

## CEDAC FINAL RECOMMENDATION and REASONS for RECOMMENDATION

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### DARUNAVIR (Prezista<sup>™</sup> – Janssen-Ortho Inc.)

#### **Description:**

Darunavir is a HIV-1 protease inhibitor (PI) which, in combination with low dose ritonavir, is approved for the treatment of HIV infection in treatment-experienced adult patients who have failed prior antiretroviral therapy, and has been issued marketing authorization with conditions, pending the results of studies to verify its clinical benefit.

#### **Dosage Forms:**

300 mg tablet. The recommended dose is 600 mg twice daily.

#### **Recommendation:**

The Canadian Expert Drug Advisory Committee (CEDAC) recommends that darunavir be listed as an alternate PI as part of a HIV treatment regimen for treatment-experienced adult patients who have demonstrated failure to multiple PIs and in whom less expensive PIs are not a treatment option.

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

1. In comparison with other PIs boosted with ritonavir, treatment with darunavir boosted with ritonavir resulted in statistically significant improvements in virologic and immunologic response in patients with evidence of virologic failure to other PIs.
2. Darunavir costs \$27.84 per day, which is more expensive than other PIs (approximately \$15 – 20 per day), but less expensive than tipranavir (\$33.00 per day). The Committee felt that darunavir was cost-effective when used in accordance with the above recommendation.

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

The Committee considered a systematic review of randomized controlled trials (RCTs) comparing darunavir, boosted with ritonavir, with other treatments in patients who had experienced virologic failure to other antiretroviral therapy. Two open-labelled RCTs met the criteria for the review, both of which compared darunavir with other PIs, each boosted with ritonavir, in treatment experienced patients with at least one primary PI mutation. Patients in both trials had their background antiretroviral therapy optimized prior to randomization. The randomized phase of each RCT was 24 weeks with an open-label extension to 96 weeks. The studies are not yet complete and the Committee based its review on the analyses of endpoints at 24 and 48 weeks.

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### Common Drug Review

In comparison with other PIs boosted with ritonavir, regimens that included darunavir boosted with ritonavir were associated with statistically significant improvements in virologic response and CD4 cell counts. These results were consistent at both 24 and 48 weeks of treatment. There were no statistically significant differences in quality of life between groups in either of the RCTs.

The overall incidence and severity of adverse events was similar in patients treated with darunavir versus other PIs, with the exception of the incidence of *Herpes simplex* infections and increased serum triglycerides, both of which occurred more frequently in darunavir treated patients. Interpretation of adverse event rates is complicated by the open label design of the RCTs and the high number of patients who were converted from comparator PIs to darunavir at week 12 of the trial.

An economic evaluation submitted by the manufacturer in treatment-experienced HIV-1 infected patients who have failed at least one PI, reported that the use of darunavir, in combination with ritonavir and optimized background antiretroviral therapy, results in an incremental cost per quality-adjusted life year gained of \$31,000 when compared to treatment with other PIs. The Committee felt that restricting the use of darunavir to patients in whom all of the less expensive PIs are no longer an option would optimize the use of this medication.

**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.