

Etravirine

Product:

ETRAVIRINE (Intelence®)
100mg tablet

Class of drugs:

Antiretroviral agent; non-nucleoside reverse transcriptase inhibitor (NNRTI)

Indication:

Treatment of Human Immunodeficiency Virus type-1 (HIV-1) infection

Manufacturer:

Janssen-Ortho Inc.

CED Recommendation

The CED recommended that etravirine (Intelence) not be listed on the Ontario Drug Benefit Formulary, unless the price was reduced. The CED noted that etravirine (Intelence) has been demonstrated to be efficacious in patients whose HIV infection is resistant to multiple treatments and this drug would provide reasonable value for money if the price was reduced.

Executive Officer Decision

Based on the CED's recommendation and a subsequent pricing agreement, the Executive Officer decided to list etravirine (Intelence) on the Ontario Drug Benefit Formulary.

Status

Listed on the Ontario Drug Benefit Formulary.

Highlights of Recommendation:

- ◆ Etravirine (Intelence) is an antiretroviral medication indicated for the treatment of Human Immunodeficiency Virus (HIV). Etravirine (Intelence) belongs to a class of antiretroviral medications called non-nucleoside reverse transcriptase inhibitor (NNRTI). It is licensed for use in combination with other antiretroviral drugs in patients whose infection is resistant to multiple treatments (i.e. highly "treatment-experienced" patients).
- ◆ The Committee reviewed two clinical studies comparing etravirine (Intelence) to placebo in patients whose HIV infection had become resistant to multiple antiretroviral drugs. The studies found that etravirine (Intelence) suppressed HIV viral replication and improved immune function as measured by a rise in the CD4 cell count. It was also reported that patients on etravirine (Intelence) had a lower incidence of AIDS-defining illness, such as infections and cancers to which patients with HIV are vulnerable.
- ◆ A common side effect with etravirine (Intelence) is skin rash. Other side effects include diarrhea, nausea, abdominal pain, vomiting, tiredness, tingling or pain in hands or feet, numbness, headache, and high blood pressure.
- ◆ Etravirine (Intelence) costs \$21.80 per day. It is more expensive than other agents in the NNRTI drug class. Given that etravirine (Intelence) is used in patients who are resistant to multiple therapies and have limited remaining treatment options, the Committee indicated that this drug would provide reasonable value for money if the price was reduced.
- ◆ The Committee expressed concerns regarding the risk for off-label use in "treatment-naïve" patients (i.e. those who have not tried any antiretroviral treatments and in whom many other drugs are still effective). The efficacy and cost-effectiveness of etravirine (Intelence) in treatment-naïve patients have not been established.

- ◆ Overall, the Committee acknowledged the clinical benefits of etravirine (Intelence) in patients whose HIV infection is resistant to multiple antiretroviral drugs and noted that this drug would provide reasonable value for money if the price was reduced.

Background:

Human Immunodeficiency Virus (HIV) is the virus that causes acquired immunodeficiency syndrome (AIDS). Although there is no cure for HIV, 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 (called the viral load). This leads, in most cases, to an improvement in immune system function (measured by the CD4 cell count).

Etravirine (Intelence) belongs to the class of antiretroviral drugs called non-nucleoside reverse transcriptase inhibitor (NNRTI). NNRTIs work by blocking the action of an enzyme (reverse transcriptase) necessary for the HIV virus to reproduce.

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Detailed Discussion:

- ◆ The Committee reviewed two double-blind, randomized controlled studies (*DUET-1 and Duet-2. Lancet 2007; 370:29-48*) evaluating the efficacy and safety of etravirine (Intelence) versus placebo, on an optimized background regimen, in highly treatment-experienced patients.
- ◆ The studies reported that, after 24 weeks of treatment, a higher proportion of patients who received etravirine (Intelence) achieved virological suppression (i.e. a viral load of less than 50 copies/mL) compared with those in the placebo group (56% vs. 39% in DUET-1 and 62% vs. 44% in DUET-2). The studies also reported that patients using etravirine (Intelence) had higher increases in their CD4 cell count and a lower incidence of AIDS-defining illness compared to patients on placebo.
- ◆ An analysis of the study results found that much of the observed benefits of etravirine (Intelence) depended on whether the patient was being treated concurrently with enfuvirtide (another antiretroviral drug) and, if so, whether the patient was using enfuvirtide for the first time. Significant benefits were only demonstrated in patients who either did not use enfuvirtide concurrently or had used enfuvirtide before and were reusing it. Patients who were concurrently being treated with enfuvirtide and were using enfuvirtide for the first time did not experience significant benefits from etravirine (Intelence).
- ◆ The Committee also noted that most patients in the two studies were male and that all patients were being treated concurrently with darunavir/ritonavir in their combination antiretroviral regimen. Data from further studies on female patients, as well as in patients not being treated concurrently with darunavir/ritonavir, would be informative.
- ◆ A common side effect reported with etravirine (Intelence) is skin rash. In the two studies, most of the skin reactions occurred within the first four weeks of treatment and were generally mild.
- ◆ Etravirine (Intelence) is associated with many known and potential drug interactions, including interactions with other antiretroviral medications. Caution and dose adjustments should be made if etravirine (Intelence) is to be used in these circumstances.
- ◆ Etravirine (Intelence) costs \$21.80 per day. It is more expensive than other agents in the NNRTI drug class. Given that etravirine (Intelence) is used in patients who are resistant to multiple therapies and have limited remaining treatment options, the Committee indicated that this drug would provide reasonable value for money if the price was reduced.
- ◆ The Committee expressed concerns regarding the risk for off-label use in "treatment-naïve" patients (i.e. those who have not tried any antiretroviral treatments and in whom many other drugs are still effective). The efficacy and cost-effectiveness of etravirine (Intelence) in treatment-naïve patients have not been established.
- ◆ Overall, the Committee acknowledged the clinical benefits of etravirine (Intelence) in patients whose HIV infection is resistant to multiple antiretroviral drugs and noted that this drug would provide reasonable value for money if the price was reduced. Etravirine (Intelence) should be used in combination with an optimized background regimen, for the treatment of HIV-1 infection in treatment-experienced adult patients who have failed prior anti-retroviral therapies and have HIV-1 strains resistant to multiple antiretroviral agents, including protease inhibitors (PIs) and other non-nucleoside reverse transcriptase inhibitors (NNRTIs).

Funding Status:

Etravirine (Intelence) is listed on the Ontario Drug Benefit Formulary with the following therapeutic note:

For use in combination with an optimized background regimen, for the treatment of HIV-1 infection in treatment-experienced adult patients who have failed prior anti-retroviral therapies and have HIV-1 strains resistant to multiple antiretroviral agents, including protease inhibitors (PIs) and other non-nucleoside reverse transcriptase inhibitors (NNRTIs).

The prescriber must be approved for the Facilitated Access mechanism.

CEDAC Recommendation:

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

The Canadian Expert Drug Advisory Committee (CEDAC) recommended that etravirine (Intelence), 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.



Ministry of
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