



## FINAL RECOMMENDATION and REASONS for RECOMMENDATION

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### PEGINTERFERON ALFA-2a plus RIBAVIRIN (Pegasys® RBV™ –Hoffmann-La Roche)

**Description:**

Pegasys® RBV™ is a combination of peginterferon alfa-2a and ribavirin (RBV). The interferon in this agent is a covalent conjugate of interferon alfa-2a with a single branched polyethylene glycol (PEG) chain. Interferon is an immunomodulator and inhibits proliferation and viral replication in affected cells. Ribavirin is a synthetic nucleotide analog and has direct antiviral and immunomodulatory properties. Peginterferon alfa-2a plus ribavirin (Pegasys® RBV™) is approved in Canada for the treatment of chronic hepatitis C in adult patients without cirrhosis and in adult patients with compensated cirrhosis.

**Recommendation:**

The Canadian Expert Drug Advisory Committee recommends that the combination of peginterferon alfa-2a plus ribavirin (Pegasys® RBV™) be listed in a similar manner to other interferon plus ribavirin products used in the treatment of chronic hepatitis C.

**Reasons for recommendation:**

1. In all relevant clinical trials considered in this submission, there is a significantly higher percentage of patients who had a sustained virological response (SVR), which equates to the absence of detectable virus (< 100 copies /ml) on a qualitative based serum HCV RNA PCR assay at 3 to 6 months after completion of therapy, when peginterferon alfa-2a plus ribavirin (Pegasys® RBV™) was compared to interferon alfa-2b plus ribavirin (Rebetron®).
2. There was no statistically significant difference in morbidity with respect to emergency room visits and hospitalizations in patients receiving the peginterferon alfa-2a plus ribavirin (Pegasys® RBV™) compared to those receiving interferon alfa- 2b plus ribavirin.
3. The acquisition costs of peginterferon alfa-2a plus ribavirin (Pegasys® RBV™) and peginterferon alfa-2b plus ribavirin (Pegetron®), the latter which is already listed in most jurisdictions in Canada, are essentially identical.
4. When comparing peginterferon alfa-2a plus ribavirin (Pegasys® RBV™) versus no treatment, the estimates for incremental cost-effectiveness ratios are approximately \$11,000 per QALY gained and within the limitations of the pharmacoeconomic model used, peginterferon alfa-2a

plus ribavirin (Pegasys® RBV™) was dominant with respect to the other comparators of interferon alfa-2b plus ribavirin (Rebetron®) and peginterferon interferon alfa-2b plus ribavirin (Pegetron™). The main limitations of the model used were the exclusion of adverse events from the analysis, the lack of head-to-head trials between pegylated formulations of interferon and the methodologic limitations of using SVR as a valid endpoint for long term response in chronic HCV infection.

**Of Note:**

1. No head to head trial evidence is available to suggest that peginterferon alfa-2a plus ribavirin (Pegasys® RBV™) is superior to peginterferon alfa-2b plus ribavirin (Pegetron™) with respect to the outcomes of SVR or histologic responses.
2. The recommended dose of peginterferon alfa-2a plus ribavirin (Pegasys® RBV™), with respect to the interferon dosing, may have an advantage of convenience with once weekly versus multiple weekly dosing for non-pegylated products.
3. Rigorous evidence that any interferon plus ribavirin therapy improves the long term outcome in chronic HCV infection is lacking. In addition, the studies to support the validity of using SVR as a surrogate marker for improved long term outcome have significant methodological limitations.