PrEP Provider FAQs

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1. What is PrEP?

PrEP stands for **pre**-exposure prophylaxis. It is the use of antiretroviral medication to prevent acquisition of HIV infection. PrEP is used by HIV uninfected people who are at risk of being exposed to HIV through sexual contact or injection drug use. At present, the only medication with an FDA-approved indication for PrEP is oral tenofovir disoproxil fumarate-emtricitabine (TDF-FTC), which is available as a fixed combination tablet called Truvada. This medication is also commonly used in the treatment of HIV.

PrEP should be considered part of a comprehensive prevention plan that includes adherence, risk reduction counseling, HIV prevention education and provision of condoms.

Recently, a fixed-dose combination similar to Truvada, Descovy, was approved for HIV treatment; this pill includes a novel, tenofovir pro-drug (tenofovir alafenamide) in addition to emtricitabine. However, data are not yet available to support the use of Descovy as PrEP.

2. What are the guidelines for prescribing PrEP?

Two sets of guidelines for prescribing PrEP exist:

- Los Angeles County Public Health Guidelines [1] - which focuses on the identification of individuals at highest risk for HIV who would be ideal candidates for PrEP
- Centers for Disease Control (CDC) Guidelines [2], including a Clinical Providers' Supplement [3]

Find both sets of guidelines at GetPrEPLA.com

The Clinical Providers' Supplement contains additional tools for clinicians providing PrEP, such as a patient/provider checklist, patient information sheets, provider information sheets, a risk incidence assessment, supplemental counseling information, billing codes and practice quality measures.

If PrEP questions arise, clinicians should consult the University of California, San Francisco Clinician Consultation Center Line. This line can also assist with questions pertaining to post-exposure prophylaxis (PEP).

University of California San Francisco (CCC) Line
1-855- HIV- PREP (Monday to Friday, 11 a.m. to 6 p.m. PST) for PrEP calls

3. To whom should I offer PrEP?

Per CDC Guidelines, PrEP may be appropriate for the following populations:

Men Who Have Sex with Men	Heterosexual Woman and Men	Injection Drug Users
• HIV-positive sexual partner • Recent bacterial STI • High number of sex partners • History of inconsistent or no condom use • Commercial sex work	• HIV-positive sexual partner • Recent bacterial STI • High number of sex partners • History of inconsistent or no condom use • Commercial sex work • Person living in high-prevalence area or network	• HIV-positive injecting partner • Sharing injection equipment • Recent drug treatment (but currently injecting)

Per LAC Guidelines, clinicians should also discuss PrEP with the following non-HIV- infected individuals (other than those mentioned above):

- Male-to-female and female-to male transgender individuals engaging in condomless anal intercourse with men
- Individuals who report the use of mood-altering substances during sex (e.g. alcohol, methamphetamine, cocaine, ecstasy, poppers etc.)
- MSM or transgender people engaging in condomless anal receptive sexual intercourse
- Transgender people engaging in transactional sex, providing sex in exchange for money or drugs
- Diagnosis of urethral gonorrhea or rectal chlamydial infection within the prior 12 months
- Persons seeking a prescription for PrEP (as they may be a high risk of HIV acquisition but uncomfortable providing a full sexual history to the provider)
- Individuals who have been prescribed PEP for non-occupational exposures and demonstrate continued high-risk behavior, or have used multiple courses of PEP, among men who have sex with men (MSM).

4. Who can prescribe PrEP?

Any licensed prescriber can prescribe TDF-FTC as PrEP. Specialization in Infectious Disease or HIV Medicine is NOT required. In fact, primary care providers who see members of populations at high risk of HIV on a routine basis should consider offering PrEP to all eligible patients.

5. How is TDF-FTC for PrEP prescribed?

TDF-FTC for oral PrEP is taken once daily by mouth. No other dosing strategy is currently recommended.

1st prescription:	30 days of medication (1 month without refill)
2nd prescription:	60 days of medication (1 month with 1 refill)*
Subsequent prescriptions:	90 days of medication (1 month with 2 refills; each prescription must be preceded by a negative HIV test)

*HIV testing only indicated if concern for acute HIV infection exists.

PrEP should be discontinued immediately if: (1) the patient becomes HIV-infected, or (2) the patient experiences toxicities or symptoms that cannot be managed.

Condoms and supportive counseling, both for adherence and risk reduction, are required.

6. What is the evidence base for PrEP?

Clinical trials of oral daily PrEP show these results:

Study	Population	N	Results
iPrEX [6] *Brazil, Ecuador, Peru, S. Africa, Thailand, U.S.A*	MSM	2,499	44% efficacy TDF-FTC
Partners PrEP Study [7] *Kenya, Uganda*	Heterosexual Couples	4,758	67% efficacy TDF 75% efficacy TDF-FTC
TDF2 Study [8] *Botswana*	Young men and women	1,200	62% efficacy TDF-FTC
Bangkok Tenofovir Study (BTS) [9] *Thailand*	Injection Drug Users	2,400	49% efficacy TDF

*Overall risk reduction; intention to treat analysis.

Studies among women only are discussed in question 11.

7. How important is adherence to PrEP?

Adherence is critical. In all PrEP clinical trials to date, PrEP efficacy appeared to depend on adherence [12, 13]. According to a dedicated analysis of adherence of those trials, PrEP was non-efficacious when adherence was low, but when moderate or high adherence was achieved, efficacy was modest or relatively high, respectively [13]. Among the study subjects with detectable plasma tenofovir levels in iPrEx, Partners PrEP, TDF2 and BTS, efficacy ranged from 74 to 92% [6, 7, 8, 9].

Adherence to PrEP was also found to be highly associated with reduction of HIV risk in an open-label study (iPrEX OLE) [14]. Among participants with drug detected by dried blood spot, HIV incidence ranged from 4.7 infections per 100 person-years (no drug detected) to 0.6 per 100 person-years (two to three tablets per week). There were no HIV infections in participants using four or more tablets per week.

Another study suggested that an "on demand" regimen (i.e., use of PrEP just before and after sex) might also reduce HIV acquisition among MSM (IPERGAY [15]), although the frequency of sexual acts among men in that study was high enough that they closely approximated four tablets weekly (which, as mentioned above, provides very high levels of protection). The effectiveness of "on demand" PrEP among those using PrEP less frequently is unknown. At this time, the only recommended PrEP dosing strategy is daily [16].

8. How quickly does PrEP provide protection?

Data from pharmacokinetic studies suggest that individuals need to take PrEP for:

- At least 7 days to achieve protective levels in rectal tissue and plasma [3,17]
- At least 20 days to achieve protective levels in cervicovaginal tissue

9. Is PrEP safe?

TDF-FTC as PrEP is considered safe and well-tolerated. Although TDF-FTC has caused renal toxicity and decreased bone mineral density when used for HIV treatment and administered for months and years, in PrEP studies to date, TDF-FTC has not caused serious safety concerns [5, 18, 19].

PrEP is considered safe for women of child-bearing age. Available data suggest that TDF-FTC does not increase risk of birth defects, although there are not enough data to exclude the possibility of harm. TDF-FTC is considered in Pregnancy Class B. PrEP is often used in pregnancy if the risk of ongoing HIV transmission is sufficiently high (such as in a sero-different partnership) and because pregnancy itself is associated with an increased risk of HIV acquisition. Per CDC guidelines, if pregnancy is intended in a sero-different relationship, PrEP can also be used periconceptionally by the uninfected partner to reduce the risk of sexual HIV acquisition. Expert consultation is recommended for these couples.

Since TDF-FTC is actively eliminated by the kidneys, it should be co-administered with care in patients taking medications that are eliminated by active tubular secretion (e.g., acyclovir, adefovir dipivoxil, cidofovir, ganciclovir, valacyclovir, valganciclovir, aminoglycosides and high-dose or multiple NSAIDs). Drugs that decrease renal function may also increase concentrations of TDF-FTC.

10. Who is not eligible for PrEP?

- **HIV-positive people**. Individuals must be confirmed as HIV-negative before initiating PrEP. Excluding those with acute HIV infection is critically important, as there is a risk of developing resistant HIV if they are inadvertently started on TDF-FTC as PrEP. (TDF-FTC is an appropriate component of a regimen to treat HIV, but must be combined with an additional agent from an other class of antiretroviral to provide effective treatment.)
- **People with renal insufficiency.** Providers should confirm that the patient's calculated creatinine clearance is > 60 mL/minute (Cockcroft-Gault formula) before initiating PrEP.

Additionally, those who indicate that they are not ready to adhere to daily oral TDF-FTC should not be prescribed PrEP (since efficacy is extremely limited when patients do not adhere, as described above).

11. Does PrEP work in women?

Current clinical guidelines include women as appropriate candidates for PrEP. As with all PrEP patients, adherence is critical. Two trials of PrEP in women were stopped early for futility by their respective data safety and monitoring boards [20, 21].

A determination of futility is made when it appears that no evidence of efficacy would be found in the future based on the results collected up to that point. Low adherence among the participants was thought to be a substantial factor in the futility finding. Other studies that included both men and women (TDF-2, Partners PrEP) in which higher levels of adherence were achieved did show efficacy among women. Recent data suggest that women may need higher levels of adherence than men, in order to achieve protective levels of drug in the female genital tract.

12. Can adolescents take PrEP?

Based on the experience of using TDF-FTC for HIV treatment and PEP among adolescents, the CDC and the International Antiviral Society-USA now recommend the use of TDF-FTC as PrEP for adolescents at high sexual or other behavioral risk for HIV infection. However, studies are still underway, and pilot data suggest that these young people may have special issues maintaining sufficiently high adherence for HIV prevention [23, 24].

As with every patient, but especially with younger adolescents:

- Carefully weigh the potential benefits and risks, including acquiring HIV infection.
- Refer to the institution's policy or consult with the institution's legal department about consent to care for adolescents under 18 years of age according to California State law.
- Make clear that the efficacy of PrEP is highly dependent on strict adherence.

13. What baseline assessment is required for individuals beginning PrEP?

The most important aspect of the baseline assessment is ascertaining that the patient is not already HIV-infected. HIV testing should be conducted immediately prior to starting PrEP, ideally on the same day the prescription is provided.

LAC Guidelines recommend that baseline testing should be conducted with a lab-based fourth-generation (preferred) or viral load (for a list of FDA-approved third- and fourth-generation tests, go to **http://www.cdc.gov/hiv/testing/lab/guidelines**).