

## **CEDAC FINAL RECOMMENDATION and REASONS for RECOMMENDATION**

### **MARAVIROC RESUBMISSION (Celsentri™ – Pfizer Canada Inc.)**

#### **Description:**

Maraviroc is a chemokine (CC-motif) receptor 5 (CCR5) antagonist. In combination with other antiretroviral agents, it is indicated for treatment-experienced adult patients infected with CCR5-tropic human immunodeficiency virus (HIV) type 1, who have evidence of resistance to multiple antiretroviral agents. Maraviroc was previously submitted to the Common Drug Review, but the submission was withdrawn prior to the Canadian Expert Drug Advisory Committee (CEDAC) deliberations.

#### **Dosage Forms:**

150 mg and 300 mg tablets. The recommended dose is 300 mg taken twice daily.

#### **Recommendation:**

The Canadian Expert Drug Advisory Committee recommends that maraviroc, given in combination with other antiretroviral agents, be listed for treatment of HIV-1 infection in patients:

- who have CCR5 tropic viruses and
- who have documented resistance to at least one agent from each of the three major classes of antiretroviral agents (nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, protease inhibitors).

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

1. Maraviroc has been shown to improve immunologic and virologic responses when added to an optimized antiretroviral background regimen in patients demonstrating resistance to, or who have extensive experience with other therapies and who have a CCR5 tropic virus that is susceptible to maraviroc.
2. The daily drug cost for maraviroc is \$33, which is more than some of the antiretroviral agents used in treatment-experienced patients who are not responding adequately to prior therapy, such as raltegravir (\$27), but less than other agents (tipranivir/ritonavir, \$39.74/day).

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

The Committee considered a systematic review of two double-blind randomized controlled trials (RCTs) evaluating maraviroc, in combination with other antiretroviral agents, in treatment-experienced adult patients with CCR5 tropic HIV-1 infection (N=1040). The data from the maraviroc 300 mg twice daily and placebo arms were considered. The two trials were 48 weeks in duration, had identical designs and

compared maraviroc, in addition to optimized background therapy (OBT), with OBT alone. The primary efficacy endpoint of both trials was the mean change from baseline in HIV-1 viral load at week 48.

Pooled analyses from the two RCTs reported statistically significant differences in favour of maraviroc in the mean change from baseline in viral load at week 48, and the proportion of patients with viral load less than 50 copies/mL (number needed to treat, NNT = 4 at 48 weeks). Changes in CD4 cell count from baseline were also statistically significantly greater in the maraviroc group in both trials, compared to placebo. Maraviroc increased the time to treatment failure, compared to placebo in both trials. The Committee did have some concern regarding the study validity due to the high rate of study withdrawal (35% of maraviroc patients and 68% of placebo patients) and failure to follow these patients beyond a short period. Lack of efficacy was the primary reason for withdrawal from the studies (23% of maraviroc patients and 54% of placebo patients).

There were no statistically significant differences in withdrawals due to adverse events or total adverse events. Patients receiving maraviroc experienced a higher rate of infections compared to placebo, largely attributable to upper respiratory tract infections, but adverse events were not analyzed based on duration of treatment. The long term beneficial and harmful effects of CCR5-antagonism is unknown.

#### **Of Note:**

1. Both published and unpublished data were reviewed and taken into consideration in making this recommendation.
2. The optimal frequency of testing for CCR5 tropism has not been established. The CCR5 test is currently provided free of charge by the manufacturer, but it is unknown how long this service will be provided. Rates of false positives and false negatives of the CCR5 test have not been reported and therefore the reliability of the test results are unknown. Given that testing for CCR5 is required for use of this agent, participating drug plans should acquire information on the accuracy and availability of this test in the future.
3. The long term incidence of viral resistance to maraviroc and emergence of CXCR4 tropism or dual tropism is unknown.
4. Initial prescribing of maraviroc 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.

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### **Common Drug Review**