CEDAC FINAL RECOMMENDATION AND REASONS FOR RECOMMENDATION

RALTEGRAVIR
(Isentress™ – Merck Frosst Canada Ltd.)

Description:
Raltegravir inhibits the catalytic activity of HIV integrase, an HIV-encoded enzyme that is required for viral replication. When used in combination with other antiretroviral agents, raltegravir is approved for the treatment of HIV-1 infection in treatment-experienced adult patients who have evidence of viral replication and HIV-1 strains resistant to multiple antiretroviral agents. It has been issued a Notice of Compliance with Conditions from Health Canada (NOC/c), pending the results of studies to verify its clinical benefit.

Dosage Forms:
400 mg tablets. The recommended dose is 400 mg taken twice daily.

Recommendation:
The Canadian Expert Drug Advisory Committee (CEDAC) recommends that raltegravir be listed for the treatment of HIV infection in patients who are antiretroviral experienced and have virologic failure due to resistance to at least one agent from each of the three major classes of antiretroviral agents, nucleoside/tide reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors and protease inhibitors.

Reasons for the Recommendation:
1. Raltegravir has been shown to improve virologic and immunologic outcomes in patients who have experienced virologic failure with other antiretroviral therapy.

2. Raltegravir is similar or lower in cost compared to other antiretroviral agents currently listed by drug plans for treatment of patients who have experienced virologic failure with other antiretroviral therapy.

Summary of Committee Considerations:
The Committee considered a systematic review of double blind, randomized, placebo controlled trials of raltegravir, in combination with other treatments, in patients who had experienced virologic failure with other antiretroviral therapy, and with resistance to at least one drug from each major antiretroviral drug class. Three trials met the inclusion criteria for the systematic review, though the Committee focused its review on two identically designed trials of 48 weeks duration in a total of 699 patients which compared

raltegravir in addition to optimized background antiretroviral therapy with optimized background antiretroviral therapy alone. The third trial in the systematic review was a small phase II trial.

Pooled analyses from the two key trials reported statistically significant differences in favour of raltegravir for the number of patients with HIV-1 RNA levels <400 copies/mL (number needed to treat [NNT] = 3), the number of patients with HIV-1 RNA levels <50 copies/mL (NNT = 4), and the mean increase in CD4 cell count.

There were no statistically significant differences in the incidence of serious adverse events, withdrawals due to adverse events or drug-related adverse events.

Raltegravir costs $27 per day, which is similar or less than other antiretroviral agents approved for use in treatment-experienced patients who are not responding to initial therapy: $31 per day for darunavir boosted with ritonavir, $40 per day for tipranavir boosted with ritonavir, and $79 per day for enfuvirtide.

Of Note:

1. Both published and unpublished data were reviewed and taken into consideration in making this recommendation.

2. Drug plans may seek further advice from the Committee when the results of studies to verify its clinical benefit are available.

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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