

## CEDAC FINAL RECOMMENDATION on RECONSIDERATION and REASONS for RECOMMENDATION

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### TELBIVUDINE (Sebivo™ – Novartis Pharmaceuticals Canada Inc.)

#### **Description:**

Telbivudine is a synthetic thymidine nucleoside analogue that is approved for the treatment of chronic hepatitis B in adults 16 years and older with compensated liver disease with evidence of viral replication and active liver inflammation.

#### **Dosage Forms:**

600 mg tablets. The recommended dose is 600 mg taken once daily.

#### **Recommendation:**

The Canadian Expert Drug Advisory Committee (CEDAC) recommends that telbivudine not be listed.

#### **Reasons for the Recommendation:**

1. While telbivudine has been shown to be superior to lamivudine in improving histologic and viral outcomes in patients not previously treated with nucleoside analogues, a relatively high proportion of patients will develop resistance to telbivudine.
2. The annual cost of telbivudine is \$6,200 per patient, compared to \$1,600 for lamivudine. The manufacturer submitted an economic evaluation comparing telbivudine to lamivudine which estimated an incremental cost per quality adjusted life year (QALY) of \$33,300 for hepatitis B virus e antigen positive patients and \$107,900 per QALY for hepatitis B virus e antigen negative patients. However, the evaluation was based on a time horizon of 30 years that assumed that telbivudine resulted in a reduced incidence of hepatocellular carcinoma and the development of cirrhosis. Given that the incidence of viral resistance to telbivudine in patients who were hepatitis B virus e antigen positive at two years has been reported to be 18%, this will clearly impact the long-term effectiveness of this drug. It was unclear how resistance was incorporated into the cost-effectiveness analysis and therefore, the Committee felt that the true cost-effectiveness of telbivudine over the long-term was uncertain.

#### **Summary of Committee Considerations:**

The Committee considered a systematic review of randomized controlled trials (RCTs) in adult patients with chronic hepatitis B infection. Four double blind RCTs comparing telbivudine with lamivudine, all in nucleos(t)ide-naïve patients with compensated liver disease, met the inclusion criteria for the review. One

of these trials was small and two are still ongoing. The Committee focused its review on a two year trial in 1367 patients which assessed treatment effects on serologic, virologic and biochemical effects.

In patients who were hepatitis B virus e antigen positive, telbivudine resulted in statistically significant improvements in the proportion of patients with undetectable hepatitis B viral DNA (number needed to treat [NNT] of 6) and normalization of alanine aminotransferase (NNT=13). There were also significant differences in the proportion of patients who developed virologic breakthrough: 19% of telbivudine patients versus 33% of lamivudine patients. There were no statistically significant differences in the rate of loss or seroconversion of hepatitis B virus e antigen. Inconsistent histologic response results were reported – there was a statistically significant improvement in favour of telbivudine in the number of patients with histologic response assessed by the Knodell Histology Activity Index score on liver biopsy at one year compared to baseline (NNT=12) but no statistically significant difference between groups in the Ishak fibrosis score at one year compared to baseline.

In patients who were hepatitis B virus e antigen negative, telbivudine resulted in statistically significant improvements in the proportion of patients with undetectable hepatitis B viral DNA (NNT=4) and development of viral resistance (NNT=13) but there were no significant differences in histologic or serologic measures of effectiveness.

There was no difference between telbivudine and lamivudine in the incidence of serious adverse events or withdrawals due to adverse events. The most common adverse event related to telbivudine was elevation of creatine kinase.

**Of Note:**

1. Both published and unpublished data were reviewed and taken into consideration in making this recommendation.
2. The Committee recognizes that the management of chronic hepatitis B infection is rapidly evolving and recommends that drug plans seek further advice from the Committee based on emerging treatment options and strategies for the treatment of chronic hepatitis B infection.

**Background:**

CEDAC provides formulary listing recommendations to publicly funded drug plans. Recommendations are based on an evidence-based review of the medication’s effectiveness and safety and an assessment of its cost-effectiveness in comparison to other available treatment options. For example, if a new medication is more expensive than other treatments, the Committee considers whether any advantages of the new medication justify the higher price. If the recommendation is not to list a drug, the Committee has concerns regarding the balance between benefit and harm for the medication, and/or concerns about whether the medication provides good value for public drug plans.

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**Common Drug Review**