# Supplement to Application for Inclusion of Tenofovir Disoproxil Fumarate (DF), Emtricitabine, and Emtricitabine/Tenofovir DF Fixed-Dosed Combination on WHO Model List of Essential Medicines

## Submitted By


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With this supplement to our application for the 15th edition of the WHO Essential Medicines List submitted on 12th September 2006 (tenofovir DF, and emtricitabine and tenofovir DF fixed-dose combination tablet) and 24th October 2006 (emtricitabine), Gilead Sciences would like to address specific issues that were raised related to the original application for these drugs, which were submitted for the 14th edition (March 2005) of the WHO Essential Medicines List.

**Tenofovir DF**

- Accessibility of clinical data found within the application
  - All the clinical data found in the current application (12th September 2006) are in the public domain. References have been provided.
- Independent renal safety analyses
  - As part of this supplement, we are providing three independent renal analyses.
    - Johns Hopkins HIV Clinical Cohort Database[1,2]
    - Chelsea and Westminster Hospital[3,4]
    - DART: Development of AntiRetroviral Therapy in Africa[5]
- Clinical data from resource-limited settings
  - As part of this supplement, we are providing data from three clinical trials that support the use of TDF in resource-limited settings.
    - ANRS 1207/IMEA 025: Evaluation of TDF/FTC/EFV once daily first line regimen in West Africa[6]
    - DART: Development of AntiRetroviral Therapy in Africa[7,8]
    - Family Health International: Findings from a double-blind, randomized, placebo-controlled trial of TDF for the prevention of HIV infection in women[9]
- Co-administration of TDF with ddI
  - References related to the mitochondrial safety profile when TDF and ddI are co-administered are included with this supplement.[10-28]
- Use of TDF in paediatric patients
  - In this supplement, we include 11 additional references to further characterize the use of TDF in this patient population[29-38]
- Effects of TDF on bone mineral density
  - Published and presented data related to the effects of TDF on bone mineral density are included in this supplement to better characterize this issue.[10,39-45]

**Emtricitabine**

- Hyperpigmentation resulting in failure of compliance
  - This topic is discussed thoroughly in the separate emtricitabine application

**Emtricitabine/Tenofovir DF Fixed Dose Combination Tablet**

- Bioequivalence data to support the fixed dose combination are the same as the two components given separately:
    - Publicly presented data related to the potential for drug-drug interactions between emtricitabine and tenofovir DF, as well as the pharmacokinetics, bioequivalence, and safety of the fixed dose combination of emtricitabine and tenofovir DF are included in the Emtricitabine and Tenofovir DF Fixed Dose Combination Tablet application.[46,47]
- Additional clinical data specific to the individual components of the emtricitabine and tenofovir DF fixed dose combination tablet are addressed separately in the applications for emtricitabine and tenofovir DF, as well as in this supplement.

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