CEDAC FINAL RECOMMENDATION and REASONS for RECOMMENDATION

ETRAVIRINE
(Intelence™ – Janssen-Ortho Inc.)

Description:
Etravirine is a human immunodeficiency virus non-nucleoside reverse transcriptase inhibitor (NNRTI) which, in combination with other antiretroviral agents, is approved for the treatment of HIV-1 infection in treatment-experienced adult patients who have failed prior therapy and have HIV-1 strains resistant to multiple antiretroviral agents, including NNRTIs.

Dosage Forms:
100 mg tablets. The recommended dose is 200 mg taken twice daily.

Recommendation:
The Canadian Expert Drug Advisory Committee (CEDAC) recommends that etravirine, in combination with other antiretroviral agents, be listed for the treatment of HIV-1 infection in treatment-experienced patients who have failed prior antiretroviral therapy, and have HIV-1 strains resistant to multiple antiretroviral agents, including other NNRTIs.

Reasons for the Recommendation:
1. Etravirine has been shown to improve immunologic, virologic and clinical responses when added to an optimized background antiretroviral regimen in patients who have experienced virologic, immunologic or clinical failure on prior therapy.

2. Etravirine costs $21.80 per day, which is less expensive than other antiretroviral agents approved for use in treatment-experienced patients, such as raltegravir ($27 per day).

Summary of Committee Considerations:
The Committee considered a systematic review of double-blind randomized controlled trials (RCTs) evaluating etravirine, in combination with other antiretroviral agents, in treatment-experienced adult patients with HIV-1 infection who had failed prior therapy and had HIV-1 strains resistant to multiple antiretroviral agents, including NNRTIs. Two identically designed double-blind RCTs of 96 weeks duration in a total of 1,203 patients were included in the systematic review. Both RCTs compared etravirine to placebo with an optimized background regimen comprised of darunavir boosted with ritonavir and investigator-selected nucleoside/nucleotide reverse transcriptase inhibitors and optional enfuvirtide. Patients were

stratified prior to randomization by previous enfuvirtide use. The primary efficacy endpoint in both trials was the proportion of patients with viral load < 50 copies/mL.

Pooled analyses from the two RCTs reported statistically significant differences in favour of etravirine for the number of patients with viral load less than 50 copies/mL (number needed to treat [NNT] = 6 at 24 weeks and NNT = 5 at 48 weeks). Changes in CD4 cell count from baseline were also statistically significantly greater in the etravirine group in both trials. Although not a primary outcome in either trial, pooled analyses reported fewer etravirine treated patients with any AIDs-defining illness compared to placebo (relative risk of 0.51 [0.33-0.79]).

There were no statistically significant differences in withdrawals due to adverse events, total adverse events or grade 3 or 4 adverse events between treatment groups.

The daily drug cost for etravirine is $21.80, which is less than other antiretroviral agents approved for use in treatment-experienced patients who are not responding adequately to prior therapy.

Of Note:

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

2. Initial prescribing of etravirine should be guided by physicians with significant expertise in HIV care.

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.