

CEDAC FINAL RECOMMENDATION and REASONS for RECOMMENDATION

TENOFOVIR/EMTRICITABINE/EFAVIRENZ (Atripla™ – Bristol-Myers Squibb Canada and Gilead Sciences Canada, Inc.)

Description:

Atripla™ is a fixed dose combination of two nucleoside/nucleotide reverse transcriptase inhibitors (tenofovir and emtricitabine) and a non-nucleoside reverse transcriptase inhibitor (efavirenz) that is approved for use alone as a complete regimen or in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults.

Dosage Forms:

Tablet containing emtricitabine 200 mg, tenofovir disoproxil fumarate 300 mg and efavirenz 600 mg. The recommended dose is one tablet once daily.

Recommendation:

The Canadian Expert Drug Advisory Committee (CEDAC) recommends that Atripla™ be listed as an option for the treatment of HIV-1 infection where the virus is susceptible to each of tenofovir, emtricitabine and efavirenz, and:

- Atripla™ is used to replace existing therapy with its component drugs, or
- the patient is treatment naïve, or
- the patient has established viral suppression but requires antiretroviral therapy modification due to intolerance or adverse effects.

Reasons for the Recommendation:

1. The Committee considered the data from an open label randomized controlled trial (RCT) of 48 weeks duration in treatment naïve patients that compared a regimen of zidovudine, lamivudine and efavirenz, against a combination of tenofovir, emtricitabine and efavirenz. At 48 weeks the combination of tenofovir, emtricitabine and efavirenz was associated with statistically significant improvements in patients with HIV-1 RNA levels <400 or <50 copies/mL (number needed to treat [NNT] of 9 and 11 respectively). After 144 weeks of follow-up, there was a statistically significant difference in the number of subjects with HIV-1 RNA levels <400 copies/mL (NNT=8) but not for HIV-1 RNA levels <50 copies/mL. More patients in the zidovudine, lamivudine and efavirenz group (6%) discontinued therapy due to virologic failure than in the tenofovir, emtricitabine and efavirenz group (2%). There were fewer withdrawals due to adverse effects in the tenofovir, emtricitabine and efavirenz arm and this was primarily due to a lower incidence of anemia.
2. Atripla™ costs \$39.11 per day, which is equivalent to the combined cost of Truvada™ (tenofovir/emtricitabine) and efavirenz. While Atripla is slightly more costly than the combination

Common Drug Review

of abacavir/lamivudine/efavirenz (~ \$36.00 per day), it is less costly than protease inhibitor containing regimens which could also be chosen for primary therapy.

Summary of Committee Considerations:

The Committee considered a systematic review of RCTs of tenofovir, emtricitabine and efavirenz, given either as the fixed dose combination or as individual components with the same dose as Atripla™, in adult patients infected with HIV-1. Three open label trials were included in the systematic review: one compared the combination of tenofovir, emtricitabine and efavirenz with the combination of zidovudine, lamivudine and efavirenz in treatment naïve patients while the other two trials randomized patients who had achieved virologic suppression to either continue their antiretroviral regime or switch to the combination of tenofovir, emtricitabine and efavirenz. The results of the trial in treatment naïve patients are summarized above.

In the two trials which switched patients to the tenofovir, emtricitabine and efavirenz combination, measures of virologic response were similar between treatment groups.

Of Note:

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

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.