

Drug Coverage Decision for B.C. PharmaCare

About PharmaCare

B.C. PharmaCare is a government-funded drug plan. It helps British Columbians with the cost of eligible prescription drugs and specific medical supplies.

Details of Drug Reviewed

Drug	Tenofovir alafenamide
Brand Name	Vemlidy™
Dosage Form(s)	25 mg tablet
Manufacturer	Gilead Sciences Canada Inc.
Submission Type	New Submission
Use Reviewed	Treatment of chronic hepatitis B (CHB)
Common Drug Review (CDR)	Yes, CDR recommended: to Reimburse with clinical criteria and/or conditions . Visit the CDR website for more details: https://www.cadth.ca/sites/default/files/cdr/complete/SR0537_Vemlidy_complete_Mar-28-18.pdf
Drug Benefit Council (DBC)	DBC met on April 9, 2018. DBC considered various inputs including: clinical and pharmaco-economic evidence review material and the recommendation from the Canadian Drug Expert Committee (CDEC). The DBC also considered Patient Input Questionnaire responses from one patient and one Patient Group, CDR Patient Input, Clinical Practice Reviews from one specialist, Other Drug Agencies Review Recommendations document from the Canadian Agency for Drugs and Technologies in Health (CADTH), and a Budget Impact Assessment.
Drug Coverage Decision	Non-Benefit
Date	December 18, 2018
Reason(s)	Drug coverage decision is consistent with the CDEC and DBC recommendations. <ul style="list-style-type: none"> • DBC concurred with CDEC recommendation that the drug plan cost of Vemlidy™ should not exceed that of the lowest-cost preparation of tenofovir disoproxil fumarate (generics). • The drug was similar to or demonstrated some advantage over tenofovir disoproxil fumarate with respect to efficacy and safety. Quality of life was not assessed in the studies. • Based on the submitted product price, Vemlidy™ was substantially more expensive than the lowest-cost preparation of tenofovir disoproxil fumarate. • Based on the CDR recommendation, an attempt by the pan-Canadian Pricing Alliance (pCPA) was unsuccessful to address the concerns on cost and cost effectiveness.
Other Information	None

The Drug Review Process in B.C.

A manufacturer submits a request to the Ministry of Health (Ministry).

An independent group called the [Drug Benefit Council \(DBC\)](#) gives advice to the Ministry. The DBC looks at:

- whether the drug is safe and effective
- advice from a national group called the [Common Drug Review \(CDR\)](#)
- what the drug costs and whether it is a good value for the people of B.C.
- ethical considerations involved with covering or not covering the drug
- input from physicians, patients, caregivers, patient groups and drug submission sponsors

The Ministry makes PharmaCare coverage decisions by taking into account:

- the existing PharmaCare policies, programs and resources
- the evidence-informed advice of the DBC
- the drugs already covered by PharmaCare that are used to treat similar medical conditions
- the overall cost of covering the drug

Visit the [The Drug Review Process in B.C. - Overview](#) and [Ministry of Health - PharmaCare](#) for more information.

This document is intended for information only.

It does not take the place of advice from a physician or other qualified health care provider.

Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

FINAL

tenofovir alafenamide (Vemlidy™)

Gilead Sciences Canada Inc.

Description

Drug review of **tenofovir alafenamide (Vemlidy™)** for the following Health Canada approved indication(s):

For the treatment of chronic hepatitis B (CHB) in adults with compensated liver disease.

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on March 26, 2018, which included clinical and pharmacoeconomic evidence review material and the recommendations from the Canadian Drug Expert Committee (CDEC). The DBC also considered Patient Input Questionnaire responses from one patient and one Patient Group, CDR Patient Input, Clinical Practice Reviews from one specialist, an Other Drug Agencies Review Recommendations document from the Canadian Agency for Drugs and Technologies in Health (CADTH), and a Budget Impact Assessment.

Dosage Forms

Vemlidy™ is available as tenofovir alafenamide 25 mg oral tablet.

Recommendations

1. The Drug Benefit Council (DBC) recommends that tenofovir alafenamide (Vemlidy™) not be listed at the submitted price.

Reasons for the Recommendation

1. Summary

- In two double-blind randomized controlled trials (RCTs) comparing tenofovir alafenamide (TAF) with tenofovir disoproxil (TDF) in patients with chronic hepatitis B, the proportion of patients who achieved undetectable hepatitis B virus (HBV) DNA with TAF was non-inferior to TDF at week 48.
- The trials were not designed to assess key clinical outcomes such as morbidity, mortality, or health-related quality of life.
- The trials reported statistically significant improvements in bone mineral density (hip or spine) for TAF versus TDF at 48 weeks. There were no statistical differences between the TAF and TDF groups experiencing renal events.
- At the manufacturer submitted price, TAF is significantly more expensive than TDF.

2. Clinical Efficacy

- The DBC considered the CDR systematic review, which included two manufacturer-sponsored, multi-centre, double-blind RCTs comparing TAF with TDF in patients with chronic hepatitis B (hepatitis B e antigen-negative patients in Study 108, and hepatitis B e antigen-positive patients in Study 110).

- The primary outcome in both trials was the proportion of patients with hepatitis B virus (HBV) DNA of < 29 IU/mL at 48 weeks, testing the non-inferiority of TAF to TDF. Other outcomes included fibrosis, bone health, renal function, alanine aminotransferase (ALT) normalization, lipid measures, and adverse events, serious adverse events, and withdrawals due to adverse events.
- The proportion of patients who achieved undetectable HBV DNA with TAF was noninferior to TDF at week 48 in both Study 108 and in Study 110. There was no statistically significant difference between TAF and TDF groups after 48 weeks in either Study 108 or Study 110. Similar results were observed at 96 weeks, with no statistically significant difference between groups in each study.
- The proportion of patients who achieved undetectable HBV DNA at 96 weeks, who experienced hepatitis B surface antigen (HBsAg) loss, or who experienced HBeAg loss or seroconversion (Study 110 only), was similar between TAF and TDF treatment arms.
- The trials were not designed to assess key clinical outcomes such as morbidity and mortality, and health-related quality of life was not assessed in either study.
- For detailed information on the systematic review of tenofovir alafenamide (Vemlidy™) please see the CDEC Final Recommendation at: <https://www.cadth.ca/tenofovir-alafenamide>.

3. Safety

- There were similar overall adverse events and similar serious adverse events with TAF and with TDF in both studies after 96 weeks.
- The TAF formulation allows patients to receive a lower dosage than the TDF formulation yet achieve therapeutic levels of tenofovir, thereby reducing systemic exposure to tenofovir. This implies that TAF has the potential to reduce the toxicity associated with TDF, particularly the bone and renal effects.
- Secondary outcomes of the trials included those related to bone mineral density (hip and spine) and assessment of renal function (serum creatinine and proteinuria).
- The assessment of the key safety outcome of bone disorders relied on bone mineral density, a surrogate marker, instead of clinical outcomes such as fractures. Statistically significant improvements in bone mineral density were reported for TAF versus TDF at 48 weeks.
- There were no statistical differences between the TAF and TDF groups experiencing renal events, including proteinuria. In study 110, there was a smaller increase in serum creatinine in the TAF versus TDF groups after 48 weeks, and these differences persisted at 96 weeks. There was no difference in the increase in serum creatinine between TAF and TDF groups in study 108.
- For detailed information on the safety and tolerability of tenofovir alafenamide (Vemlidy™), please see the CDEC Final Recommendation at the links above.

4. Economic Considerations

- At the manufacturer submitted price, the annual cost of TAF is approximately four times the cost of generic TDF.
- The manufacturer submitted a cost analysis assuming equivalent efficacy and safety between TAF and TDF, and therefore it was impossible for the CDR to assess the cost-effectiveness of TAF versus TDF considering the two drugs' potential advantages or disadvantages in terms of adverse event profile over the long term.
- The CDR recommended that the drug plan cost of TAF should not exceed that of the lowest-cost preparation of TDF.

5. Of Note

- The Patient Input Questionnaire responses received from one patient and one Patient Group reported that, although the current drugs for treatment of hepatitis B were effective and well tolerated, the adverse event profile for TAF appeared to be better in regards to bone and renal events.