



Indian Health Service
National Pharmacy and Therapeutics Committee
Formulary Brief: HIV Pre-Exposure Prophylaxis (PrEP)
-August 2018-



Background:

The Indian Health Service National Pharmacy and Therapeutics Committee (NPTC) reviewed pre-exposure prophylaxis (PrEP) against HIV infection during the August 2018 meeting. Previously, tenofovir/emtricitabine (Truvada[®]) was added to the National Core Formulary for HIV post-exposure prophylaxis (PEP) only. The NPTC **added PrEP (in addition to PEP) as an indication for tenofovir/emtricitabine on the National Core Formulary.**

Human Immunodeficiency Virus (HIV) infection is a prevalent condition with nearly 40,000 new diagnoses in the United States each year¹. Mostly commonly, HIV is transmitted among males who have sex with males or others, but is also transmitted in heterosexual couples and injection drug users. A 38% increase in HIV diagnoses in American Indians/Alaska Natives (AI/AN) was observed from 2011 to 2015 while HIV diagnoses in the U.S. population, as a whole, decreased by 5%¹. Additionally, AI/AN have the 4th highest rate of HIV diagnoses of all ethnicities/races and the 2nd highest rate of sexually transmitted infections for chlamydia and gonorrhea¹. There continue to be challenges disproportionately affecting AI/AN including stigma, cultural diversity, socioeconomic issues, increased alcohol and illicit drug use and data limitations¹.

Tenofovir disoproxil fumarate 300mg combined with emtricitabine 200mg (Truvada[®]) is a nucleoside and nucleotide reverse transcriptase inhibitor combination². It is currently the only FDA approved medication for pre-exposure prophylaxis to HIV-1 infection, in combination with safer sex practices. It is dosed once daily in patients ≥ 35 kg who have normal renal function and a HIV-negative status². HIV status must be evaluated before prescribing tenofovir/emtricitabine (TDF/FTC) as there is an associated risk of resistance if the person is HIV positive¹⁻³. In addition, there is a risk of severe, acute exacerbation of Hepatitis B virus (HBV) in HBV-infected patients who discontinue TDF/FTC².

The U.S. Centers for Disease Control and Prevention and U.S. Public Health Service jointly published [updated guidelines in 2017](#) for prevention of HIV infection⁴. Of note, they recommend PrEP therapy be used in those who are HIV negative and at substantial risk for HIV. This includes men who have sex with men (MSM) and heterosexual women and men with a HIV-positive sexual partner, a recent bacterial STI (within past 6 months), high number of sex partners, history of inconsistent or no condom use, or those who engage in commercial sex work. The guidelines also recommend PrEP in those who inject drugs (within past 6 months), who have an HIV-positive injecting partner or share injecting equipment. Prior to starting PrEP, clinical eligibility must be determined which includes documented negative HIV test, no signs or symptoms of acute HIV infection, normal renal function, no contraindications to medications, and documented HBV infection and vaccination status. Follow-up should continue every 3-6 months.

Discussion:

Several clinical trials have evaluated the safety and efficacy of PrEP in prevention of HIV-1 infections in MSM. The Preexposure Prophylaxis Initiative (**IPrEX**) trial was a randomized, double-blind, placebo controlled trial in MSM and others⁵. The results demonstrated a 44% reduction (RR 0.56, 95% CI: 0.37 to 0.85) in HIV in those enrolled in the TDF/FTC arm. In those with detectable plasma levels of TDF/FTC, a 92% reduction in HIV incidence (RR 0.18, 95% CI: 0.4 to 0.99) was found. The On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection (**IPERGAY**) trial was a randomized, double-blind, placebo controlled trial in MSM with an "on-demand" TDF/FTC schedule⁶. On-demand participants were instructed to take two pills 2-24 hours before sex, followed by a third and fourth dose within 24 and 48 hours of the first 2 doses, respectively. On average, the participant group took 15 pills/month and had an 86% reduction in HIV incidence (95% CI: 40% to 98%; p=0.002). The Preexposure prophylaxis to prevent acquisition of HIV-1 infection (**PROUD**) study was an open label, randomized trial that evaluated the incidence of HIV infection in a real world setting with an immediate and deferred treatment group⁷. The

incidence of HIV was noted to be significantly lower in the immediate group (1.2 cases/100 person years, 90% CI: 0.4 to 2.9) compared to the deferred group (9 cases/100 person years, 90% CI: 6.1-12; p=0.0001).

There are two studies that have evaluated the effectiveness of PrEP in heterosexual couples, the FEM-PrEP and VOICE, of which neither found benefit for HIV prevention. The **FEM-PrEP** study (Preexposure prophylaxis for HIV infection among African women) had an adherence rate of 39% in the treatment arm and showed no significant reduction in HIV infections (HR: 0.94, 0.59 to 1.52)⁸. The **VOICE** study (Tenofovir-based preexposure prophylaxis for HIV infection among African Women) also failed to show significant reduction in HIV infections (oral TDF: HR 1.49 (0.97-2.29, p=0.07), TDF/FTC: HR 1.04 (0.73-1.49; p=0.81), tenofovir gel: HR 0.85 (0.61-1.21; p=0.37)⁹. Overall, for the oral treatment arm, the study drug was only detected in 30% of participants. Interestingly, the study with the best evidence for sero-discordant heterosexual partners was the **Partners PrEP Study** (Antiretroviral prophylaxis for HIV-1 prevention among heterosexual men and women)¹⁰. This randomized, double-blind, placebo controlled trial in heterosexual couples found the incidence of HIV infection was reduced with both TDF alone and with the TDF/FTC combination. Overall, HIV incidence was reduced by 67% in the TDF arm (95% CI: 44% to 81%, p<0.001) and 75% in the TDF/FTC arm (95% CI: 58% to 87%, p<0.001).

A 2012 Cochrane Review analyzed six randomized controlled trials, which included almost 10,000 patients who were HIV-negative MSM, sero-discordant couples and high-risk men and women¹¹. The results showed the combination of TDF/FTC provided a 51% reduction in HIV infection (RR 0.49, 95% CI: 0.28 to 0.85; n=8918 participants) while TDF alone offered a 67% reduction (RR 0.33, 95% CI: 0.20 to 0.55, n=4027 participants). Adverse drug reactions were not statistically significant (RR 1.0; 95% CI: 0.83 to 1.19, n=6862 participants) between groups.

Findings:

TDF/FTC has been shown to be extremely effective (up to 92%) in preventing HIV infections in MSM, heterosexual couples and injection drug users when medication adherence is high. Treatment with TDF/FTC demonstrated a high safety profile with low overall incidence of adverse drug reactions. It should be used with safe sex practices, including condom use. Education about medication adherence and safe sex practices along with routine medical follow-up is critical in the prevention of HIV infection.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the [NPTC website](#).

References:

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