
Although advances in treatment have improved the quality and length of life for individuals infected with HIV, more than 50,000 new infections occur each year in the United States. Fortunately, clinicians now have an unprecedented and expanding number of effective HIV prevention tools at their fingertips, including behavioral and biomedical interventions that can play a critical role in reducing the incidence of new infections. This guide summarizes how clinicians can be most effective at preventing new HIV infections and provides information on one of the most promising new prevention tools: the use of daily antiretroviral medications by high-risk HIV-uninfected individuals as pre-exposure prophylaxis, or “PrEP.” PrEP has been shown to protect against HIV acquisition and has been approved by the FDA.

HIV testing: Still the critical first step in HIV prevention
In the United States, 21% of HIV-infected persons do not know they are infected. Therefore, the CDC recommends that all persons aged 13 to 64 be tested for HIV at least once, independent of risk, and on a regular basis if they are at high-risk for HIV acquisition (http://www.cdc.gov/MMWR/preview/mmwrhtml/rr5514a1.htm). HIV test results will determine whether HIV treatment or preventive services are indicated. Those patients who are HIV-infected should be immediately evaluated for HIV treatment, as early treatment can reduce their risk of HIV-related complications and greatly decreases their likelihood of transmitting HIV to their sexual partners.

Creating a patient-centered prevention plan
HIV-uninfected individuals should be offered a selection of prevention services, based on an individualized risk assessment. Those at increased risk for HIV acquisition include:

- People with sexual partner(s) known to be HIV-infected.
- Men who have sex with men; in particular, those who report inconsistent condom use, use recreational drugs or alcohol in conjunction with sex, or have been diagnosed with sexually transmitted infections.
Sex workers or anyone who exchanges sex for money, goods, or services.
Injection drug users.

Selection of the optimal prevention package will depend on each individual’s risk factors for HIV acquisition, their personal preferences, and the presence of medical co-morbidities. Key components of an individual’s prevention package may include:

- Safer-sex counseling, focusing on reduction in the number of sexual partners, avoidance of high-risk behaviors (e.g., unprotected receptive anal or vaginal sex), and correct and consistent condom and lubricant use.
- Provision of condoms and lubrication.
- Screening and treatment for other sexually transmitted infections, as these can facilitate HIV acquisition.
- Post-exposure prophylaxis, or “PEP,” consisting of antiretroviral medications taken for 28 days following a high-risk exposure to HIV.
- The PrEP Package: Antiretroviral medications coupled with the behavioral interventions listed above, for individuals at ongoing, high risk for HIV acquisition.
- Provision of clean syringes for injection drug users.

What is the PrEP Package? A Pill and a Process!
The term “PrEP Package” is preferred over the shorter term “PrEP” to emphasize that taking a pill alone has not been proven to be effective for HIV prevention without an integrated package of evidence-based behavioral interventions. The PrEP Package consists of the prescription of antiretroviral medications to high-risk persons in addition to ongoing safer-sex counseling, condom provision, treatment of other sexually transmitted infections, and monitoring for adherence and adverse effects. In essence, it involves taking a pill as part of a process aimed at optimizing the prevention effect. In the United States, once-daily tenofovir-emtricitabine (TDF-FTC) is the only medication that is FDA-approved for use as part of the PrEP Package.

How effective is TDF-FTC as part of the PrEP Package?
Daily oral TDF-FTC has been evaluated in several large clinical trials in a range of high-risk populations, including men who have sex with men and sero-discordant heterosexual couples (i.e., couples in which one partner is infected with HIV and the other is not). In these studies, TDF-FTC reduced the risk of HIV acquisition by 44% to 75%, although two studies in African women did not show a benefit.
Overall, these studies demonstrated that the effectiveness of TDF-FTC is contingent upon medication adherence. Those who were more adherent attained the greatest prevention benefit. It is not yet known how frequently one must take TDF-FTC in order to be protected from HIV; daily use is recommended until further data are available. A study to test the efficacy of PrEP among injection drug users is ongoing.

**How safe is TDF-FTC as part of the PrEP Package?**

How safe is TDF-FTC as part of the PrEP Package? There have been no differences in serious adverse effects between the use of TDF-FTC and placebo medications in clinical trials of PrEP to date. Use of TDF-FTC may be associated with nausea or other gastrointestinal symptoms (in less than 5% of study participants) that generally resolve within days, and certainly within 4 weeks of use. Counseling patients about this possibility could decrease self-discontinuation of TDF-FTC. When used for the long-term treatment of HIV infection, TDF-FTC has been associated with renal toxicity and decreased bone mineral density, but clinically significant changes in these parameters have not been seen in PrEP trials. However, the duration of follow-up for study participants has generally been about 1-2 years, so clinicians must be alert for potential adverse effects as long-term safety data are not yet available. Use of TDF-FTC in those with pre-existing renal failure or osteoporosis is not recommended.

It is possible that PrEP use could be associated with an increase in high-risk sexual behaviors or with selection of antiretroviral resistance in those who acquire HIV while using TDF-FTC as PrEP. However, in the context of clinical studies, all of which have featured intensive behavioral counseling, PrEP use has not been associated with increased sexual risk, and antiretroviral resistance among those who acquire HIV while using PrEP has been rare.

**How do I prescribe TDF-FTC for the PrEP Package?**

Before prescribing TDF-FTC, clinicians should consider whether the patient is capable of taking a pill daily and of regularly following up for testing, adherence, adverse effects, and safer sex counseling.

In addition, all patients should have:

- Documentation of a negative HIV antibody test.
- Assessment for acute HIV with an HIV RNA test if the patient has signs or symptoms consistent with acute
infection (e.g., fever, rash, lymphadenopathy, a “viral syndrome”) or a recent, high-risk exposure.
  o Baseline creatinine assessment to document an estimated creatinine clearance ≥ 60 mL/minute.
  o Screening for hepatitis B infection, as both TDF and FTC can be used to treat this condition, and their abrupt discontinuation can cause flares of chronic hepatitis B.
  o Screening for, and treatment of, other sexually transmitted infections.
  o Safer-sex counseling.
  o Determination if women are pregnant, planning to become pregnant, or are breastfeeding, and counseling around the use of barrier and hormonal contraception while using PrEP. TDF-FTC is not recommended for women who are breastfeeding.

During prescription of TDF-FTC, all patients should have:

  o HIV antibody tests every 2-3 months. If patients experience signs or symptoms of acute HIV infection, HIV RNA testing should be performed.
  o Follow-up visits at least every 2-3 months to assess medication adherence and adverse effects, to evaluate for sexually transmitted infections, and to provide safer-sex counseling and condoms.
  o Screening for sexually transmitted infections at least every six months, even if asymptomatic, with treatment as needed.
  o Serum creatinine checked after 3 months on the medication and yearly thereafter if baseline and 3 month values are within normal limits.
  o For women, pregnancy testing every 3 months. In case of pregnancy, continued use of the medication should be discussed with the patient and their prenatal-care provider given limited safety data for the fetus in this setting.

Reimbursement
Public and private payors are currently undergoing a review process to determine if they will provide reimbursement for PrEP, as they typically do for newly approved treatments. Clinicians and patients will need to determine whether each patient’s insurer will cover the cost of PrEP. Some payors have already agreed to cover payment, while others are considering it.
What are other resources on the use of TDF-FTC?

- Interim guidelines for health care providers who may prescribe PrEP have been published by the CDC (http://www.cdc.gov/hiv/prep/pdf/PrEPfactsheet.pdf).
- Gilead Sciences, the manufacturer of TDF-FTC, has developed a website which contains an online training module and checklist for clinicians providing PrEP as well as information on identifying individuals at high risk of HIV acquisition (https://truvadapreprems.com).
- The CDC’s Compendium of Evidence-Based Behavioral HIV Interventions (www.cdc.gov/hiv/topics/research/prs/prs_rep_debi.htm) provides extensive information on risk-reduction counseling and other non-pharmacologic strategies to help prevent HIV infection.
- The CDC has published recommendations for HIV testing in health care settings (www.cdc.gov/MMWr/preview/mmwrhtml/rr5514a1.htm).

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INFORMATION FOR PATIENTS
Protecting Yourself from HIV through Pre-Exposure Prophylaxis (PrEP):
What you need to know

What are you doing to protect yourself from HIV? Better treatments have improved the quality of life for people living with HIV. But HIV can still make people very sick, and more than 50,000 people still get HIV each year in the United States.

This informational guide will tell you about some important ways that you and your health care provider can work together to protect you against HIV. One of the most promising new ways is known as PrEP ("pre-exposure prophylaxis").

PrEP is the use of HIV treatment medications by HIV-negative people to protect them from getting HIV. Recently, the Food & Drug Administration (FDA) approved such a medication, tenofovir-emtricitabine, for PrEP.

**Step 1: Getting tested for HIV**
- In the United States, one in five people with HIV do not know they are infected.
- Everyone aged 13 to 64 should be tested for HIV at least once, even if they do not think they are at risk for HIV.
- People who are at high risk for HIV infection should be tested more often.
- You have a high risk of becoming infected with HIV if:
  - You have sex with people who have HIV
  - You are a man who has sex with other men (especially if you don’t always use condoms, have had sexually transmitted infections, or use drugs or alcohol while having sex)
  - You trade sex for money, things you need, or services
  - You inject drugs to get high

**Step 2: What is the best way to protect yourself?**
If you are HIV-negative, there are many ways to lower your chances of becoming infected with HIV. Different ways include:
- Safer-sex counseling from your health care provider or HIV testing counselor. Here, you will get information to help you make choices about how many people you have sex with, what types of sex you have, and how to protect yourself from HIV and other sexually transmitted infections (STIs).
- Using condoms and lubrication every time you have sex. Be sure to use lubrication that is safe to use with condoms, such as water-based ones.
- Testing and treatment for other STIs. Having an STI can increase your chance of becoming infected with HIV.
- Taking **PEP** (post-exposure prophylaxis): PEP is an emergency medication taken after a high-risk exposure to HIV. PEP is available in many providers’ offices and emergency departments and must be taken as soon as possible after sex (or other high-risk exposure) in order to be effective.
- Using the **PrEP Package** (pre-exposure prophylaxis): The PrEP package involves taking an anti-HIV medication every day, using condoms as much as possible, getting frequent HIV and STI testing, and seeing your health care provider. It is only for people at high risk of getting HIV.
- Using sterile syringes and not sharing works with other people when injecting drugs.

**Using PrEP: More Than Just Taking a Pill**

Studies have shown that people who were given PrEP had a lower chance of getting HIV compared to people who were not given PrEP. But PrEP is more than just taking an anti-HIV pill. To protect you, PrEP must include:
- Taking the pill every day, without missing a single dose. In PrEP studies, people who took the pill as directed had the lowest chance of becoming infected with HIV.
- Seeing your health care provider on a regular basis to discuss: if you are having any side effects from PrEP; if you are having trouble taking the medication as directed; and to have testing for HIV and sometimes other blood tests to make sure the pill is not harming you.
- Ongoing safer-sex counseling with your provider.
- Using condoms and lubrication as much as possible when you have sex. PrEP is not fool-proof, so condoms provide a second level of defense against HIV. Condoms also protect against other STIs, like gonorrhea and chlamydia. The PrEP pill does not protect against these other STIs.
- Testing and treatment for other STIs.

PrEP is not 100% effective at preventing HIV. Even if you take the pill as directed, you may still become infected with HIV. While using PrEP, it is important that you continue to use the other ways to protect yourself, as discussed above.
**How Safe Is It To Use PrEP?**

- In the United States, only one drug, tenofovir-emtricitabine, has been FDA-approved for use as part of the *PrEP Package*. So far, studies have shown that tenofovir-emtricitabine is safe and has few side effects when used for PrEP.
- Tenofovir-emtricitabine may cause nausea or other gastrointestinal symptoms in less than 5% of people who take it for PrEP. These side effects usually go away after a few days to a few weeks.
- Tenofovir-emtricitabine can cause kidney or bone problems for a small number of people who take it for PrEP. You should not use it for PrEP if you have problems with your kidneys or bones.
- Talk to your health care provider, or see the websites below, for more information on how using this pill for PrEP might be harmful or cause side effects for some people.

**Insurance coverage**

You should contact your health insurance organization to learn if they will cover part or all of the cost of PrEP. Some insurers have already agreed to pay for PrEP. Other insurers have not yet decided if they will pay for PrEP.

**Other things to think about before using PrEP**

*Before being prescribed tenofovir-emtricitabine, you will need to have:*
- A negative test for HIV.
- A blood test to see how well your kidneys work.
- Testing and treatment for STIs, including hepatitis B.
- Safer-sex counseling.
- If you are a woman, a pregnancy test. If you are planning to become pregnant, you should discuss this with your provider. You will also need to discuss which birth control options may be right for you while using PrEP. Women who breastfeed must not use PrEP.

*While using tenofovir-emtricitabine, you will need to have:*
- HIV testing every 2-3 months or sooner if you have symptoms that could be a sign of HIV infection.
- Follow-up visits with your health care provider at least every 2-3 months to discuss: whether you are able to continue taking the drug as directed; whether you are having side effects; and to have testing for STIs. At these visits, you should also discuss ways to have safer sex and whether you are able to use condoms when you have sex.
- If you are a woman, you will need pregnancy testing every 3 months. If you become pregnant, it will be important to discuss with
your health care providers whether or not you should keep taking PrEP.

**Other websites about PrEP**
- Information about taking PrEP from Gilead Sciences, a company that makes the PrEP pill: [http://www.truvadapreprems.com/pre-exposure-prophylaxis](http://www.truvadapreprems.com/pre-exposure-prophylaxis)

**Key Points**
- Pre-exposure prophylaxis (PrEP) means taking an HIV medication every day in order to prevent HIV infection.
- PrEP is only appropriate for those at high risk of becoming infected with HIV.
- The drug tenofovir-emtricitabine is FDA-approved for PrEP.
- Tenofovir-emtricitabine is not 100% effective at preventing HIV. You should still try to use condoms and practice safer sex if using PrEP.
- If you take tenofovir-emtricitabine for PrEP, you must see your health care provider every 2-3 months for check-ups, tests, and safer sex counseling.
- There are several ways to protect yourself against HIV. Talking to your health care provider can help you choose what options are best for you.

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