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Research

Variable access to antiviral treatment of chronic hepatitis B in Canada: a descriptive study

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Abstract

Background: Antiviral treatment for chronic hepatitis B is costly, which presents challenges for universal drug coverage for the estimated 480 000 people with the disease in Canada. We appraised criteria for reimbursement of chronic hepatitis B antivirals by public drug plans in Canada.

Methods: In this descriptive study, we reviewed the reimbursement criteria for lamivudine, adefovir, tenofovir, entecavir, telbivudine, pegylated or standard interferon, and emtricitabine–tenofovir in the 10 provinces and the Yukon Territory as well as 3 federal programs: Correctional Services Canada, Veterans' Affairs and the Non-Insured Health Benefits Program. We extracted data from publicly available formularies. The primary outcomes extracted were prescriber details, reimbursement regulations and published list price.

Results: All public drug insurance plans limit access to antiviral treatment in patients with chronic hepatitis B based on viral characteristics, fibrosis stage and/or specialist approval. Lamivudine use is restricted only in British Columbia and Ontario. Six plans (43%) cover entecavir or tenofovir with no restriction, and 8 plans (57%) cover these agents if patients have advanced fibrosis/cirrhosis. Nine plans (64%) provide coverage of interferon, although 4 of these programs reimburse only nonpegylated interferon, which is not currently recommended for chronic hepatitis B treatment.

Interpretation: We found substantial variability among jurisdictions in reimbursement criteria for the treatment of chronic hepatitis B in Canada. The findings can inform health policy and support the development and adoption of a national chronic hepatitis B strategy to ensure equitable and timely access to treatment no matter where patients reside in Canada.

Chronic hepatitis B is a global infection affecting over 250 million people.[1] The prevalence varies depending on the geographic region. In Canada, up to 480 000 people are infected, mostly people or populations that have not received routine vaccinations including immigrants from endemic countries, indigenous populations and street-connected people.[2,3] Treating chronic hepatitis B can reduce the risk of transmission and prevent or reverse progression to cirrhosis and liver cancer.[4] Current Canadian guidelines recommend treatment of patients with cirrhosis, or with elevated alanine aminotransferase (ALT) levels and hepatitis B DNA levels over 2000 IU/mL with tenofovir, entecavir or interferon, depending on patient characteristics.[3] Orally administered agents for hepatitis B are well-tolerated once-daily medications but require indefinite use; older medications have high rates of resistance, which is not seen with tenofovir and entecavir. Interferon offers the advantage of a fixed course of therapy but often is poorly tolerated and is not recommended in cirrhosis. For these reasons, tenofovir, entecavir and interferon are the preferred agents for the treatment of hepatitis B.[3,5–7]

In Canada, once a drug has Health Canada approval, reimbursement recommendations are made by the Canadian Drug Expert Committee (CDEC), part of the Canadian Agency for Drugs and Technologies in Health, for all federal plans and all provinces and territories except Quebec.[8] In Quebec, recommendations are made by the Institut national d'excellence en santé et en services sociaux. Each plan then makes a final decision regarding reimbursement. Reimbursement decisions may limit the ability of physicians to deliver safe, effective and tolerable antivirals. A major barrier to adequate care for chronic hepatitis B in Canada remains provincial restrictions

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on reimbursement, with 64% of patients receiving treatment requiring reimbursement through public drug programs.[9] As Canada remains a top destination for immigrants, and despite implementation of a universal vaccination program, the chronic hepatitis B population will continue to rise or, at the very least, will stay constant because of immigration. Thus, the primary aim of this study was to appraise reimbursement criteria in Canada for all commercially approved therapies for chronic hepatitis B, including lamivudine, adefovir, tenofovir, entecavir, telbivudine, pegylated or standard interferon, and emtricitabine–tenofovir.

Methods

Data sources

We collected reimbursement criteria for tenofovir, entecavir, interferon formulations, lamivudine, telbivudine, adefovir and emtricitabine–tenofovir for all Canadian provinces and the Yukon Territory as well as the federal programs of Correctional Services Canada, Veterans' Affairs and the Non-Insured Health Benefits (NIHB) Program for First Nations and Inuit. Nunavut and the Northwest Territories do not have their own formulary but cover all drugs approved by the NIHB formulary.[10,11] Each provincial/territorial health ministry sets its own reimbursement criteria; thus, we collected information from jurisdiction websites. We extracted data from publicly available online reimbursement information (Appendix 1, available at www.cmajopen.ca/content/7/1/E182/suppl/DC1). We obtained formulary information through a database of provincial and territorial formularies[12] as well as by searching the provincial/territorial health websites for supplemental information when required. Information about the Veterans' Affairs formulary was found through an Internet search, and the Correctional Services Canada formulary was obtained by request. These formularies are official government documents so were not formally validated. When information could not be retrieved or was not available (e.g., the therapy was not reimbursed), we labelled data "NA" (not available). In all but 1 case, the formularies provided sufficient information; we contacted Manitoba Pharmacare for further clarification, which was provided. Data searches and abstraction were performed by both authors separately and cross-checked; the data obtained were congruent between the 2 authors.

Data collection

The data collected were based on minimum fibrosis stage required and prescriber type restrictions. We organized the data into categories so that criteria could be compared across jurisdictions. We categorized fibrosis data as the minimum fibrosis stage required (categories: no restrictions, stage ≥ F2, stage ≥ F3 or stage F4 of the Meta-Analysis of Histologic Data in Viral Hepatitis scoring system or equivalent). We categorized prescriber data as 1) any provider could prescribe the medication, 2) there was restriction by specialty (e.g., internal medicine, hepatology, gastroenterology or infectious diseases) or 3) a provider with experience treating patients with chronic hepatitis B could prescribe treatment once designated prescriber status as defined by the jurisdiction was met.

Statistical analysis

We employed descriptive statistics using Microsoft Excel to show the proportion of public health plans that restrict drug coverage by primary outcome.

Ethics approval

Ethics approval was not required as the data used in this study came from publicly available data from government agencies.

Results

Prescriber limitations

Prescriptions for chronic hepatitis B were restricted to specialists/designated prescribers in 5 (36%) of 14 plans. In Saskatchewan, Nova Scotia and the Yukon Territory, specialist recommendation/consultation is encouraged, although the definition of a specialist is not explicit. In New Brunswick, permissible prescribers include hepatologists, gastroenterologists and infectious diseases specialists, and in Alberta, all internal medicine specialists are authorized prescribers. For both Alberta and New Brunswick, practitioners with experience in chronic hepatitis B management can apply to become designated prescribers.

Reimbursement requirements for drugs (Table 1)

Lamivudine

Lamivudine is covered by all provincial and federal plans, although there are substantial differences in coverage requirements between jurisdictions. In Manitoba, Quebec, the Yukon Territory, Prince Edward Island, Newfoundland and Labrador, and all 3 federal programs, there is no restriction on access or who can prescribe lamivudine for chronic hepatitis B. Notably, Newfoundland and Labrador restricts prescriptions to 30 days and uses a 150-mg formulation, which is not the recommended dosage of 100 mg. Alberta, New Brunswick, Nova Scotia and Saskatchewan restrict prescribers, as described above, although Saskatchewan recommends only consultation with a specialist. Ontario covers patients with hepatitis B virus (HBV) DNA levels greater than 1000 IU/mL and elevated liver enzyme levels or evidence of fibrosis/cirrhosis. The most restrictive province is British Columbia, with specific requirements for HBV DNA levels and ALT levels in patients without cirrhosis but covering all those with cirrhosis.

Adefovir

The majority of public drug plans restrict (8/14) or do not cover (4/14) adefovir, with the fewest restrictions found in Alberta, which requires only an authorized prescriber. Correctional Services Canada had no restrictions reported. Adefovir is not covered by Manitoba, Ontario, New Brunswick or Veterans Affairs. For many public plans (Saskatchewan, Quebec, New Brunswick, Prince Edward Island, the Yukon

Table 1: Criteria for reimbursement of chronic hepatitis B medications in Canada*

Province/territory or federal plan	Lamivudine	Adefovir	Emtrictiabine–tenofovir	Tenofovir disoproxil fumarate†	Entecavir	Interferon
CDEC	NA	Take with lamivudine for lamivudine failure	NA	Cirrhosis with HBV DNA level > 2000 IU/mL	Cirrhosis with HBV DNA level > 2000 IU/mL	NA
British Columbia	ALT and viral load requirement OR cirrhosis	Lamivudine resistance	NA	Cirrhosis and viral load ± ALT requirement OR lamivudine resistance	Cirrhosis and viral load ± ALT requirement	Alfa-2b HBeAg+ with ALT and viral load requirement
Alberta	No restrictions for specialists	No restrictions for specialists	NA	No restrictions for specialists	No restrictions for specialists	Pegylated interferon alfa-2a No restrictions for specialists
Saskatchewan	No restrictions for specialists	As per CDEC with specialist consultation	NA	As per CDEC with specialist consultation	As per CDEC with specialist consultation	Alfa-2b Up to 6 mo with specialist consultation
Manitoba	No restrictions	NA	NA	As per CDEC OR cirrhosis with lamivudine resistance	No restrictions	NA
Ontario	HBV DNA level ≥ 1000 IU/mL with ALT level > ULN or fibrosis/cirrhosis	NA	NA	HBV DNA level ≥ 1000 IU/mL with ALT level > ULN or fibrosis/ cirrhosis	HBV DNA level ≥ 1000 IU/mL with ALT level > ULN or fibrosis/cirrhosis	Alfa-2b Age < 50 yr, ≤ stage F3 fibrosis with ALT and DNA requirements
Quebec	No restrictions	As per CDEC OR > Child–Pugh class A6 OR after liver transplantation with DNA requirement	No restrictions	No restrictions	No restrictions	Pegylated interferon alfa-2a No restrictions
New Brunswick	No restrictions for specialists	NA	No restrictions	No restrictions for specialists	No restrictions for specialists	Pegylated interferon alfa-2a HBeAg–, liver inflammation, failed lamivudine
Nova Scotia	No restrictions with specialist request	As per CDEC	NA	As per CDEC	As per CDEC	NA
Prince Edward Island	No restrictions	As per CDEC	NA	No restrictions	As per CDEC	NA
Newfoundland and Labrador	No restrictions	As per CDEC	NA	As per CDEC	As per CDEC	Alfa-1a/-2b HBeAg–, liver inflammation, lamivudine failure with specialist consultation
Yukon Territory	No restrictions	As per CDEC with specialist recommendation	Case by case with specialist recommendation	Case by case with specialist recommendation	Case by case with specialist recommendation	NA
Non-Insured Health Benefits Program	No restrictions	As per CDEC	No restrictions	As per CDEC	As per CDEC	Pegylated interferon alfa-2a No cirrhosis, with DNA requirements and specialist request
Correctional Services Canada	No restrictions	No restrictions	No restrictions	No restrictions	No restrictions	Pegylated interferon alfa-2a/-2b No restrictions
Veterans Affairs	No restrictions	NA	No restrictions	No restrictions	NA	Interferon alfa-2b

Note: ALT = alanine aminotransferase, CDEC = Canadian Drug Expert Committee, HBeAg= hepatitis B e-antigen, HBV = hepatitis B virus, NA = no recommendation or not listed, ULN = upper limit of normal.
*No public health plans reimburse telbivudine.
†No public health plans reimburse tenofovir alafenamide fumarate.

Territory and the NIHB Program), adefovir is covered in combination with lamivudine if the patient experienced lamivudine failure, based on a DNA level greater than 1 log above the nadir after 3 months of treatment, provided that noncompliance was not the reason for failure, as per the CDEC recommendations. Saskatchewan and the Yukon Territory require specialist input. British Columbia also follows the CDEC recommendation but does not require lamivudine to be used with adefovir. Quebec additionally covers patients with an increase in HBV DNA level by 1 log or proven resistance, with a HBV DNA level greater than 20 000 IU/mL in patients with Child–Pugh class B/C cirrhosis, liver transplant recipients, patients coinfected with HIV but not taking antiretrovirals, and patients with an HBV DNA level greater than 20 000 IU/mL (hepatitis B e-antigen [HBeAg] positive) or greater than 2000 IU/mL in HBeAg-negative patients.

Telbivudine

No public health plan in Canada reimburses telbivudine.

Emtricitabine–tenofovir

Six public programs cover emtricitabine–tenofovir for chronic hepatitis B treatment. Quebec, New Brunswick and the federal plans have no restrictions on coverage, and the Yukon Territory covers this drug combination on a case-by-case recommendation. Saskatchewan, Manitoba, Ontario, Prince Edward Island, and Newfoundland and Labrador cover emtricitabine–tenofovir for HIV infection only. It is not covered for any indication in BC, Alberta or Nova Scotia.

Tenofovir

There are currently 2 formulations of tenofovir on the market: tenofovir disoproxil fumarate, which has recently become available as a generic formulation, and tenofovir alafenamide fumarate. The latter was approved by Health Canada in June 2017. No public health plans in Canada reimburse tenofovir alafenamide fumarate. Six plans reimburse tenofovir disoproxil fumarate with few or no restrictions: Alberta requires tenofovir be prescribed by an authorized prescriber, whereas Quebec, Prince Edward Island, New Brunswick, Correctional Services Canada and Veteran Affairs have no restrictions. Interestingly, Correctional Services Canada covers the 245-mg formulation of tenofovir, rather than the typical 300-mg formulation. Tenofovir is covered in the Yukon Territory on a case-by-case evaluation with recommendation by a specialist. In Saskatchewan, Manitoba, New Brunswick, Nova Scotia, Newfoundland and Labrador, and the NIHB Program, tenofovir is covered for patients with cirrhosis and a DNA level greater than 2000 IU/mL, which matches the CDEC recommendation; Saskatchewan also suggests specialist involvement. Manitoba additionally covers tenofovir in patients with cirrhosis resistant to lamivudine. Ontario covers tenofovir for patients with HBV DNA levels greater than 1000 IU/mL and elevated liver enzyme values or evidence of fibrosis/cirrhosis. Ontario also covers tenofovir for patients in whom other therapies have failed, for pregnant patients with DNA levels greater than 1 000 000 IU/mL and for chemoprophylaxis. British Columbia has the most restrictive guidelines for the drug, covering only patients without cirrhosis with lamivudine resistance and those who have been treated with adefovir and have detectable virus as well as lamivudine resistance; for patients with cirrhosis, either an HBV DNA level greater than 200 000 IU/mL or 2000–200 000 IU/mL together with an ALT level greater than 3 times the upper limit of normal is required for coverage.

Entecavir

Entecavir coverage requirements are similar to those for tenofovir in most provinces. Quebec, Manitoba and Correctional Services Canada cover entecavir in adults with no restrictions, and Alberta covers it at the request of an authorized prescriber. In Saskatchewan, most Atlantic provinces and the NIHB Program, the coverage criteria are identical to the CDEC guidelines: cirrhosis and an HBV DNA level greater than 2000 IU/mL. Entecavir is covered in the Yukon Territory on a case-by-case basis by specialist request and is not covered by Veteran Affairs. British Columbia and New Brunswick have the same coverage requirements for entecavir as for tenofovir. Ontario covers entecavir in patients with HBV DNA levels greater than 1000 IU/mL and elevated liver enzymes or evidence of fibrosis/cirrhosis, in those with intolerance to other HBV medications and for chemoprophylaxis.

Pegylated interferon alfa-2a/-2b

Interferon in any form is not covered for chronic hepatitis B treatment in the Yukon Territory, Manitoba, Nova Scotia or Prince Edward Island. Manitoba covers pegylated interferon alfa-2a for hepatitis C virus infection, and Prince Edward Island covers both pegylated interferon alfa-2a and pegylated interferon alfa-2b. Pegylated interferon alfa-2a is the preferred drug in Alberta (prescribed by an authorized prescriber), Quebec, New Brunswick and the NIHB Program. Quebec has no restrictions on the use of pegylated interferon alfa-2a. New Brunswick covers HBeAg-negative patients with compensated liver disease, liver inflammation and evidence of viral replication with demonstrated intolerance to or failure of lamivudine therapy for 48 weeks with specialist requests. The NIHB Program covers patients without cirrhosis with an HBV DNA level greater than 2000 IU/mL and no limitation on HBeAg status on the request of a specialist. British Columbia covers interferon alfa-2b in HBeAg-positive patients with an ALT level greater than twice the upper limit of normal for 24 weeks. Similarly, Ontario covers interferon alfa-2b in patients aged less than 50 years with stage F3 fibrosis or less on biopsy, an HBV DNA level of 10 000–10 000 000 IU/mL and 2 ALT values greater than twice the upper limit of normal in the previous 6 months. Correctional Services Canada has the most liberal coverage, allowing both pegylated interferon alfa-2a and pegylated interferon alfa-2b to be prescribed. Saskatchewan covers interferon alfa-2b for up to 6 months, Newfoundland and Labrador covers interferon

alfa-1a and alfa-2b with identical criteria to those of New Brunswick, and Veteran Affairs covers interferon alfa-2b.

Interpretation

We found substantial variability in the criteria for reimbursement of chronic hepatitis B antivirals by jurisdiction in Canada. Currently, no jurisdictions or federal plans limit reimbursement to patients with advanced fibrosis, but 2 (14%) explicitly require elevated ALT levels. Recommendations from the CDEC to limit entecavir and tenofovir to patients with cirrhosis were present in 6 programs (43%). Four (31%) of 13 jurisdictions had some form of explicit restriction of prescribers to specialists.

Some of the reimbursement requirements are somewhat perplexing, as major associations, including the Canadian Association for the Study of the Liver,[3] American Association of the Study of Liver Diseases,[6] European Association for the Study of Liver,[7] Asian Pacific Association for the Study of the Liver[5] and the World Health Organization,[13] have developed treatment algorithms documenting effective timing of therapy to prevent complications (Table 2, Table 3). It is unclear why interferon is approved only for HBeAg-negative patients in some provinces given the reasonable response rate in the HBeAg-positive population.[3,6] In addition, restrictions such as fibrosis stage are neither cost-effective nor evidence-based. Although a "one-size-fits-all" strategy has drawbacks (e.g., the ability of jurisdictions to respond to chronic hepatitis B

Table 2: Treatment recommendations by various international organizations for patients positive for hepatitis B e-antigen

Recommendation	AASLD[6] 2018 (United States)*	EASL[7] 2017 (Europe)†	CASL[3] 2018 (Canada)*	APASL[5] 201 (Asia)†	WHO[11] 2015‡
Treatment definitely recommended	• ALT level > 2× ULN and HBV DNA level > 20 000 IU/mL	• ALT level > 2× ULN and HBV DNA level > 20 000 IU/mL • ALT level > ULN and HBV DNA level > 2000 IU/mL and/or moderate/severe inflammation/fibrosis on liver biopsy • Cirrhosis	• Cirrhosis	• ALT level > 2× ULN and HBV DNA level > 20 000 IU/mL • Moderate/severe inflammation/advanced fibrosis on liver biopsy • Compensated cirrhosis and HBV DNA level > 2000 IU/mL • Decompensated cirrhosis	• Cirrhosis • Age > 30 yr, persistently abnormal ALT level and HBV DNA level > 20 000 IU/mL
Treatment should be considered	• ALT level > 2× ULN and HBV DNA level 2000–20 000 IU/mL • ALT level 1–2× ULN and HBV DNA level > 20 000 IU/mL • Age > 40 yr • Evidence of moderate/severe inflammation or fibrosis	• Elevated HBV DNA level and age > 30 yr • Family history of hepatocellular carcinoma or cirrhosis and extrahepatic manifestations	• ALT level > ULN for 3–6 mo and HBV DNA level > 2000 IU/mL • Evidence of moderate/severe inflammation or fibrosis	• Monitor all untreated patients every 3 mo • Biopsy recommended for treatment decisions if: ◊ Noninvasive tests suggest evidence of advanced fibrosis ◊ ALT level is persistently elevated ◊ Age > 35 yr ◊ Family history of hepatocellular carcinoma or cirrhosis	• Monitor all untreated patients
Monitor	• ALT level < ULN	• ALT level < ULN • HBV DNA level < 2000 IU/mL	• ALT level < ULN • HBV DNA level < 2000 IU/mL		
Preferred first-line treatment (in alphabetical order)	• Entecavir • Pegylated interferon • Tenofovir	• Entecavir • Pegylated interferon • Tenofovir	• Entecavir • Pegylated interferon • Tenofovir	• Entecavir • Pegylated interferon • Tenofovir	• Entecavir • Tenofovir

Note: AASLD = American Association of the Study of Liver Diseases, ALT = alanine aminotransferase, APASL = Asian Pacific Association for the Study of the Liver, CASL = Canadian Association for the Study of the Liver, EASL = European Association for the Study of Liver, HBV = hepatitis B virus, ULN = upper limit of normal, WHO = World Health Organization.
*Upper limit of normal for alanine aminotransferase: men 35 U/L, women 25 U/L.
†Upper limit of normal for alanine aminotransferase: 40 U/L.
‡Upper limit of normal for alanine aminotransferase: men 30 U/L, women 19 U/L.

Table 3: Treatment recommendations by various international organizations for patients negative for hepatitis B e-antigen

Recommendation	AASLD[6] 2018 (United States)*	EASL[7] 2017 (Europe)†	CASL[3] 2018 (Canada)*	APASL[5] 2015 (Asia)†	WHO[11] 2015‡
Treatment definitely recommended	• ALT level > 2× ULN and HBV DNA level > 2000 IU/mL • Cirrhosis and HBV DNA level > 2000 IU/mL	• HBV DNA level > 2000 IU/mL and ALT level > ULN and/or moderate/severe inflammation/fibrosis on liver biopsy • HBV DNA level > 20 000 IU/mL and ALT level > 2× ULN • Cirrhosis	• Cirrhosis	• ALT level > 2× ULN and HBV DNA level > 2000 IU/mL • Moderate/severe inflammation/advanced fibrosis on liver biopsy • Compensated cirrhosis and HBV DNA level > 2000 IU/mL • Decompensated cirrhosis	• Cirrhosis • Age > 30 yr, persistently abnormal ALT level and HBV DNA level > 20 000 IU/mL
Treatment should be considered	• ALT level 1–2× ULN • HBV DNA level > 2000 IU/mL • Age > 40 yr • Moderate/severe inflammation/fibrosis on liver biopsy	• Elevated HBV DNA level and age > 30 yr • Family history of hepatocellular carcinoma or cirrhosis and extrahepatic manifestations	• ALT level > ULN for 3–6 mo and HBV DNA level > 2000 IU/mL • Evidence of moderate/severe inflammation or fibrosis	• Monitor all untreated patients every 3 mo • Biopsy recommended for treatment decisions if: ◊ Noninvasive tests suggest evidence of advanced fibrosis ◊ ALT level is persistently elevated ◊ Age > 35 yr ◊ Family history of hepatocellular carcinoma or cirrhosis	• Monitor all untreated patients
Monitor	• ALT level < ULN and HBV DNA level < 2000 Liver biopsy	• HBV DNA level < 2000 IU/mL • ALT level < ULN	• ALT level < ULN • HBV DNA level < 2000 IU/mL		
Preferred first line treatment (alphabetical)	• Entecavir • Pegylated interferon • Tenofovir	• Entecavir • Pegylated interferon • Tenofovir	• Entecavir • Tenofovir	• Entecavir • Pegylated interferon • Tenofovir	• Entecavir • Tenofovir

Note: AASLD = American Association of the Study of Liver Diseases, ALT = alanine aminotransferase, APASL = Asian Pacific Association for the Study of the Liver, CASL = Canadian Association for the Study of the Liver, EASL = European Association for the Study of Liver, HBV = hepatitis B virus, ULN = upper limit of normal, WHO = World Health Organization.
*Upper limit of normal for alanine aminotransferase: men 35 U/L, women 25 U/L.
†Upper limit of normal for alanine aminotransferase: 40 U/L.
‡Upper limit of normal for alanine aminotransferase: men 30 U/L, women 19 U/L.

burdens will vary), the development and adoption of a national chronic hepatitis B strategy in Canada akin to hepatitis C care in Australia could facilitate volume-based discounting, reduce interjurisdictional heterogeneity and direct treatment to at-risk populations. Furthermore, equitable access could be broadened to eliminate the "postal code lottery" to enable safe and effective treatment of chronic hepatitis B while controlling the burden of chronic hepatitis B care in Canada. Clinician knowledge of drug prices is variable,[14] which may affect delivery of the highest-value care, and, so, in addition to further education, prudent policy coverage decisions will be critical to deliver cost-effective care.

When the CDEC made its initial recommendations, the cost of tenofovir and entecavir was about $18–22/d each, and restriction of a drug to patients with advanced fibrosis theoretically made sense from the standpoint of cost-effectiveness/budget impact. However, with the generic formulation of tenofovir entering the market, the difference between the cost of lamivudine and highly potent orally administered nucleos/tide analogues (i.e., tenofovir/entecavir) is now between $1/d and $2/d (Table 4). Lamivudine is not a favoured drug given the high rate of resistance (70% in 5 yr) and weaker viral suppression.[15] The reduced efficacy of viral suppression may allow progressive fibrosis to develop in spite of treatment, which would increase the overall economic burden on the health care system. As such, the initial savings with lamivudine will likely lead to additional costs downstream. It would be an important area of future investigation to repeat the previous economic analyses with more modern outcome data and costs as well as budget impact

Table 4: Cost per dose of chronic hepatitis B treatment

Drug	Province/territory;* cost, $								
	British Columbia†‡	Alberta	Saskatchewan	Manitoba	Ontario†	Quebec	Nova Scotia†	Newfoundland and Labrador§	Yukon Territory
Lamivudine¶	5.17	4.79	4.79	–	–	4.56	–	5.22	4.71
Originator price	3.81	3.53	3.53	–	3.53	3.53	3.53	3.85	3.53
Generic price									
Adefovir¶	26.28	23.84	24.34	–	–	23.22	–	26.53	24.34
Originator price	20.28	18.25	18.25	–	20.44	18.25	20.44	22.28	–
Generic price									
Tenofovir**	–	18.49	18.77	25.51	19.55	17.29	–	21.34	18.77
Originator price	5.28	4.89	4.89	4.89	4.89	4.89	4.89	5.33	4.89
Generic price									
Entecavir	23.76	22.00	22.00	–	–	22.00	–	23.98	22.00
Originator price	5.94	5.50	5.50	16.50	16.50	5.50	5.50	5.99	5.50
Generic price									
Emtricitabine–tenofovir	–	–	27.70	29.21	29.21	26.10	26.10	31.84	24.83
Originator price	–	–	7.30	7.30	7.30	7.30	7.30	7.96	–
Generic price									
Interferon	Alfa-2b††	Pegylated interferon 2a	Alfa-2b††	–	Alfa-2b††	Pegylated interferon 2a	–	Alfa-2b††	–
Originator price	–	–	–	–	–	–	–	–	–
Generic price	135.89	407.39	125.82		145.84	395.84		659.31	

*New Brunswick and Prince Edward Island do not report cost.
†Maximum price paid.
‡List price + 5%–8%.
§List price + 8.5%.
¶Only Apo generic.
**Apo, Teva, Mylan, Auro.
††Cost for 10 MU dosing.

analyses to improve our use of resources and patient outcomes and, it is hoped, standardize care nationally.

Based on the current list pricing of medications as well as the different populations these drugs would be considered for, we advocate for standard reimbursement nationwide for tenofovir, entecavir and interferon considering best practices and drug costs in alignment with internationally recognized guidelines. We acknowledge that the immediate budget impact may vary from jurisdiction to jurisdiction, although use of these agents is likely cost-effective in the long term and would eliminate costly and less-effective drugs from routine reimbursement. In context, the annual cost of treatment of HBV infection ($1300–$1800) is lower than that of HIV infection ($12 000)[16] or the 1-time cost of treatment of hepatitis C virus infection (about $60 000).[8]

Limitations

There were several study limitations. Not all plans provided pricing information about the medications, and there is the potential that the online criteria may be incomplete. Furthermore, criteria may have been updated after the data were extracted, although, typically, most formularies do not change substantially month to month. We lacked data for Nunavut and the Northwest Territories; however, we do not believe this affected our findings. As well, this study could not address implementation of criteria. Last, we examined only publicly available formularies, as we were unable to retrieve private health insurance criteria online for comparison.

Conclusion

The current criteria for reimbursement of antiviral medication to treat chronic hepatitis B in Canada show substantial interjurisdictional heterogeneity, with most plans having restrictions based on liver disease stage and allowing prescribing by specialists only. Given the substantial variability in access and the marked decrease in drug prices, improved access to medications nationally to ameliorate patient outcomes and eliminate geographical disparity is warranted to align with international treatment recommendations.

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