists; just that a written instruction could not be identified.

Criteria set by federal public drug plans were also reviewed. The NIHB program reimburses medications and medical services not covered under provincial/territorial or private plans for

First Nations people and Inuit. Prisoners in federal penitentiaries (sentences ≥2 years) have a similar federal plan and these criteria were reviewed. Prisoners with sentences <2 years follow criteria set by provincial corrections, which are the same criteria as the province/territory where the sentence is being served.

Data were collected by two authors (ADM and SS) and were cross-checked by each other with inconsistencies resolved through consensus. Data were organized using an Excel spreadsheet (Microsoft® Corporation, Redmond, WA, USA).

Data were organized into categories so that criteria could be compared across provinces/territories. To compare with Medicaid reimbursement criteria in the US [19], the same primary outcomes were collected: 1) minimum fibrosis stage required; 2) drug and alcohol use restrictions; 3) HIV co-infection restrictions; and 4) prescriber type restrictions. Fibrosis data were categorized as the minimum fibrosis stage required (categories: no restrictions; ≥F2; ≥F3; or F4, METAVIR or equivalent). Depending on the jurisdiction, fibrosis stage is assessed by transient elastrography (kPa) (e.g. FibroScan®), aspartate aminotransferase-to-platelet ratio index (APRI) score, Fibrosis-4 (FIB-4) index score, and liver biopsy. Drug and alcohol use criteria were categorized based on current or past drug or alcohol use restrictions (categories: yes; no). HIV co-infection data were categorized as to whether HIV co-infected persons were eligible for treatment [categories: eligible (HIV-co-infected persons had the same criteria as HCV monoinfected) or ineligible (HIV-coinfection was listed in exclusion criteria)]. Prescriber data were categorized as whether a hepatologist, gastroenterologist or infectious disease specialist prescriber was required or if non-specialist

options were permitted (categories: specialist; general practitioner). In some cases, a physician with experience treating HCV could prescribe treatment once meeting designated prescriber status as defined by the jurisdiction: this was categorised as 'general practitioner'. Treatment eligibility for decompensated cirrhosis was also noted (categories: eligible; ineligible; or may be considered). Decompensated cirrhosis was defined as Child-Pugh score >6 (class B or C) similar to the US reimbursement study [19].

Descriptive statistics were used to demonstrate the proportion of provinces/territories that restrict drug coverage by primary outcome. Data were presented in percentages. Map imagery was created with Tableau Software 9.0 (Seattle, WA, USA).

Results

Simeprevir with peginterferon plus ribavirin

Simeprevir is approved for use in genotype 1 infection in combination with peginterferon plus ribavirin. Patients with genotype 1a infection require resistance testing demonstrating the absence of the NS3 Q80K polymorphism. Prince Edward Island does not reimburse simeprevir.

As shown in Table 2, 92% (n=11) of jurisdictions require a fibrosis stage of ≥F2. Quebec does not provide this information (Figure 1A). None of the jurisdictions lists drug and alcohol use criteria. Three-quarters of provinces/territories (n=9) provide no information for HIV-HCV co-infection. In two jurisdictions (17%), Manitoba and Ontario, persons with HIV-HCV co-infection are eligible for treatment using the same criteria for HCV monoinfection. HIV co-infected persons are not eligible for treatment in Quebec. However, study authors specified that exceptions could be granted via the 'patient d'exception' route whereby a prescriber provides additional justification for treatment. Fifty percent of provinces/territories (n=6) require specialist prescription and four (33%) provide no information. Two jurisdictions (17%), British Columbia and Ontario, allow general practitioners to prescribe. More than half (n=7 [58%]) of jurisdictions do not allow treatment for patients with decompensated cirrhosis. There is no information available for the remaining provinces/territories (n=5 [42%]).

Sofosbuvir with peginterferon and/or ribavirin

Sofosbuvir is approved for use in genotypes 1-3 infections in combination with pegylated interferon and/or ribavirin. In Quebec, reimbursement for genotype 4 infection is also permitted. Prince Edward Island does not reimburse sofosbuvir.

As illustrated in Table 3, the majority of provinces/territories (n=11 [92%]) require ≥F2. Quebec does not list this information (Figure 1B). In practice, there are no fibrosis stage restrictions (Klein MB and Bruneau J, Personal Communication, October 2015). None of the jurisdictions has drug and alcohol use restrictions. There are no stated restrictions for HIV co-infected persons in nine jurisdictions (75%). Two jurisdictions (17%) do not provide information. HIV co-infected persons were not eligible for treatment in Quebec. Similar to simeprevir, exceptions could be granted through the 'patient d'exception' route. Eight jurisdictions (67%) permit general practitioners to prescribe whereas three jurisdictions (25%) require specialist prescribers. Quebec does not list this information. Treatment of decompensated cirrhosis is considered on a 'case by case basis' in most jurisdictions (n=8 [67%]) with four provinces/territories (33%) lacking information.

Ledipasvir-Sofosbuvir

Ledipasvir-sofosbuvir is approved for use in genotype 1 infection. Prince Edward Island does not reimburse ledipasvir-sofosbuvir.

As shown in Table 4, 92% of provinces/territories (n=11) require a fibrosis stage of ≥F2. In Quebec, fibrosis stage requirements depend on the number of years the DAA therapy has been on market. In year 1 (July 2015-2016), evidence of advanced fibrosis (≥F3) or cirrhosis is required (Figure 1C). In years 2-3, persons with moderate fibrosis (F2) or mild fibrosis (F1) plus an indicator of poor prognosis, such as co-infection with HIV or HBV, will be required. For years 4-6, all patients will be eligible for treatment regardless of fibrosis stage. There are no drug and alcohol use restrictions although British Columbia criteria state that 'patients who are at high risk for non-compliance' are not eligible, Saskatchewan has a Directly Observed Therapy (DOT) option, and the NIHB program requests that patients have access to multidisciplinary health teams. In all 12 jurisdictions, persons with HIV-HCV co-infection are eligible for treatment with HCV monoinfection criteria. Nine provinces/territories (75%) allow general practitioners to prescribe while three jurisdictions (25%) require specialist prescribers. Eight jurisdictions (67%) have decompensated cirrhosis restrictions. Restrictions are not listed; only that patients 'may be considered' for treatment. Three jurisdictions (25%) do not provide information. Patients with decompensated cirrhosis are eligible for treatment in Quebec.

Paritaprevir-ritonavir-ombitasvir plus dasabuvir (with or without ribavirin)

Paritaprevir-ritonavir-ombitasvir plus dasabuvir (with or without ribavirin) is approved for use in genotypes 1a or 1b subtype infections. Prince Edward Island also permits treatment of genotype 4 infection. As of January 2016, paritaprevir-ritonavir-ombitasvir plus dasabuvir was approved in 11 jurisdictions.

As illustrated in Table 5, the majority of provinces/territories [n=9 (82%)] require a fibrosis stage of ≥F2. A fibrosis stage of ≥F3 is required for Quebec in year 1, with increased eligibility in subsequent years (Figure 1D). Prince Edward Island has no fibrosis stage requirements. There are no drug and alcohol use restrictions. However, Prince Edward Island lists 'methadone or equivalent for at least 6 months' and 'stable address' in the inclusion criteria as well as active injecting drug use in the exclusion criteria, at the discretion of the physician. All 11 jurisdictions allow HIV-HCV co-infected persons to receive therapy with HCV monoinfection criteria. Prince Edward Island requires HIV co-infected persons to be treated off-island by a specialist. Three jurisdictions (27%) require a specialist prescription while eight provinces (73%) permit prescriptions by general practitioner. In most provinces/territories (n=9 [82%)], patients with decompensated cirrhosis are ineligible for treatment. There is no information for British Columbia and Prince Edward Island.

First Nations People and Inuit and Federal Prisoners

For simeprevir, sofosbuvir, ledipasvir-sofosbuvir, NIHB and CSC criteria require a fibrosis stage of ≥F2 (Tables 2-5). Paritaprevir-ritonavir-ombitasvir plus dasabuvir is reimbursed for federal prisoners and requires a fibrosis stage of ≥F2. The NIHB program approved paritaprevir-ritonavir-ombitasvir plus dasabuvir; online access was not available at time of writing. CSC criteria state that for all four regimens, treatment is prioritized for patients with F3-F4 and DOT is required. NIHB criteria request a specialist prescription for simeprevir. Further, NIHB and CSC criteria permit HIV co-infected populations to be treated with ledipasvir-sofosbuvir.

Interpretation

Findings indicate variability in HCV DAA reimbursement criteria by jurisdiction in Canada. Depending on the therapy, 82-92% of provinces/territories limit reimbursement to fibrosis stages of ≥F2. No alcohol or drug use restrictions were found. Only Quebec lists HIV co-infection restrictions. Lastly, 25-50% of jurisdictions restrict prescriber type to specialists.

In contrast to Canada, 74% of US states limit reimbursement to evidence of advanced fibrosis or cirrhosis (F3-F4) [19]. Clinical guidelines state that *all* patients with chronic HCV, irrespective of disease stage, should receive treatment [20-22], including prioritizing treatment for populations at risk of transmitting HCV, e.g. people who inject drugs (PWID) [22]. Further, a review by the Canadian Agency for Drugs and Technologies in Health (CADTH) demonstrated that treating patients across all fibrosis stages is cost-effective [28]. Given this, fibrosis stage restrictions should be re-reviewed.

While there are no drug and alcohol use restrictions for HCV DAA therapy in Canada, 50% of US states require drug and/or alcohol abstinence prior to treatment commencement [19] Considering that treatment of PWID is safe and effective [29], cost-effective [30, 31], and would prevent HCV transmission [32], absence of such restrictions is warranted. HIV co-infection restrictions are mostly non-existent in Canada whereas 25% of US states request evidence of ART therapy or suppressed HIV RNA levels [19]. Canada's broader access is more aligned with clinical guidelines [20-22]. Up to half of jurisdictions in Canada restrict prescriber type to specialists only. Specialists may be better suited for the management of DAA-based therapy in select circumstances (potential drug-drug interactions with complex HIV regimens or decompensated cirrhosis), new interferon-free DAA therapies are simple,

tolerable, and highly effective and general practitioners should not be excluded from prescribing HCV therapy. Programs to provide appropriate education, training, and linkage to HCV specialists could facilitate broadened prescribing by general practitioners.

There were several study limitations. Retrieving complete online criteria was challenging. Though ministries provided criteria when contacted, greater information transparency is needed. In addition, online criteria might not be up-to-date. NIHB criteria updates lag considerably behind other jurisdictions, possibly impeding treatment access. This study cannot speak to implementation of criteria. Further research might highlight greater inter-jurisdiction heterogeneity. For example, fibrosis cut-off values and methodologies differed by jurisdiction, which may contribute to inequitable therapy access. Lastly, study authors were unable to retrieve online private health insurance criteria for comparison. Medicaid recipients in the US are ten times more likely to be denied reimbursement for HCV therapy than those with private insurance [33]. Similar research in the Canadian context would be beneficial.

Conclusion

This first review of HCV DAA reimbursement criteria in Canada showed greater reimbursement homogeneity than the US [19]. The purchasing power of the pCPA might partly explain this result as the US lacks an equivalent committee and Medicaid cannot legally negotiate with manufacturers. The pCPA process may however inadvertently benefit jurisdictions with larger HCV affected populations (i.e. purchase more drugs). Prince Edward Island negotiated with a drug manufacturer directly and as a result, does not offer sofosbuvir

and ledipasvir-sofosbuvir [34]. The impact of the pCPA will become clearer once additional negotiations have occurred [35].

This review has considerable implications for policy. The development and adoption of a national HCV strategy akin to Australia [36] or action plans in Scotland [37, 38] could minimize criteria heterogeneity and facilitate greater information transparency. Increased uptake of HCV DAA therapy, especially by PWID, is essential to reduce HCV incidence and contribute to viral elimination in Canada, and fibrosis stage restrictions are neither evidence-based nor cost-effective. By comparison, HCV treatment in Australia will be reimbursed with no restrictions based on liver disease stage, recent drug use, HIV co-infection, or specialist prescribing, across all jurisdictions [39, 40]. In Canada, reimbursement criteria should more closely align with evidence to reduce therapy costs and better optimise treatment uptake in this groundbreaking era in HCV therapy.

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Table 1. Health ministries by province/territory in Canada

Province/Territory	Health Ministry	
British Columbia	British Columbia Ministry of Health	www.gov.bc.ca/health
Alberta	Alberta Health and Wellness	www.health.alberta.ca
Saskatchewan	Saskatchewan Health	www.health.gov.sk.ca
Manitoba	Manitoba Health	www.gov.mb.ca/health
Ontario	Ontario Ministry of Health and Long-Term Care	www.health.gov.on.ca
Quebec	Quebec Ministry of Health and Social Services	www.msss.gouv.qc.ca
New Brunswick	New Brunswick Department of Health	www2.gnb.ca/content/gnb/en/departments/health.html
Newfoundland & Labrador	Newfoundland & Labrador Department of Health and Community Services	www.health.gov.nl.ca/health
Prince Edward Island	Prince Edward Island Department of Health and Wellness	www.gov.pe.ca/health
Nova Scotia	Nova Scotia Department of Health and Wellness	novascotia.ca/DHW
Yukon	Yukon Health and Social Services	www.hss.gov.yk.ca
Northwest Territories	Northwest Territories Health and Social Services	www.hss.gov.nt.ca
Nunavut	Nunavut Department of Health	www.gov.nu.ca/health

Table 2. Key eligibility criteria for simeprevir with peginterferon plus ribavirin reimbursement by province/territory in Canada

	Restrictions				
Province/Territory	**Fibrosis stage[¶]**	**Substance use[†]**	**HIV co-infection[1]**	**Prescriber[§]**	**Decompensated cirrhosis[‡]**
British Columbia	≥ F2	None listed	None listed	General Practitioner	None listed
Alberta	≥ F2	None listed	None listed	None listed	Ineligible
Saskatchewan	≥ F2	None listed	None listed	Specialist	None listed
Manitoba	≥ F2	None listed	Eligible	Specialist	Ineligible
Ontario	≥ F2	None listed	Eligible	General Practitioner	Ineligible
Quebec	None listed	None listed	Ineligible[11]	None listed	None listed
New Brunswick	≥ F2	None listed	None listed	None listed	Ineligible
Newfoundland & Labrador	≥ F2	None listed	None listed	None listed	Ineligible
Prince Edward Island	n.a.	n.a.	n.a.	n.a.	n.a.
Nova Scotia	≥ F2	None listed	None listed	Specialist[§§]	Ineligible
Yukon	≥ F2	None listed	None listed	Specialist	Ineligible
Northwest Territories	≥ F2	None listed	None listed	Specialist[§§]	None listed
Nunavut	≥ F2	None listed	None listed	Specialist[§§]	None listed
NIHB[a]	≥ F2	None listed	None listed	Specialist[§§]	None listed
CSC[b]	≥ F2[¶¶]	None listed[††]	None listed	None listed	None listed

[a]Federally-funded public drug benefit program for First Nations people and Inuit
[b]Federally-funded public drug benefit program for federal prisoners
[¶] Minimum fibrosis stage required
[¶¶]Treatment is prioritized to F3 and F4. Treatment for patients <F3 are reviewed on a case by case basis
[†]Drug and alcohol criteria restrictions: yes; no; none listed
[††]Direct Observed Therapy (DOT) required
[1]Treatment for HIV co-infection: eligible; ineligible; none listed
[11]However, exceptions could be granted via the "patient d'exception" route
[§]Prescriber limitation: specialist (hepatologist, gastroenterologist, infectious disease specialist) or physician (experienced with treating chronic Hepatitis C)
[§§]Prescriber restrictions not listed; however, specialist is listed as requirement for PEG-IFN-based therapies
[‡]Defined as higher Child Pugh score >6. Treatment eligibility for decompensated cirrhosis was also noted (categories: eligible; ineligible; may be considered)

Table 3. Key eligibility criteria for sofosbuvir with pegylated interferon and/or ribavirin reimbursement by province/territory in Canada

	Restrictions				
Province/Territory	**Fibrosis stage[¶]**	**Substance use[†]**	**HIV co-infection[ŧ]**	**Prescriber[§]**	**Decompensated cirrhosis‡**
British Columbia	≥ F2	None listed[††]	Eligible	General Practitioner	May be considered
Alberta	≥ F2	None listed	Eligible	General Practitioner	May be considered
Saskatchewan	≥ F2	None listed[†††]	Eligible	General Practitioner	May be considered
Manitoba	≥ F2	None listed	Eligible	Specialist	May be considered
Ontario	≥ F2	None listed	Eligible	General Practitioner	May be considered
Quebec	None listed[¶¶]	None listed	Ineligible[ŧŧ]	None listed	None listed
New Brunswick	≥ F2	None listed	Eligible	General Practitioner	None listed
Newfoundland & Labrador	≥ F2	None listed	Eligible	General Practitioner	May be considered[‡‡]
Prince Edward Island	n.a.	n.a.	n.a.	n.a.	n.a.
Nova Scotia	≥ F2	None listed	Eligible	Specialist	May be considered
Yukon	≥ F2	None listed	Eligible	Specialist	May be considered
Northwest Territories	≥ F2	None listed	None listed	General Practitioner	None listed
Nunavut	≥ F2	None listed	None listed	General Practitioner	None listed
NIHB[a]	≥ F2	None listed	None listed	General Practitioner	None listed
CSC[b]	≥ F2[¶¶¶]	None listed[††††]	None listed	None listed	None listed

[a]Federally-funded public drug benefit program for First Nations people and Inuit
[b]Federally-funded public drug benefit program for federal prisoners
[¶] Minimum fibrosis stage required
[¶¶]None listed in Criteria; but in practice, there are no fibrosis stage restrictions (Klein MB and Bruneau J, Personal Communication, Oct. 2015)
[¶¶¶]Treatment is prioritized to F3 and F4. Treatment for patients <F3 are reviewed on a case by case basis
[†]Drug and alcohol criteria restrictions: yes; no; none listed
[††]No specific criteria, but exclusion criteria states: "Patients who are at high risk for non-compliance"
[†††]None listed; however the prescriber can indicate that Direct Observed Therapy (DOT) is recommended; also the patient consents (via signature) to understanding treatment adherence
[††††]DOT required
[ŧ]Treatment for HIV co-infection: eligible; ineligible; none listed
[ŧŧ]However, exceptions could be granted via the "patient d'exception" route
[§]Prescriber limitation: specialist (hepatologist, gastroenterologist, infectious disease specialist) or physician (experienced with treating chronic Hepatitis C)
[‡]Defined as higher Child Pugh score >6. Treatment eligibility for decompensated cirrhosis was also noted (categories: eligible; ineligible; may be considered)
[‡‡]Personal communication from L Barrett (Sept. 2015)

Table 4. Key eligibility criteria for ledipasvir-sofosbuvir reimbursement by province/territory in Canada

	Restrictions				
Province/Territory	**Fibrosis stage[¶]**	**Substance use[†]**	**HIV co-infection[ŧ]**	**Prescriber[§]**	**Decompensated cirrhosis[‡]**
British Columbia	≥ F2	None listed[††]	Eligible	General Practitioner	May be considered
Alberta	≥ F2	None listed	Eligible	General Practitioner	May be considered
Saskatchewan	≥ F2	None listed[†††]	Eligible	General Practitioner	May be considered
Manitoba	≥ F2	None listed	Eligible	Specialist	May be considered
Ontario	≥ F2	None listed	Eligible	General Practitioner	May be considered
Quebec	≥ F3[¶¶]	None listed	Eligible[ŧŧ]	General Practitioner	Eligible
New Brunswick	≥ F2	None listed	Eligible	General Practitioner	None listed
Newfoundland & Labrador	≥ F2	None listed	Eligible	General Practitioner	May be considered[‡‡]
Prince Edward Island	n.a.	n.a.	n.a.	n.a	n.a.
Nova Scotia	≥ F2	None listed	Eligible	Specialist	May be considered
Yukon	≥ F2	None listed	Eligible	Specialist	May be considered
Northwest Territories	≥ F2	None listed	Eligible	General Practitioner	None listed
Nunavut	≥ F2	None listed	Eligible	General Practitioner	None listed
NIHB[a]	≥ F2	None listed	Eligible	General Practitioner	None listed
CSC[b]	≥ F2[¶¶¶]	None listed[††††]	Eligible	None listed	None listed

[a]Federally-funded public drug benefit program for First Nations people and Inuit
[b]Federally-funded public drug benefit program for federal prisoners
[¶]Minimum fibrosis stage required
[¶¶]In year 1 (July 2015), only those with ≥F3 receive reimbursement
[¶¶¶]Treatment is prioritized to F3 and F4. Treatment for patients <F3 are reviewed on a case by case basis
[†]Drug and alcohol criteria restrictions: yes; none listed
[††]No specific criteria, but exclusion criteria states: "Patients who are at high risk for non-compliance"
[†††]None listed; prescriber can indicate that Direct Observed Therapy (DOT) is recommended; also the patient consents (via signature) to understanding treatment adherence
[††††]DOT required
[ŧ]Treatment for HIV co-infection: eligible; ineligible; or may be considered
[ŧŧ]Treated in year 1 (July 2015) if ≥F3
[§]Prescriber limitation: specialist (hepatologist, gastroenterologist, infectious disease specialist) or physician (experienced with treating chronic Hepatitis C)
[‡]Defined as higher Child Pugh score >6. Treatment eligibility for decompensated cirrhosis was also noted (categories: eligible; ineligible; may be considered)
[‡‡]Personal communication from L Barrett (Sept. 2015)

Table 5. Key eligibility criteria for paritaprevir-ritonavir-ombitasvir plus dasabuvir (with or without ribavirin) reimbursement by province/territory in Canada

	Restrictions				
Province/Territory	**Fibrosis stage[¶]**	**Substance use[†]**	**HIV co-infection[ı]**	**Prescriber[§]**	**Decompensated cirrhosis‡**
British Columbia	≥ F2	None listed[††]	Eligible	General Practitioner	None listed
Alberta	≥ F2	None listed	Eligible	General Practitioner	Ineligible
Saskatchewan	≥ F2	None listed[†††]	Eligible	General Practitioner	Ineligible
Manitoba	≥ F2	None listed	Eligible	Specialist	Ineligible
Ontario	≥ F2	None listed	Eligible	General Practitioner	Ineligible
Quebec	≥ F3[¶¶]	None listed	Eligible[ıı]	General Practitioner	Ineligible
New Brunswick	≥ F2	None listed	Eligible	General Practitioner	Ineligible
Newfoundland & Labrador	≥ F2	None listed	Eligible	General Practitioner	Ineligible
Prince Edward Island	No restrictions	None listed[††††]	Eligible[ııı]	General Practitioner	None listed
Nova Scotia	≥ F2	None listed	Eligible	Specialist	Ineligible
Yukon	≥ F2	None listed	Eligible	Specialist	Ineligible
Northwest Territories	n.a.	n.a.	n.a.	n.a.	n.a.
Nunavut	n.a.	n.a.	n.a.	n.a.	n.a.
NIHB[a]	n.a.	n.a.	n.a.	n.a.	n.a.
CSC[b]	≥ F2[¶¶¶]	None listed[†††††]	None listed	None listed	None listed

[a]Federally-funded public drug benefit program for First Nations people and Inuit
[b]Federally-funded public drug benefit program for federal prisoners
[¶]Minimum fibrosis stage required
[¶¶]In year 1 (July 2015), only those with ≥F3 receive reimbursement
[¶¶¶]Treatment is prioritized to F3 and F4. Treatment for patients <F3 are reviewed on a case by case basis
[†]Drug and alcohol criteria restrictions: yes; no; none listed
[††]No specific criteria, but exclusion criteria states: "Patients who are at high risk for non-compliance"
[†††]None listed; prescriber can indicate that Direct Observed Therapy is recommended; also the patient consents (via signature) to understanding treatment adherence
[††††]There were restrictions left to physician discretion (e.g. methadone or equivalent for at least 6 months)
[†††††]DOT required
[ı]Treatment for HIV co-infection: eligible; ineligible; none listed
[ıı]Treated in year 1 if ≥F3
[ııı]Must be treated by a specialist off-island if HIV co-infected
[§]Prescriber limitation: specialist (hepatologist, gastroenterologist, infectious disease specialist) or physician (experienced with treating chronic Hepatitis C)
[‡]Defined as higher Child Pugh score >6. Treatment eligibility for decompensated cirrhosis was also noted (categories: eligible; ineligible; may be considered)

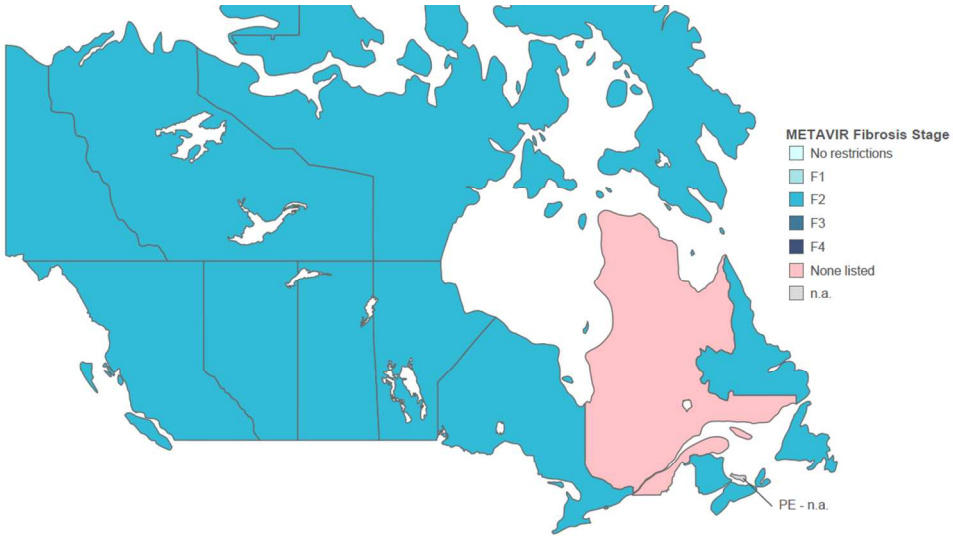

Figure 1A. Minimum fibrosis stage required for simeprevir with peginterferon plus ribavirin by province/territory in Canada.

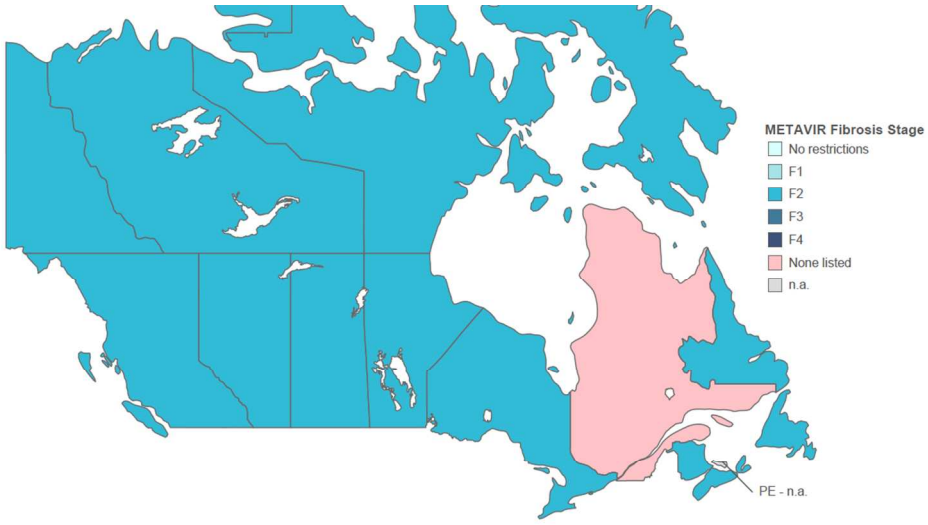

Figure 1B. Minimum fibrosis stage required for sofosbuvir with peginterferon and/or ribavirin by province/territory in Canada.

Figure 1C. Minimum fibrosis stage required for ledipasvir-sofosbuvir by province/territory in Canada.

Figure 1D. Minimum fibrosis stage required for paritaprevir-ritonavir-ombitasvir plus dasabuvir with or without ribavirin by province/territory in Canada.