

PRE-EXPOSURE PROPHYLAXIS (PREP) CLINICAL REFERENCE SHEET

GENERAL

- Pre-exposure prophylaxis (PrEP) is a medication taken daily which prevents HIV infection.
- PrEP is taken before (pre-) an exposure which is different than post-exposure prophylaxis (PEP), which is a medication regimen taken after exposure (e.g., after a needle stick).
- The medication used for PrEP for ≥ 18 years of age is a single pill comprised of 150 mg of tenofovir disoproxil fumarate (TDF) and 100 mg of emtricitabine (FTC).
- The medication was approved for ≥ 18 years of age by the United States Food and Drug Administration (FDA) in 2012 [for PrEP](#).
- The brand name is Truvada (TDF-FTC).
- The medication has been approved for the [treatment](#) of HIV in adults since 2004. Low strength TDF-FTC for pediatric use was approved by the FDA in 2016 for HIV treatment only for patients weighing 17 kg to less than 35 kg who can swallow a pill. Please see full prescribing information below for pediatric dosing.

INDICATIONS FOR PREP

Gay, Bisexual, and other Men Who Have Sex with Men (MSM), and Transgender Women: Any anal sex without condoms or sexually transmitted diseases (STDs) in the last six months, or in an ongoing relationship with an HIV+ partner, multiple sex partners.

Heterosexuals: Bisexual men, ongoing HIV+ partner, or condomless sex with 1+ partner(s) of unknown HIV status who are at increased risk of HIV such as an injection drug user or bisexual male partner, recent bacterial STD.

Injection Drug Users (IDU): HIV+ injection partner, sharing needles or risk of sexual acquisition as above.

INITIAL EFFICACY STUDIES

iPrEx: In patients that had high levels of adherence, TDF-FTC reduced the risk of HIV in gay, bisexual, and other MSM by 92%.¹ *Brazil, Ecuador, Peru, S. Africa, Thailand, USA*

Partners PrEP Trial: In patients that had high levels of adherence, TDF-FTC reduced the risk of HIV in heterosexual patients by 90%, with efficacy being lower in women than men.² *Kenya, Uganda*

TDF2 Trial: TDF-FTC reduced the risk of HIV in heterosexual patients by 62%, but this may have included people who didn't always take the medication. Efficacy was lower in women.³ *Botswana*

Bangkok Tenofovir Study: In patients that had high levels of adherence, TDF-FTC reduced the risk of HIV in IDUs by 49%.⁴ *Thailand*

- 1 Robert M. Grant, et al., "Preexposure Chemoprophylaxis for HIV Prevention in Men who Have Sex with Men," *New England Journal of Medicine* 363, no. 27 (2010): 2587-99. DOI: 10.1056/NEJMoa1011205.
- 2 Jared M. Baeten, et al., "Antiretroviral Prophylaxis for HIV Prevention in Heterosexual Men and Women," *New England Journal of Medicine* 367, (2012): 399-410, DOI: 10.1056/NEJMoa108524.
- 3 Michael C. Thigpen, et al., "Antiretroviral Preexposure Prophylaxis for Heterosexual HIV Transmission in Botswana," *New England Journal of Medicine* 367, no. 5 (2012): 423-34, DOI: 10.1056/NEJMoa1110711.
- 4 Kachit Choopanya, et al., "Antiretroviral Prophylaxis for HIV Infection in Injecting Drug Users in Bangkok, Thailand (the Bangkok Tenofovir Study): A Randomized, Double-blind, Placebo-controlled Phase 3 Trial," *Lancet* 381, no. 9883 (2013): 2083-90, DOI: 10.1016/S0140-6736(13)61127-7.

INITIATION OF PREP

- Negative HIV antibody test (within the last week; no oral rapid testing)
- Screen for acute HIV infection (recent “flu-like” symptoms. If concern, check an HIV viral load)
- Normal renal function, CrCl \geq 60 ml/min (check creatinine)
- Negative for chronic hepatitis B infection (hepatitis B surface antigen negative)
- Screen for other STDs as needed (syphilis, gonorrhea, chlamydia)
- Negative pregnancy test (for women)
- Prescription for a three (3) month supply

TIME TO ACHIEVING PROTECTION

For MSM: Maximum concentration in rectal tissue at seven days

For Women: Maximum concentration in cervicovaginal tissue at 20 days

For Transgender Women: Maximum concentration in rectal tissue at seven days

For IDUs: Maximum concentration in the blood at 20 days

POTENTIAL SIDE-EFFECTS

- **No** severe or life-threatening side-effects in the major trials [iPrEx].
- Mild gastrointestinal upset (e.g., nausea, flatulence) in 9% of individuals [iPrEx] which generally resolve in the first month.
- Other potential side-effects include fatigue, headache, and dizziness.
- TDF-FTC may cause a small decrease in bone mineral density (1%) but the clinical significance of this is unknown (i.e., does not appear to lead to fractures). In general, DEXA scans are not recommended.
- TDF-FTC is associated with renal dysfunction in <1 to 4.3% of individuals in North America.¹ Creatinine should be monitored periodically. Stopping TDF-FTC in these individuals generally leads to normalization of renal function.

¹ Nishijima Takeshi et. al., “Impact of Small Body Weight on Tenofovir-Associated Renal Dysfunction in HIV-Infected Patients: A Retrospective Cohort Study of Japanese Patients,” *PLoS ONE* 6, no. 7: e22661, DOI: 10.1371/journal.pone.0022661

POTENTIAL DRUG INTERACTIONS

Caution should be taken when using other drugs that may reduce renal function (e.g., acyclovir, adefovir dipivoxil, cidofovir, ganciclovir, valganciclovir, aminoglycosides and high doses of multiple NSAIDs) since TDF-FTC is actively eliminated by the kidney. Drugs that decrease renal function may also increase concentrations of TDF-FTC.

DRUG RESISTANCE

- No drug resistance generally found in patients who acquire HIV while on PrEP [iPrEx].
- Resistance identified in some patients who have HIV at baseline before PrEP is started [iPrEx].

PERSONS WITH A NEW HIV DIAGNOSIS

- Confirm the diagnosis with subsequent testing (may be performed through local health department).
- Check CD4 lymphocyte count.
- Check HIV viral load.
- Check HIV genotype (for drug resistance).
- Linkage to care with an HIV provider.
- If the patient is on PrEP and diagnosed with HIV, urgent consultation with an infectious disease specialist is suggested. TDF-FTC may be continued, but a third drug should be added. A three-drug regimen is the standard treatment regimen for people living with HIV.

TREATING SPECIAL POPULATIONS

PrEP During Conception, Pregnancy and Breast-feeding

See [PrEP Information Sheet: PrEP During Conception, Pregnancy, and Breastfeeding](#) (Centers for Disease Control and Prevention)

Adolescent Minors

- The CDC recommends routine HIV testing for those 13-65 years old. HIV screening is part of primary care and should be offered to all sexually active minors; those who are MSM or have a history of IDU should be screened more frequently as indicated.
- Discuss parent/guardian involvement in adolescent health care. Unless contraindicated for an adolescent's safety, parental/guardian involvement is advised.
- Be aware of consent, confidentiality, reporting, and parental disclosure laws and that these laws may also vary by local jurisdiction.
- None of the completed PrEP trials have included individuals below age 18. Consider:
 - the lack of data on safety and effectiveness of TDF-FTC taken by persons under 18 years of age, possibility of bone or other toxicities among youth who are still growing, safety data available when TDF-FTC is used in treatment regimens for youth living with HIV.
 - Weigh these factors against the potential benefit of providing TDF-FTC for an individual adolescent at substantial risk of HIV acquisition.

Transgender Women¹

- Transgender women are at increased risk of HIV infection due to multiple factors dominated by stigma and discrimination, including sex practices (vaginal sex and/or receptive anal sex), and substance use.
- Some limited studies demonstrated efficacy of TDF-FTC in trans women who were adherent to TDF-FTC.
- More research is needed to understand the interaction between feminizing hormones and TDF-FTC and impact on the buildup of TDF-FTC to protective levels in rectal tissue.
- Counsel clients on balancing possible TDF-FTC efficacy with risk of HIV acquisition.

Patients with Chronic Active Hepatitis B Infection

- Refer to a clinician experienced in managing TDF-FTC.

Patients with Chronic Renal Failure

- Refer to a clinician experienced in managing TDF-FTC.

1 Samantha Marquez, Sean Cahill, "Transgender Women and Pre-exposure Prophylaxis: What We Know and What We Still Need to Know," *National Center for Innovation in HIV Care*, November 2015.

MEDICATION ADHERENCE COUNSELING

Establish trust and bidirectional communication

Provide simple explanations and education

- Medication dosage and schedule
- Management of common side-effects
- Relationship of adherence to the efficacy of TDF-FTC
- Signs and symptoms of acute HIV infection and recommended actions

Support adherence

- Tailor taking the medication to the patient's daily routine.
- Identify reminders and devices to minimize forgetting doses
- Identify and address barriers to adherence

Monitor medication adherence in a non-judgmental manner

- Normalize occasional missed doses, while ensuring patient understands importance of daily dosing for optimal protection
- Reinforce success
- Identify factors interfering with adherence and plan with patient to address them
- Assess side-effects and plan how to manage them

BEHAVIORAL RISK-REDUCTION COUNSELING

Establish trust and two-way communication

Provide feedback on HIV risk factors identified during sexual and substance use history taking

- Elicit barriers to, and facilitators of, consistent condom use
- Elicit barriers to, and facilitators of, reducing substance abuse

Support risk-reduction efforts

- Assist patient to identify one or two feasible, acceptable, incremental steps towards risk reduction
- Identify and address anticipated barrier to accomplishing planned actions to reduce risk

Monitor behavioral adherence in a non-judgmental manner

- Acknowledge the effort required for behavior change
- Reinforce success
- If not fully successful, assess factors interfering with completion of planned actions and assist patient to identify next steps

Adapted from [Pre-exposure Prophylaxis for the Prevention of HIV Infection in the United States—2014 Clinical Practice Guideline](#) (Centers for Disease Control and Prevention)

MORE INFORMATION

- [Full prescribing information](#)
- [United States Public Health Service Pre-exposure Prophylaxis for the Prevention of HIV Infection in the United States 2014: A Clinical Practice Guideline](#)
- [United States Public Health Service, Pre-exposure Prophylaxis for the Prevention of HIV Infection in the United States 2014: Clinical Providers' Supplement](#)
- [Taking a Sexual History](#)
- To speak with a clinician experienced in managing PrEP, contact the University of California San Francisco [Clinician Consultation Center](#), (855) 448-7737 or (855) HIV-PrEP