Emtricitabine/Tenofovir disoproxil fumarate

Product:
EMTRICITABINE/TENOFOVIR DISOPROXIL FUMARATE (Truvada®) 200mg/300mg tablet

Class of drugs:
Antiretroviral agent

Indication:
Treatment of HIV infection

Manufacturer:
Gilead Sciences Canada Inc.

CED Recommendation

The CED recommended that emtricitabine/tenofovir (Truvada) 200mg/300mg tablet not be listed on the Ontario Drug Benefit (ODB) Formulary, on the basis that there is inadequate evidence of clinical superiority to justify its price premium over alternative therapies.

Executive Officer Decision

Based on the CED's recommendation and a subsequent listing agreement that addresses both price and utilization, the Executive Officer decided to list emtricitabine/tenofovir (Truvada) on the ODB Formulary via the Facilitated Access mechanism.

Status

Funding available through the Ontario Public Drug Programs.

Highlights of Recommendation:

- Emtricitabine/tenofovir (Truvada) is a combination antiretroviral drug used for the treatment of Human Immunodeficiency Virus (HIV).
- The Committee reviewed information from one study that compared emtricitabine/tenofovir (Truvada) against zidovudine/lamivudine, an alternative combination antiretroviral medication.
- The study reported that patients who were on the regimen containing emtricitabine/tenofovir (Truvada) experienced greater improvements in virologic response. However, the Committee noted that this reported advantage might have been influenced by the way the study was designed.
- With respect to side effects, the study reported that fewer patients in the emtricitabine/tenofovir (Truvada) group discontinued treatment, primarily because emtricitabine/tenofovir (Truvada) was associated with a lower incidence of anemia. However, the overall adverse event rates between the different regimens were similar.
- Emtricitabine/tenofovir (Truvada) costs $25.05 per day. This is more costly than other combination anti-retroviral products. Combination lamivudine/zidovudine (Combivir) costs approximately $20.00 per day.
- **Overall, the Committee acknowledged the clinical efficacy of emtricitabine/tenofovir (Truvada) but noted that convincing evidence of clinical superiority is lacking to justify its price premium over alternative therapies**.

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 avoid the clinical consequences of HIV infection by restoring immune function, improving quality of life and reducing HIV-related complications and death. Antiretroviral therapy reduces the amount of HIV in a patient's blood (called the viral load), leading in most cases to an increase in T-helper cells. Reducing the amount of HIV in the blood and increasing the T-helper cell count help to decrease the risk of infections and cancer in patients living with HIV.

The combination of emtricitabine and tenofovir (Truvada) blocks an enzyme that the HIV virus requires to reproduce.

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Detailed Discussion:

- The Committee considered the funding of emtricitabine/tenofovir (Truvada) on two occasions, initially in October 2006 and again in March 2007.
- The Committee considered data from one open-label, randomized-controlled trial in treatment-naïve patients with HIV (*Gallant JE et al, NEJM 2006*). This study evaluated the combination of tenofovir, emtricitabine, and efavirenz against the combination of zidovudine, lamivudine, and efavirenz.
- The study reported statistically significant improvement in virologic response for the tenofovir (TDF) + emtricitabine (FTC) + efavirenz (EFV) arm, versus the zidovudine (AZT)/lamivudine (3TC) + EFV arm. Limitations of the trial included its open-label design and the fact that more patients in the AZT/3TC + EFV arm discontinued therapy and were classified as treatment failures. Because of these limitations, it is difficult to conclude that emtricitabine/tenofovir (Truvada) is virologically superior to zidovudine/lamivudine.
- There were no statistically significant differences between the two treatment arms in the occurrence of virologic failure (inability of the treatment to reduce viral load) or viral resistance (loss of sensitivity to treatment).
- Mortality was similar between the two treatment arms at 48 weeks.
- There were no statistically significant differences in overall adverse event rates between the treatment groups. There were fewer withdrawals due to adverse events in the TDF + FTC arm, primarily due to a lower incidence of anemia.
- The major safety concern with TDF + FTC therapy is nephrotoxicity. Renal failure and elevated creatinine have been reported with the use of TDF in clinical practice.
- There are no randomized controlled trials (RCTs) comparing emtricitabine/tenofovir (Truvada) to other antiretroviral therapies in treatment-experienced patients with stable or unstable virologic control.
- The Committee noted the potential for off-label use in treatment-experienced patients or in patients with Hepatitis B.
- Emtricitabine/tenofovir (Truvada) costs $25.05 per day. This is more costly than other combination products. The manufacturer's pharmacoeconomic analysis was biased in favour of emtricitabine/tenofovir (Truvada), as it assumed therapeutic superiority of this product. Value for money was not demonstrated when the assumptions were adjusted for bias.
- Overall, the Committee acknowledged the clinical efficacy of emtricitabine/tenofovir (Truvada) but indicated that the price premium was not justified.

CEDAC Recommendation:

(http://www.cadth.ca/index.php/en/cdr/recommendations)

The Canadian Expert Advisory Committee (CEDAC) recommended that emtricitabine/tenofovir (Truvada) be listed as an alternative for the initial phase of treatment of adult patients with HIV infection who have experienced intolerance or adverse events with other nucleoside combinations including lamivudine in combination with zidovudine, abacavir, stavudine or didanosine and, who have not developed virologic failure or clinical progression on initial antiretroviral therapy.

Ontario

Ministry of
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