A VA Clinician's Guide to PrEP for HIV (2023)

VA

U.S. Department of Veterans Affairs

Veterans Health Administration

PBM Academic Detailing Services

Contents

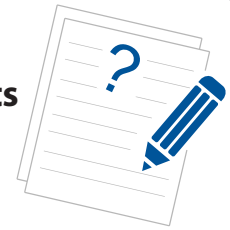
Pre-exposure prophylaxis (PrEP) for human immunodeficiency virus (HIV)

Pre-exposure prophylaxis (PrEP) for human immunodeficiency virus (HIV) infection is a safe and effective way to prevent HIV acquisition in people who have risk factors for HIV infection.[1]

FDA-approved PrEP medications include:

- **Tenofovir disoproxil fumarate (TDF) 300 mg with emtricitabine (FTC) 200 mg (Truvada® and generics)**
    - Approved by the FDA in 2012 for PrEP, FTC/TDF has a long history of safety and efficacy in multiple populations, including cis-gender men who have sex with men (MSM), transgender and gender diverse persons (TGD), cis-gender women, and persons who inject drugs ((PWID) – TDF alone). It is also available as a low-cost generic.[2-5]
- **Tenofovir alafenamide (TAF) 25 mg with emtricitabine (FTC) 200 mg (Descovy®)**
    - Approved by the FDA in 2019 for PrEP in cis-gender MSM and transgender women (TGW), based on the DISCOVER trial, which found it to be non-inferior to FTC/TDF in this population.[6] Please note, this medication is not indicated for individuals at risk of HIV infection from receptive vaginal sex.[1,7]
- **Cabotegravir (CAB) 600 mg intramuscular injection (Apretude®)**
    - Approved by the FDA in 2021, based on the results of two large trials comparing it to FTC/TDF, one in cis-gender MSM/TGW and one in cis-gender heterosexual females.[1,8,9] CAB is given as a long-acting injection, every 2 months, after 2 initial monthly doses.

Did you know?

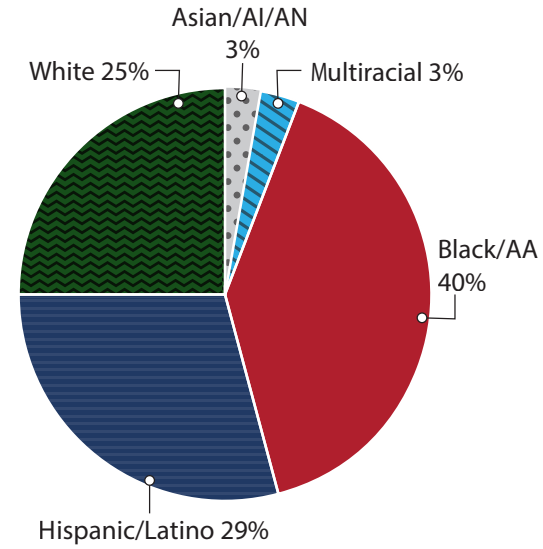


PEP is not PrEP! PEP is POST-EXPOSURE prophylaxis, which consists of taking 3 HIV medications for 4 weeks and must be started WITHIN 72 HOURS of exposure to prevent contraction of HIV.
If evaluating a patient for PrEP and they mention a possible exposure (e.g., unprotected sex or sharing of needles), refer the patient to the Emergency Department for PEP!

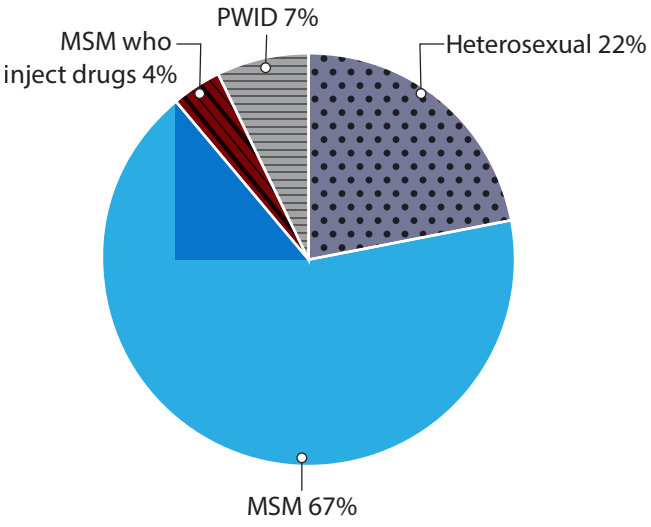
PrEP for HIV and health equity opportunities

Every year, approximately 35,000 new HIV infections are diagnosed in the U.S. While PrEP utilization is increasing, as of 2021 only 30% of the 1.2 million people for whom PrEP is recommended were prescribed it. In addition, there are opportunities to reduce disparities in receipt of PrEP among those with indications.[1,10,11]

Figure 1. New HIV infections in the U.S. by race/ethnicity and risk category, 2021[11]

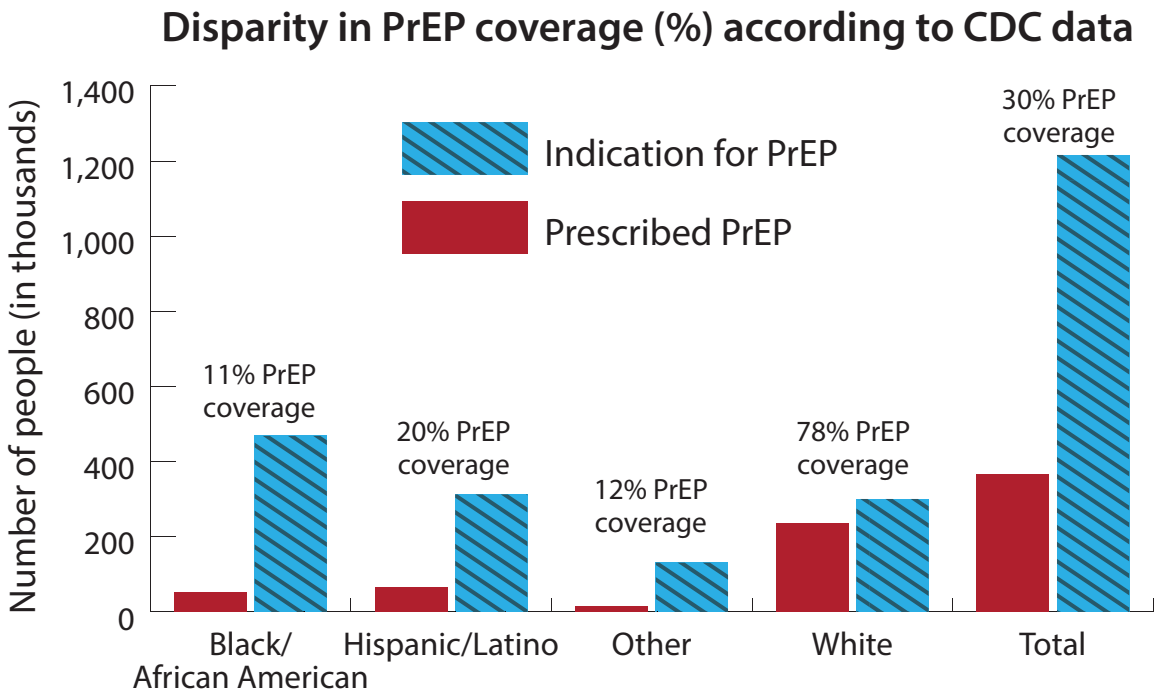


AA = African American, AI = American Indian, AN = Alaska Native



MSM = men who have sex with men, PWID = persons who inject drugs

Figure 2. Receipt of PrEP in those with indications by race in the U.S., 2021[10]



Who can prescribe PrEP?

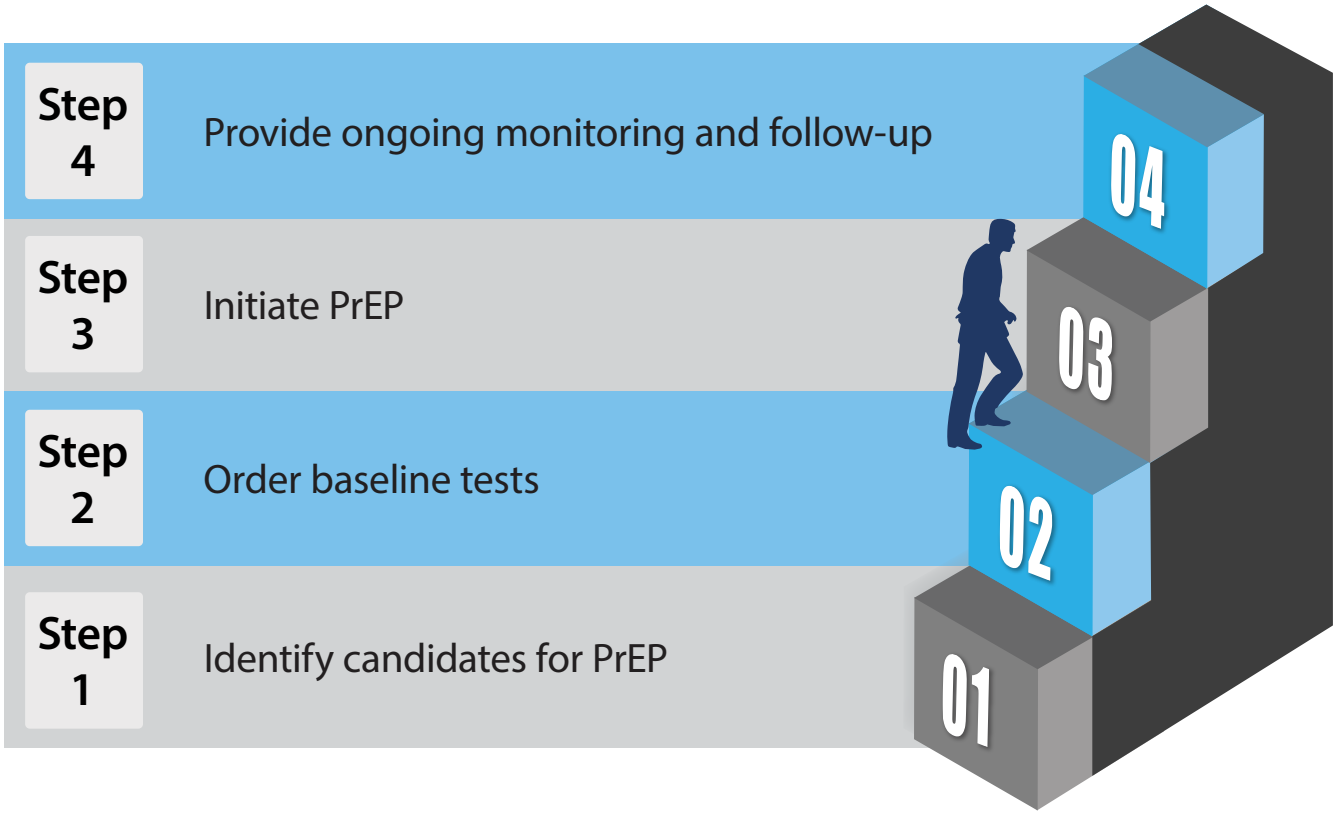
PrEP has typically been managed by infectious disease (ID) or HIV experts. However, many different prescribers have a role in expanding access to this care. Primary Care Providers (PCPs) can capitalize on trusted relationships with their patients to effectively advocate for, and prescribe, PrEP and other risk reduction strategies. HIV/ID specialists can help manage complex cases, provide guidance on indeterminate testing, and manage patients who become HIV infected while on PrEP.

To help reduce health disparity and expand access to PrEP, it is critical that we utilize a comprehensive team approach.

Prescribing PrEP - Follow the steps!

Using a stepwise approach is useful to ensure PrEP is prescribed appropriately by specialists and non-specialists.

Figure 3. Stepwise approach to prescribing PrEP for HIV



Step 1

Key message: Identify candidates for PrEP

Start by discussing sexual and injection drug practices.

Anyone who is sexually active or shares injection drug equipment is potentially at risk for HIV. Ask patients about their sexual behaviors and injection drug use in an open-ended, non-judgmental way to better understand their risk for HIV. See the PrEP Quick Guide for more tips on having the conversation.

Figure 4. Tips for talking about sex and injection drug use

SLANG

Ask Veterans to explain unfamiliar slang.

If a patient asks why you're asking, let them know that sexual health is a part of overall health, and that it helps tailor healthcare to the patient's needs.

Use eye contact and a tone or inflection that allows for honest and forthcoming responses to questions.

Keep in mind factors such as race, ethnicity, religion, sexual orientation, gender identity, and others when talking with Veterans.

- Ask about the name, gender, and pronouns they prefer.
- Discuss how they refer to their anatomy used in sex acts.
- Incorporate this language into sexual health questions.

Identify patients who may benefit from PrEP

Risk of HIV acquisition is determined by both **frequency of specific risk behaviors** and the **likelihood the partner has HIV**. Many factors may increase risk of HIV exposure such as condomless sex, sexual activities, multiple partners, drug and alcohol use, and others. Identifying populations with a higher incidence of HIV is critical for reducing health inequity and increasing access to PrEP. **PrEP is an option for anyone requesting it, as they may be uncomfortable or unwilling to disclose these activities, but still have risk.**

In addition, people who use injection drugs may be at risk from sharing injection equipment. Keep in mind that these injection practices may apply to substances beyond illicit drugs such as gender-affirming hormone therapy or other injected medications. PWID also frequently have sexual risk for HIV, even in absence of sharing injection drug supplies, and should be offered PrEP.

Table 1. Populations for whom PrEP should be considered[1]

	Applies to	PrEP Indicated if Any is True
Sexually active adults and adolescents	Those having anal or vaginal sex in the past 6 months	• Condoms are inconsistently used • Sexual partner is HIV-positive or HIV status is unknown • Bacterial sexually transmitted infection (STI) in the past 6 months (e.g., gonorrhea, syphilis, or chlamydia)
Persons who inject drugs (PWID)	Any injection drug use in the past 6 months	• Sharing of injection equipment • Risk of sexual acquisition as above
Others	Those requesting PrEP from their provider	• Anyone without contraindications even if they have reported no risk factors

Who should not receive PrEP?

- HIV positive or unknown HIV status
- Creatinine clearance (CrCl) < 60 mL/min for FTC/TDF or CrCl < 30 mL/min for FTC/TAF
- Those receiving contraindicated concomitant drugs which cannot be avoided (for FTC/TAF and CAB)
    - Rifampin, rifapentine
    - Anticonvulsants (phenytoin, phenobarbital, carbamazepine, oxcarbazepine)
    - St. John's Wort

Once candidates for PrEP have been identified, it's important to explain what PrEP is to the patient and how it would be beneficial to reduce the risk of HIV infection. Keep in mind that even if a Veteran does not currently engage in behaviors that put them at higher risk, they may still be candidates for PrEP if they perceive that their risk may be higher soon.

Step 2

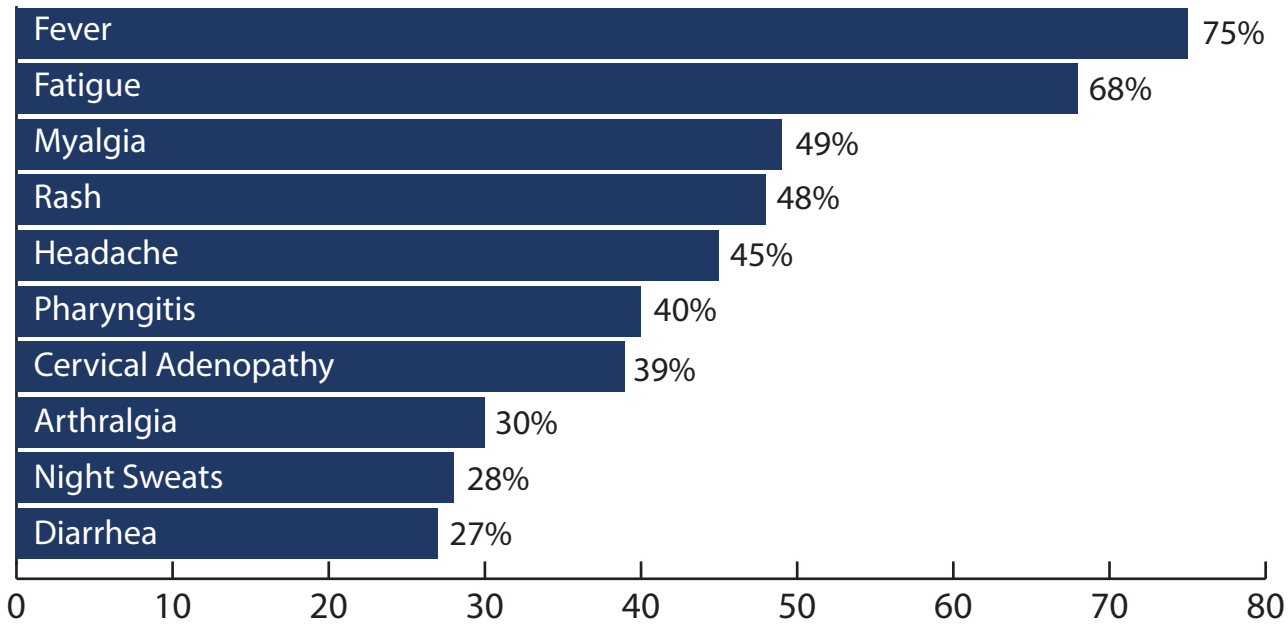
Key message: Rule out HIV and check appropriate baseline tests

HIV infection must be ruled out prior to initiation of PrEP. All patients must be tested for HIV, ideally **within 1 week prior to PrEP initiation.** HIV status should be confirmed with an initial HIV antibody/antigen test from plasma.[1]

Additionally, an HIV-1 RNA test (i.e., HIV viral load) should be obtained in all patients who have:

- Had unprotected sex or shared injection equipment in the last four weeks with a partner of unknown HIV status
- Taken oral PrEP or PEP in the last 3 months or received CAB in the past 12 months
- Signs or symptoms of acute HIV

Figure 5. Possible signs or symptoms of acute HIV infection[1]



Did you know?

PrEP should not be started in anyone with signs/symptoms of acute HIV or recent potential exposure until acute HIV infection has been excluded.

Other important considerations

Some situations may benefit from the involvement of an expert in HIV or ID. If these exist, refer the patient to the HIV or ID specialist:

- HIV testing in those who were previously on PrEP but stopped within the prior 3 months (oral) or prior 12 months (injectable)
- Those with symptoms of acute HIV infection
- Those with indeterminate or positive HIV test results

What to do if the HIV test comes back positive

- For positive HIV results from a point of care test, **confirm results with a plasma test.** For questions about test results or next steps, consider reaching out to an ID specialist for consultation.
- **Communicate HIV positive test results** to the patient in a sensitive, empathetic manner. It may require a scheduled visit at a time convenient to the patient. Please see VHA Directive 1088, Communicating Test Results to Providers and Patients (https://www.va.gov/vhapublications/ViewPublication.asp?pub_ID=10366) for additional guidance.
- **Immediately link patients to HIV care** after diagnosis is established to initiate an HIV suppressive regimen.
- **Consider the impact of a positive HIV test result** on the patient's mental health needs and suicide risk.
    - For Veterans with a High Risk for Suicide – Patient Record Flag, coordinate communication of results to the patient with mental health. Please see VHA Directive 1088, Communicating Test Results to Providers and Patients (link referenced above) for additional guidance.

Strategies to deliver results and access mental health needs:

Your care team understands that receiving these test results must be difficult for you and your loved ones. We know it may help to talk to someone about how you're feeling and to support you during this time.

- Inquire if the Veteran would like to speak with someone today and, if so, engage your local Same Day Access process.
- If a Veteran declines same day services, contact information for local Mental Health services and the Veterans Crisis Line should be provided.

Other baseline testing prior to initiating PrEP

In addition to HIV testing, other laboratory testing may be needed prior to initiation of PrEP to ensure safe and appropriate use. See Table 2 for more information.

Table 2. Baseline laboratory tests for PrEP

Test	Why it's recommended	How to use the information
Serum creatinine with estimated creatinine clearance (CrCl)	Renal function is used to inform medication selection	• FTC/TDF (generic Truvada®) can be safely used if CrCl ≥ 60 mL/min • FTC/TAF (Descovy®) can be safely used if CrCl ≥ 30 mL/min • CAB can be safely used in patients with any degree of renal dysfunction
Tests for other sexually transmitted infections (STIs)* • Gonorrhea • Syphilis (RPR or FTA) • Chlamydia	• To guide treatment • Presence of STIs increases the risk of exposure to HIV	• Treat positive results • Remind patients PrEP does not prevent other STIs • Discuss other prevention methods (e.g., condom use) and consider doxy PEP after condomless sex in MSM or TGW[12,13]
Hepatitis B virus (HBV) • HBV surface antigen • HBV surface antibody • HBV core antibody	• Patients with active HBV infection may have hepatitis flares if tenofovir based PrEP is stopped (FTC/TDF or FTC/TAF) • Identify opportunities to vaccinate	• If HBV surface antigen is positive – refer to hepatitis specialist for care and explain that HBV may flare when oral PrEP is stopped • If HBV surface antibody is negative, initiate HBV vaccine
Serum lipid panel	Patients on FTC/TAF may have increases in serum lipids	• Initiate therapy for hyperlipidemia if indicated
Hepatitis A (HAV) or C (HCV) virus antibody	To determine the need for vaccination (for HAV) or treatment (for HCV)	• Hepatitis A should be checked in MSM • Hepatitis C should be checked in MSM and PWID
Pregnancy test	• In persons of childbearing potential to guide therapy • Identifies sexual risk behaviors that also may transmit HIV	• Pregnant patients may be able to receive FTC/TDF

*Gonorrhea and chlamydia nucleic acid amplification tests (NAAT) should be done from all anatomically exposed sites (e.g., genital, rectal, pharyngeal), test based on existing anatomy and sexual behaviors, including extra-genital testing; RPR = rapid plasma regain; FTA = fluorescent treponemal antibody

Step 3

Key message: Initiate PrEP for HIV

Selection of therapy

- Three PrEP options exist: two oral agents (FTC/TDF and FTC/TAF) taken once daily, and one injectable drug (CAB) given intramuscularly (IM) every 2 months (after 2 initial doses 1 month apart).[1]
- FTC/TDF (generic Truvada®) is the preferred first-line medication for PrEP in VHA due to a long history of efficacy and safety in multiple populations (e.g., cis-gender MSM, TGD, HIV-discordant couples, cis-gender women). Most patients can use FTC/TDF for PrEP.[2-5]
- FTC/TAF and CAB have a role for some patients who may not be able to take FTC/TDF.[1,6,8,9]
- All three agents are available for prevention of HIV infection in patients at high-risk in VHA.

Table 3. Comparison of PrEP medications[1-9]

Regimen	Recommended for	Considerations	Side Effects
FTC/TDF (generic Truvada®) tablets Dose: 1 tablet daily	• **Preferred medication for PrEP in VA** • Can be used by all at-risk populations (cis-gender MSM, TGD, cis-gender women, PWID) • Safe in those with CrCl ≥ 60 mL/min	**Avoid in:** • Patients with CrCl < 60 mL/min • Some providers may wish to avoid in osteoporosis or significant osteopenia	• Headache, nausea (first month) • Renal insufficiency *(usually mild initial decrease in renal function which stabilizes, but rarely causes acute kidney injury)* • May decrease bone mineral density (BMD) with prolonged use
FTC/TAF (Descovy®) tablets Dose: 1 tablet daily	• CrCl 30-60 mL/min • Patients with osteoporosis or significant osteopenia	**Avoid in:** • Cis-gender female patients (only studied in cis-gender MSM and TGW) • Patients on drugs that may reduce PrEP efficacy (e.g., rifampin/rifapentine, St. John's Wort, certain seizure medications)	• Headache, nausea (first month) • Can cause weight gain and unfavorable lipid changes • Less impact on renal function and BMD than FTC/TDF
Cabotegravir (Apretude®) injection Dose: 3mL IM monthly for 2 doses then every 2 months	• Renal impairment: • (CrCl < 30 mL/min) • Intolerance to FTC/TDF or FTC/TAF • Other issues that impact daily PrEP adherence (e.g., unstable housing, cognitive impairment)	**Avoid in:** • Patient who cannot commit to clinic visits for injections • Patients on drugs that may reduce PrEP efficacy (e.g., rifampin/rifapentine, St John's Wort, some seizure drugs)	• Injection site reactions: pain, swelling (common but decrease over time) • Headache, nausea • Insomnia, abnormal dreams • Anxiety

Important points about oral PrEP medications

- Efficacy of oral PrEP is greatly impacted by adherence, especially with less than 4 pills / week (in cis-gender MSM and TGW), and probably less than 6 pills/week in women.
    - "On-demand PrEP," also known as 2-1-1, may be an option for selected MSM patients. The CDC recommends daily PrEP as the most effective option to reduce the risk of HIV infection.[1]
- PrEP for HIV does not prevent other STIs. Patients should be educated to combine PrEP with other measures, such as consistent use of condoms, clean injection equipment, and biomedical prevention such as doxy PEP.[12,13]

Doxy PEP: Doxycycline for post-exposure prophylaxis (PEP) to prevent gonorrhea, chlamydia, and syphilis is an emerging practice. In MSM or TGW receiving PrEP, 200 mg doxycycline taken within 72 hours of condomless sex reduced rates of gonorrhea, chlamydia, and syphilis.[13] CDC acknowledges the practice but has not made a formal recommendation on the practice.[12]

Initial assessment steps

- HIV negative
- CrCl
- Lipid profile
- Screened for:
    - HBV
    - HCV
    - Pregnancy
    - STIs (Syphilis, G/C)
- Drug-drug interactions

Tips for prescribing oral PrEP:

- Prescriptions should be for no more than a 90-day supply to ensure follow up occurs before additional medication is given.
- HIV infection should be excluded before each renewal.
- Adherence to clinic visits should be reviewed at each visit, and re-evaluation for continued appropriateness in patients who repeatedly miss appointments.

Important points about injectable PrEP

- CAB is a long-acting injectable medication for PrEP, that may be appropriate in some patients who cannot be treated with oral PrEP agents, such as those with CrCl < 30 mL/min or inability to use oral PrEP (e.g., gastrointestinal malabsorption, unstable housing or cognitive difficulties that impact adherence).
- Injection site reactions are common with CAB but usually are mild to moderate and may diminish over time. CAB may also cause weight gain and rarely, hypersensitivity reactions.
- While not required, oral CAB can be given initially to assess for tolerability prior to initiation of the injection.
- Given the long-half life, it is very important HIV is ruled out prior to treatment and before each subsequent injection with a qualitative or quantitative HIV-RNA test as resistance may occur with delayed diagnosis of new HIV infection.
- If CAB is being discontinued, convert patients to an oral PrEP regimen within 30 days after the last injection and continue HIV testing quarterly for at least 12 months after the last injection.

For patients on PrEP, offer treatment or referrals as indicated to manage other mental health or medical comorbidities.

Step 4

Key message: Monitor patients on PrEP

Monitoring and follow-up should occur every 3 months for patients on oral PrEP and every 2 months for patients on injectable PrEP.

At **EVERY** visit, patients should be assessed for medication adherence and signs or symptoms of acute HIV infection. The continued need for PrEP should be evaluated annually.

Specific recommendations for monitoring tests can be found in Tables 4 and 5.

Table 4. Frequency of monitoring patients on oral PrEP (FTC/TDF and FTC/TAF)[1]

Test	At initiation	Every 3 months	Every 6 months	Every 12 months
Laboratory tests				
HIV Ag/Ab Test*	X	X		
BUN/SCr	X		If age ≥50 or CrCl <90 mL/min at PrEP initiation	If age <50 and CrCl ≥90 mL/min at PrEP initiation
Chlamydia, gonorrhea, and syphilis	X	Cis-gender MSM, TGW	Heterosexually active women and men**	
Lipid panel (for FTC/TAF)	X			X
Hepatitis B serology	X			
Hepatitis C serology	Cis-gender MSM, TGW, and PWID			Cis-gender MSM, TGW, and PWID
Pregnancy test (persons of child-bearing potential)	X	X		

*HIV RNA should be ordered if there is concern or risk for acute HIV infection (e.g., symptoms);
**May consider reducing frequency to every 12 months if multiple negative tests over time and patient is in a monogamous relationship; use clinical judgment
X = Most monitoring tests for patients on oral PrEP need to be completed at initiation. Some should be performed every 3 months, every 6 months, or every 12 months. Please see the medication package insert for complete medication monitoring instructions.

Table 5. Frequency of monitoring patients on injectable PrEP (CAB)[1]

Test	At initiation	Month 1 visit	Every 2 months	Every 4 months	Every 6 months
Laboratory tests					
HIV RNA	X	X	X		
Chlamydia, gonorrhea, and syphilis	X			Cis-gender MSM, TGW	Heterosexually active women and men only*
Pregnancy test (persons of child-bearing potential)	X	X	X		
Clinical follow-up at every visit					
Assess for signs or symptoms of acute HIV infection Assess for adverse effects or new drug-drug interactions Review adherence to injection appointments					

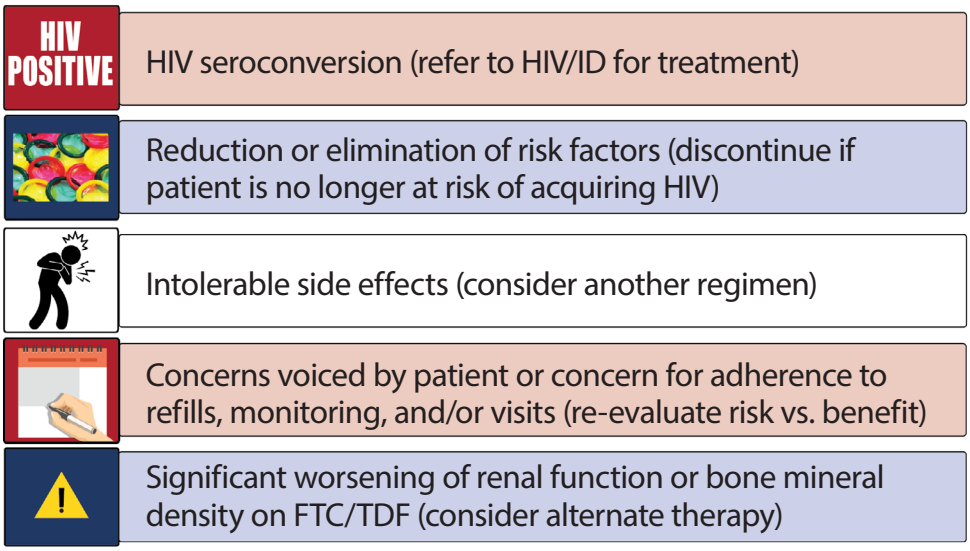
*May consider reducing frequency to every 12 months if multiple negative tests over time and patient is in a monogamous relationship; use clinical judgment

What about drug resistance?

Failure to reliably take PrEP may result in drug-resistance which can limit treatment options should the patient become HIV infected. While rare with oral PrEP, it is often tied to poor adherence and most commonly results in the M184V mutation which confers resistance to emtricitabine.

In the trials of CAB, resistance occurred rarely. However, in those few cases diagnosis was often delayed after HIV infection occurred. Use of an HIV antigen/antibody test with a discussion about risky behaviors or signs or symptoms of acute HIV infection should prompt an HIV RNA test to rule out new infection. If a patient tests positive for HIV infection, they should be referred to an HIV/ID specialist and switched to an HIV suppressive regimen as soon as possible.

Figure 6. When to consider stopping or changing PrEP regimen



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This reference guide was created to be used as a tool for VA providers and is available to use from the Academic Detailing Services SharePoint.

These are general recommendations only; specific clinical decisions should be made by the treating provider based on an individual patient's clinical condition.

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