PUBLIC SUMMARY DOCUMENT
Product: Tenofovir disoproxil fumarate with emtricitabine, tablet, 300 mg -200 mg, Truvada®
Sponsor: Gilead Sciences Australia Pty Ltd
Date of PBAC Consideration: November 2005

1. Purpose of Application
The application sought listing on the PBS as a Section 100 item (Highly Specialised Drug) for the treatment of Human Immunodeficiency Virus (HIV) infection.

2. Background
This was the first application seeking listing of this combination product on the PBS.

3. Registration Status
Truvada is TGA-registered for the treatment of HIV infected adults over the age of 18 years, in combination with other antiretroviral agents. This indication is based on analyses of plasma HIV-1 RNA levels and CD4 cell counts in controlled studies of VIREAD® and EMTRIVA® in treatment-naive and treatment experienced adults.

4. Listing Requested and PBAC's View
Section 100
Private hospital authority required
Treatment of HIV infection in patients with:
(a) CD4 cell counts of less than 500 per cubic millimetre; or
(b) viral load of greater than 10,000 copies per mL.

The PBAC noted that the requested listing was identical to the listings for the individual components.

5. Clinical Place for the Proposed Therapy
Combination therapy, comprising of at least three antiretroviral (ARV) agents, is standard care in the management of HIV infection. As part of this therapy, dual Nucleotide Reverse Transcriptase Inhibitor (NRTI) use is widely recommended. The combination product would replace use of the two drugs administered as separate products, reducing the pill burden and assisting in maintaining adherence to a treatment regime.

6. Comparator
The submission nominated concomitant tenofovir disoproxil fumarate and emtricitabine as the comparator. This was considered appropriate by the PBAC.

7. Clinical Trials
The basis of the submission was 1) one randomised open-label cross-over trial evaluating the pharmacokinetic interactions between tenofovir disoproxil fumarate and emtricitabine at steady state, and 2) one randomised, cross-over trial evaluating the bioequivalence of tenofovir disoproxil fumarate with emtricitabine fixed dose combination versus concomitant tenofovir & emtricitabine. Both of these trials were in healthy volunteers. A supporting randomised trial was also included comparing tenofovir disoproxil fumarate with emtricitabine and efavirenz with Combivir® (lamivudine with zidovudine) and efavirenz in treatment naïve HIV-1 infected patients.

8. Results of Trials

The PBAC noted the pharmacokinetic parameters were comparable when either tenofovir disoproxil fumarate or emtricitabine were given alone or in combination. The pharmacokinetic parameters of tenofovir disoproxil fumarate and emtricitabine were also similar whether given in a fixed dose combination or concomitantly.

In the supporting trial, concomitant tenofovir disoproxil fumarate and emtricitabine (and efavirenz) resulted in 81% of patients in the Intention to Treat (ITT) population being classified as responders at 48 weeks of treatment. Virological failure occurred in only 7/255 (2.7%) of tenofovir disoproxil fumarate with emtricitabine (and efavirenz) treated patients.

The PBAC noted that similar levels of adverse events occurred in normal subjects dosed with the fixed dose combination tablet compared to concomitant tenofovir disoproxil fumarate and emtricitabine. In antiretroviral treatment naïve HIV-1 infected patients at 48 weeks of tenofovir disoproxil fumarate with emtricitabine (and efavirenz) treatment the most common adverse events were dizziness, nausea, diarrhoea, abnormal dreams, fatigue, headache and insomnia. A total of 37/257 (14%) of patients reported treatment-emergent adverse events.

9. Clinical Claim

The submission described tenofovir disoproxil fumarate with emtricitabine fixed dose combination tablet as having similar effectiveness and toxicity compared to concomitant tenofovir disoproxil fumarate and emtricitabine. The claim was accepted by the PBAC.

10. Economic Analysis

The submission presented a preliminary economic evaluation. The choice of the cost-minimisation approach was considered valid. The resources included were drug costs. The overall comparative costs for each alternative (the fixed dose combination of tenofovir disoproxil fumarate with emtricitabine and concomitant tenofovir disoproxil fumarate and emtricitabine) were the same. In the context of cost-minimisation the equi-effective doses were tenofovir disoproxil fumarate 300mg with emtricitabine 200mg fixed dose combination tablet and concomitant tenofovir disoproxil fumarate 300mg and emtricitabine 200mg.

11. Estimated PBS Usage and Financial Implications

The submission calculated that there would be no cost to the PBS since tenofovir disoproxil fumarate with emtricitabine fixed dose combination tablet would only substitute for concomitant tenofovir disoproxil fumarate and emtricitabine. However, the PBAC noted the possibility that the fixed dose combination may replace other NRTI combinations of a lower cost, and it was thus likely there would some additional cost to the PBS.

12. Recommendation and Reasons

Consistent with its policy on fixed dose combination products, the PBAC recommended listing on a cost-minimisation compared to the corresponding strengths of the individual components, as the data presented indicate that Truvada, as requested, has similar safety and efficacy compared to concomitant tenofovir 300mg and emtricitabine 200mg daily.

Recommendation

List

TENOFOVIR DISOPROXIL FUMARATE with EMTRICITABINE, tablet,

300 mg-200 mg

Restriction:	Section 100 (Highly Specialised Drug) Private hospital authority required Treatment of HIV infection in patients with: (a) CD4 cell counts of less than 500 per cubic millimetre; or (b) viral load of greater than 10,000 copies per mL.
Pack Size:	30

13. Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

14. Sponsor's Comment