

Maraviroc

Product:

MARAVIROC (Celsentri®) 150mg, 300mg tablets

Class of drugs:

Antiretroviral agent

Indication:

Treatment of HIV-1 infection

Manufacturer:

Pfizer Canada Inc.

CED Recommendation

The CED recommended that maraviroc (Celsentri) be funded through the Exceptional Access Program according to specific criteria. The CED noted that reimbursement should be limited to patients whose HIV infection is resistant to multiple therapies and who are infected with a specific subtype of virus that is susceptible to the effect of maraviroc (Celsentri).

Executive Officer Decision

Based on the CED's recommendation, the Executive Officer approved funding for maraviroc (Celsentri) through the Exceptional Access Program according to specific criteria.

Status

Funding available through the Ontario Public Drug Programs via the Exceptional Access Program.

Highlights of Recommendation:

- ◆ Maraviroc (Celsentri) is an antiretroviral medication used for the treatment of Human Immunodeficiency Virus (HIV) infection. It is indicated for people whose HIV infection is resistant to multiple antiretroviral drugs (i.e. treatment-experienced patients). Maraviroc (Celsentri) is effective only in patients with a specific type of HIV infection called the CCR5-trophic virus.
- ◆ Studies in treatment-experienced adult patients with CCR5-trophic HIV infection have shown that maraviroc (Celsentri), when used in combination with other antiretroviral drugs, is effective at suppressing HIV viral replication and at improving immune function.
- ◆ The efficacy of maraviroc (Celsentri) has not been established in patients who have no, or limited, resistance to other available antiretroviral drugs (i.e. treatment-naïve patients).
- ◆ The most common side effects observed with maraviroc (Celsentri) are cough, fever, colds, rash, muscle and joint pain, stomach pain, and dizziness. An increased risk of some infections, liver problems, and cardiac events (e.g. heart attacks) have also been reported in some patients using this drug.
- ◆ The long-term safety of maraviroc (Celsentri) is unknown. Because maraviroc (Celsentri) works on immune system cells, potential harms include impaired immune function, which may increase the risk of developing infections and cancers.
- ◆ Maraviroc (Celsentri) costs \$33 per day, which is more expensive than some comparator agents.
- ◆ **Given that efficacy has only been established in treatment-experienced patients with CCR5-trophic HIV infection and the concerns over long-term safety, the Committee indicated that funding for maraviroc (Celsentri) should be provided through the Exceptional Access Program.**

Background:

Human Immunodeficiency Virus (HIV) is the virus that causes acquired immunodeficiency syndrome (AIDS). There is currently no cure for HIV infection; however, antiretroviral drugs can help patients delay or prevent the clinical consequences of HIV infection by restoring immune system function, improving quality of life, and reducing HIV-related complications and death. Antiretroviral drugs work by lowering the amount of virus in the patient's blood; this is called the viral load. A reduction in viral load leads, in most cases, to an improvement in immune system function, measured by the CD4 cell count.

There are two types of receptors on immune cells, CCR5 receptors and CXCR4 receptors. The HIV virus must bind to one of these two receptors to enter and infect the immune cells. People with HIV can be infected with CCR5-trophic virus, CXCR4-trophic virus, or a mixture of CCR5- and CXCR4-trophic viruses. Maraviroc (Celsentri) belongs to a new class of antiretroviral medications called chemokine receptor 5 (CCR5) antagonists and works by blocking the CCR5 receptor and preventing the entry of HIV into cells.

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Detailed Discussion:

- ◆ The Committee reviewed two double-blind randomized controlled trials evaluating the efficacy and safety maraviroc (Celsentri) in treatment-experienced adult patients with CCR5-trophic HIV infection. The two studies combined enrolled more than 1,000 patients and assigned them to receive maraviroc (Celsentri) or placebo, plus an optimized background regimen. *(An optimized background regimen is made up of antiretroviral drugs that are chosen on the basis of a patient's HIV resistance testing and treatment history.)*
- ◆ After 48 weeks of treatment, a higher proportion of patients who received maraviroc (Celsentri) achieved virological suppression (i.e. a viral load of less than 50 copies/mL) compared with those in the placebo group. Patients who were treated with maraviroc (Celsentri) also had higher increases in their CD4 cell count versus those on placebo.
- ◆ Maraviroc (Celsentri) is not effective in patients with CXCR4-trophic virus or a mixture of CXCR4- and CCR5-trophic viruses. For this reason, the Committee indicated that funding for maraviroc (Celsentri) should be considered in patients infected with only CCR5-trophic virus.
- ◆ Because efficacy in treatment-naïve patients has not been established, maraviroc (Celsentri) funding should also be restricted to treatment-experienced patients who are resistant to multiple antiretroviral drugs.
- ◆ Maraviroc (Celsentri) is the first agent in a class of antiretroviral drugs that targets the immune system. The long-term effects of maraviroc (Celsentri) on immune function are currently unknown. Potential harms include impaired immune function, which may increase the risk of developing infections and cancers.
- ◆ The daily drug cost for maraviroc (Celsentri) is \$33. It is more expensive than some antiretroviral agents that are also used in treatment-experienced patients.
- ◆ In light of the above, the Committee recommended that maraviroc (Celsentri) be funded through the Exceptional Access Program (EAP) according to the specific criteria.

EAP Criteria:

The CED recommended that maraviroc (Celsentri) be funded through the Exceptional Access Program (EAP) according to the following criteria:

*For the treatment of HIV-1 infection in patients with:
CCR5- trophic virus only; AND
Evidence of virologic failure despite optimal antiretroviral therapy AND with documented genotypic (or phenotypic) resistance to at least one of each: NRTI, NNRTI, and PI.*

Renewals:
Viral load is undetectable (i.e. < 50 copies/mL) OR CD₄ count is increasing or is stable (i.e., two recent CD₄ counts are at least within 20% of one another).

CEDAC Recommendation:

<http://www.cadth.ca/index.php/en/cdr/recommendations>

The Canadian Expert Drug Advisory Committee (CEDAC) recommended that maraviroc (Celsentri), given in combination with other antiretroviral agents, be listed for treatment of HIV-1 infection in patients who have CCR5 trophic viruses and have documented resistance to at least one agent from each of the three major classes of antiretroviral agents (NRTI, NNRTI, and PI).



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