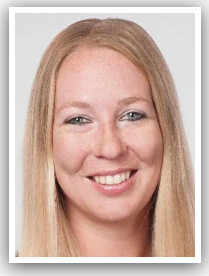
POINT OF CARE 301

PHARMACY PrEP EDUCATION A "HOW TO" SERIES SPANNING POLICY TO PRACTICE

EARN 2.0 CPE CREDITS

PROVIDING PEP/PrEP IN THE PHARMACY SETTING

A COMPREHENSIVE USER GUIDE



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HOW TO OBTAIN CREDIT

Participants must complete the preactivity questionnaire, complete and receive a minimum score of 70% on the posttest, and complete the program evaluation online at www.ExchangeCME.com/PrEPpharmacyMonograph.

Estimated time to complete this activity is 2 hours.

This activity is jointly provided by Global Education Group and Integritas Communications.

This activity is supported by an educational grant from Gilead Sciences, Inc.

DESCRIPTION

This comprehensive electronic/downloadable monograph has been developed to specifically support the needs of pharmacists now challenged to come up to speed on guidelines and protocols for HIV preexposure and postexposure prophylaxis (PrEP and PEP). A number of states in the United States have expanded the pharmacy scope of practice and this continuing education activity will provide the necessary clinical information for initiating and monitoring PrEP and PEP treatment in a pharmacy setting. In December 2021, the Centers for Disease Control and Prevention (CDC) released the 2021 Updated PrEP Clinical Practice Guidelines, and pharmacists now need education to incorporate these updated guidelines into their daily practice. In addition, with 2.0 contact hour(s) (0.10 CEUs) from the Accreditation Council for Pharmacy Education, this monograph addresses all content necessary to fulfill most state Board of Pharmacy training requirements for pharmacists wishing to become PrEP and PEP providers, such as:

- HIV epidemiology
- Pharmacology, safety, and efficacy of HIV medications used for PEP and PrEP (including oral tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC), oral tenofovir alafenamide (TAF)/FTC and cabotegravir long-acting injectable)
- Assessment of sexual health and HIV risk
- Patient counseling
- Screening for HIV and sexually transmitted infections (STIs), and laboratory testing to determine PrEP/PEP eligibility
- 2021 CDC Updated PrEP Clinical Practice PEP for PrEP eligibility, prescribing, and management
- Clinical Practice Guidelines for nPEP eligibility, prescribing, and management
- In-pharmacy implementation
- Trauma-informed care

TARGET AUDIENCE

The educational design of this monograph addresses the needs of clinical and community pharmacists involved in the treatment of patients at risk for HIV infection as well as managed care pharmacists, pharmacy benefit managers, and specialty pharmacists.

EDUCATIONAL OBJECTIVES

After completing this activity, the participant should be better able to:

- Describe the legal and professional parameters that allow for pharmacist-led or pharmacy-based direct delivery of PEP and PrEP services
- Assess patient's risk of HIV acquisition based on the type of exposure
- Determine patients' PEP/PrEP eligibility through HIV testing, sexual history-taking, and appropriate laboratory testing
- Implement guideline-driven PEP/PrEP-prescribing principles regarding treatment initiation, monitoring, and referral
- Identify infrastructure needs for in-pharmacy implementation of a PEP/PrEP prescribing initiative

PHARMACIST ACCREDITATION STATEMENT

Global Education Group is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education with Commendation.

CREDIT DESIGNATION

Global Education Group designates this continuing education activity for 2.0 contact hour(s) (0.20 CEUs) of the Accreditation Council for Pharmacy Education. (Universal Activity Number 0530-9999-22-063-H02-P)

This is a knowledge-based activity.

INSTRUCTIONS TO RECEIVE CREDIT

In order to receive credit, participants must complete the following:

- Read the educational objectives, accreditation information, and faculty disclosures at the beginning of this activity
- Complete the Preactivity Questions
- Review the activity content
- Achieve a grade of 70% on the Postactivity Test Questions and complete the Evaluation
- CE credits will be uplaoded to CPE Monitor within 60 days of completion

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The **faculty** have the following relevant financial relationships with ineligible companies:

Melissa Badowski, PharmD, MPH, FCCP, FIDSA, BCIDP, BCPS, AAHIVP	Nothing to disclose
Shauna Applin, ARNP, CNM, AAHIVMs	Consulting Fee: Gilead Sciences, Inc., Janssen Pharmaceutical Companies, Merck & Co., Inc.; Contracted Research: Gilead Sciences, Inc. (PI); Speakers' Bureau: Gilead Sciences, Inc., Merck & Co., Inc.

The **planners and managers** have the following relevant financial relationships with ineligible companies:

Lindsay Borvansky	Nothing to disclose
Andrea Funk	Nothing to disclose
Liddy Knight	Nothing to disclose
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Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this activity is not meant to serve as a guideline for patient management. Any procedures, medications, or other courses of diagnosis or treatment discussed in this activity should not be used by clinicians without evaluation of patient conditions and possible contraindications or dangers in use, review of any applicable manufacturer's product information, and comparison with recommendations of other authorities.

GLOBAL CONTACT INFORMATION

For information about the accreditation of this program, please contact Global at 303-395-1782 or cme@globaleducationgroup.com.

FEE INFORMATION & REFUND/CANCELLATION POLICY

There is no fee for this educational activity.

INTRODUCTION: PHARMACIST'S EXPANDING ROLE IN HIV PREVENTION

Human immunodeficiency virus (HIV) preexposure prophylaxis (PrEP) remains underutilized in the United States.[1] As 85% to 90% of PrEP medications are filled at community pharmacies, pharmacists have the capability to join others in ending the HIV epidemic by 2030.[2,3] Pharmacists have legal authority in most states to prescribe and dispense PrEP in collaboration with other clinicians.[4] Recently, some states (including California, Colorado, Nevada, Oregon, and Virginia) have granted pharmacists legal authority to prescribe and dispense PrEP independently.[5] Pharmacists could facilitate PrEP uptake and adherence through consultations with and HIV screening for interested patients, point-of-care testing for HIV and other sexually transmitted infections (STIs), PrEP prescriptions, and PrEP adherence counseling.[6] Pharmacy-based interventions such as refill reminders and adherence counseling have improved adherence to antiretroviral therapy (ART) regimens among people living with HIV (PLWH).[7-9] Because interventions that integrate pharmacists into the PrEP care continuum are increasing, pharmacists must have a thorough understanding of PrEP as well as the essential roles that they serve when caring for patients who may be at risk of acquiring HIV.[10,11]

HIV Epidemiology and the Burden of Disease

Approximately 1.2 million people in the United States are living with HIV, and 1 in 7 individuals infected with HIV are unaware of their infection. Latest estimates from the Centers for Disease Control and Prevention (CDC) indicate that there were 36,740 new HIV infections in the United States in 2019.[12] Populations including men who have sex with men (MSM), transgender persons, and black and Hispanic/Latinx individuals continue to be disproportionally affected. While new annual infections in the United States have been reduced by more than two thirds since the mid-1980s when HIV initially emerged, black and Hispanic/ Latinx populations are among those that continue to have high rates of undiagnosed infections (**Figure 1**).[13-15]

HIV burden has often been measured by the number of individuals dying from acquired immunodeficiency syndrome (AIDS)-related complications. Although on an international level, HIV/AIDS remains among the leading fatal infectious diseases, AIDS-related deaths in the United States have dramatically dropped because of advances in HIV treatment and management.[16,17] Nonetheless, the United States government continues to spend more than $20 billion annually in direct health expenditures related to HIV care and prevention. This underscores HIV as a persistent public health threat despite greater disease awareness, highly effective ART, and proven prevention strategies and tactics.[3]

The advent and continual evolution of ART has allowed people with HIV (PWH; or people living with HIV [PLWH]) to enjoy longer, healthier lives through reduction in HIV-related morbidity and mortality at all stages of HIV infection.[18] ART has also given rise to modalities designed to limit HIV acquisition in HIV-negative individuals—notably, specific antiretroviral drug combinations used as PrEP and postexposure prophylaxis (PEP). PrEP is prescribed for HIV-negative people who are at high ongoing risk of HIV exposure, whereas PEP is prescribed for HIV-negative people who have had a single high-risk exposure.[19]

Despite oral PrEP demonstrating efficacy in reducing HIV transmission rates by as much as 74% to 99% when taken daily (depending on mode of transmission—sexual or injection drug use [IDU]), fewer than 1 in 4 potential candidates receive PrEP (**Figure 2**).[20,21,23]

High-risk populations with the lowest rates of PrEP uptake include young MSM, racial or ethnic minority groups, and individuals living in the South or Southeast regions of the United States. Without preventive efforts, 1 in 2 black MSM and 1 in 5 Hispanic/Latinx MSM will contract HIV in their lifetimes.[24,25] The majority of PrEP uptake (75%) has been among white gay and bisexual men, predominantly those living in the Northeast or

FIGURE 1. HIV Infections by Race and Transmission Group, 2015 vs 2019[13]

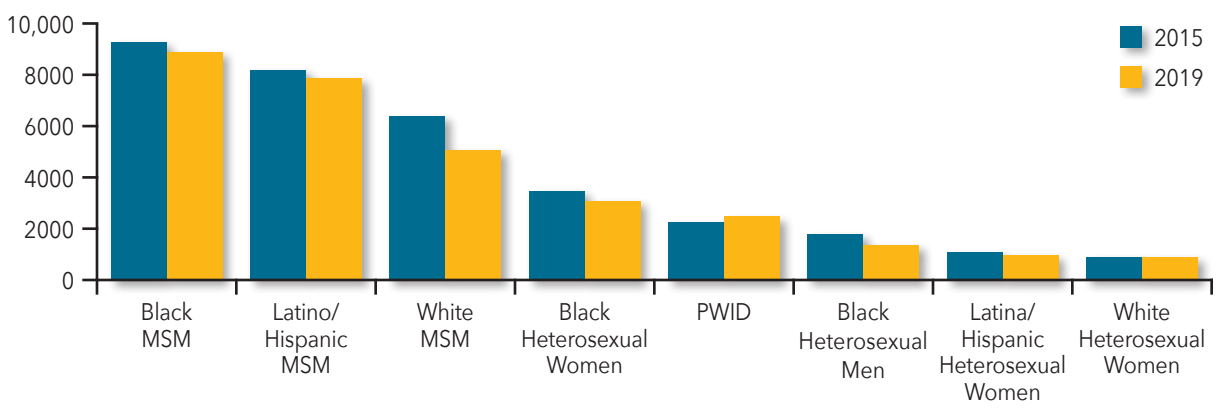
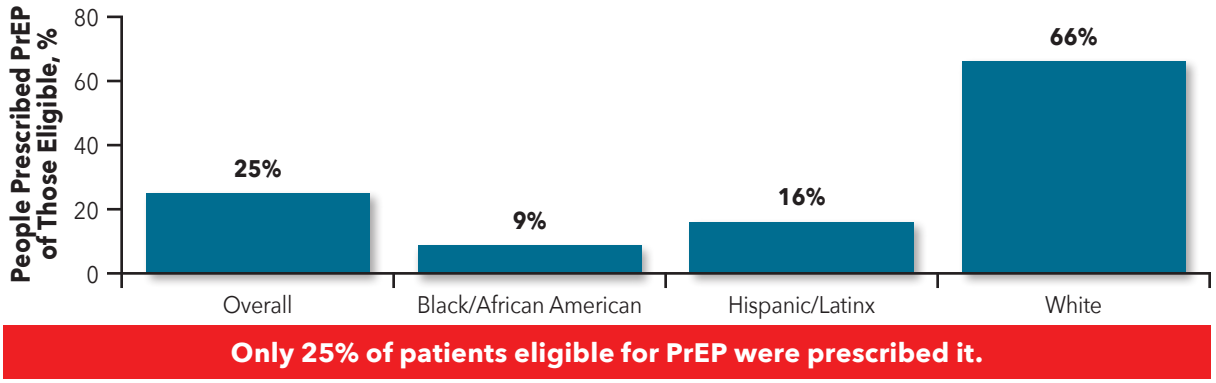


FIGURE 2. PrEP Coverage in the US by Race/Ethnicity, 2020[20]



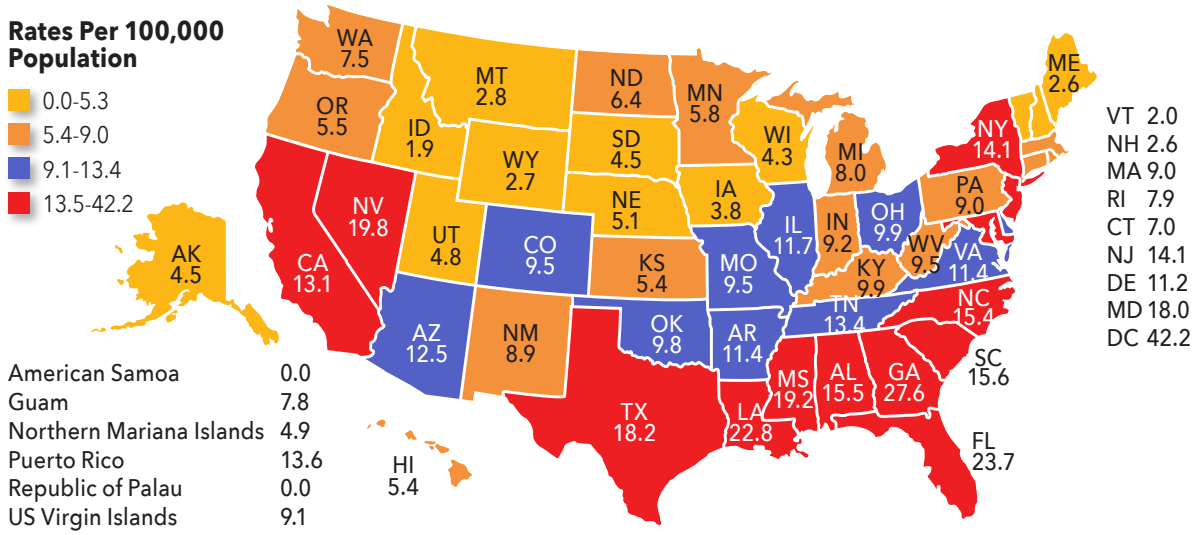
Only 25% of patients eligible for PrEP were prescribed it.

on the West Coast.[26] As of 2017, the *PrEP-to-Need ratio* (ie, the number of PrEP users divided by new HIV diagnoses) was lowest among individuals aged ≤24 years or ≥55 years. Geographically, lowest ratios were seen throughout the South, despite 52% of new HIV diagnoses in the United States being attributable to this region (**Figure 3**).[12]

Perceived stigma, distrust of the medical system, lack of PrEP awareness among patients and clinicians, and limited access due to cost are theorized as potential reasons why PrEP uptake is currently low. Distrust of the medical system may be tied to stigma, as patients are often reluctant to speak with their health care providers about their sexual activity or behaviors of increased risk. This is especially true among MSM.[27]

Further, clinicians may be uncomfortable with sexual history-taking and unfamiliar with baseline laboratory testing and how to initiate and monitor patients on PrEP. In addition, they may not realize that a less costly generic PrEP formulation is now available.[28] In many locales, required prior authorization has been one of the most common barriers to prescribing PrEP, according to primary care and HIV-treatment providers.[24] Without adequate insurance coverage, the annual cost of continuous PrEP use (including guideline-based interval visits, laboratory testing, and prescription refills) is more than $10,000. Although there are federal and state-level programs to increase access to PrEP, cost and lack of awareness of PrEP resources may be barriers for young black and Latinx MSM and transgender women who may benefit the most from PrEP, many of whom are likely to be uninsured or underinsured.[26]

FIGURE 3. New HIV Infections in the US, 2019[12]



CDC. HIV Surveillance Report: Diagnoses of HIV Infection in the United States and Dependent Areas, 2019. https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-2018-updated-vol-32.pdf. Accessed March 20, 2022.

Building on an Established Practice Foundation

Through expansion of scopes of practice, pharmacists are demonstrating their ability to work in chronic disease management and to dispense or administer certain drugs and biologic products.[25,29] Many states, in an effort to curb the soaring rates of drug overdose, now allow pharmacists to dispense naloxone without a prescription.[26,30] Frequently, pharmacists in patient-centered medical homes lead medication-management services. This entails helping patients meet clinical-management goals as diverse as control of glycated hemoglobin (HbA1c), systolic blood pressure, and serum lipids as well as increasing vaccination rates and medication adherence.[31] In certain states, upon meeting additional education, credentialing, or board recognition, pharmacists are authorized to independently prescribe or furnish and dispense contraceptives, tobacco cessation therapy, and travel medications.[24,29] Further, community pharmacists are extremely well-positioned to address certain public health problems, since high-risk patients visit their community pharmacies more often than their primary care providers (PCPs) and may be more comfortable in a pharmacy setting.[31]

Within the realm of HIV disease management in an HIV clinic setting, pharmacists are part of the HIV care team. They have already demonstrated high levels of success in recommending HIV regimen starts and modifications, increasing ART adherence via identification of patient-specific barriers (eg, health literacy, cognitive factors, mental-health and substance-use comorbidities, economic factors); detecting therapy-related barriers (eg, adverse effects, drug-drug interactions); and recognizing service-delivery barriers (eg, patient-provider relationships, providers' cultural competencies). Pharmacists also expand access to these medications by assisting in prior authorization, activating copayment cards, patient assistance programs, state AIDS Drug Assistance Programs (ADAP), or identifying other resources to assist the patient in securing access to PrEP.[32]

An obvious next step in expanding the pharmacist's role in HIV care is the prescribing and management of PrEP and PEP. Experienced in the principles and practices of chronic-disease medication management, and knowledgeable about HIV pharmacology, the pharmacist can play an essential role in HIV prevention across diverse practice venues.[33-35]

HIV Prevention and the Evolving Scope of Pharmacy Practice[35]

One state that recently increased the scope of practice for pharmacists is Colorado. Despite a relatively low HIV incidence, new cases in 2019 reflected an approximate 13% increase over cases reported in 2018.[36] This contrasts with overall US HIV incidence rates, which remained stable or showed slight decreases between 2014 and 2018.[37]

Responding to this public health imperative to reduce HIV incidence in Colorado, legislation to expand PrEP and PEP access through inclusion of pharmacists as providers of HIV prevention passed both the State Senate and House in June 2020. **Table 1** shows what is mandated in Colorado and may serve as an example for others interested in advocating in their own states.[29,38]

Other states have also passed new laws granting community pharmacists the authority to prescribe HIV PrEP medications. For example, in 2019, California passed a landmark bill, Senate Bill 159, that allows pharmacists to initiate PrEP and PEP. Pharmacists can initiate between a minimum of a 30- to 60-day supply of PrEP, provided that the patient has been tested and is in accordance with the guidelines. Pharmacists are required to complete a 90-minute state-required training prior to initiating PrEP. Moreover, this bill eliminated prior authorization requirements for PrEP in the state of California.[39] States like California and Colorado may serve as models for other states interested in authorizing pharmacists to prescribe HIV PrEP medications in the future.

TABLE 1. Summary of Updates to the Definition of Practice of Pharmacy per Colorado Revised Statutes[38]

Colorado Statute Section	Update
2	Provides for coverage of pharmacy-based clinical or administrative (HIV-prevention) services, either through direct medical billing or enhanced dispensing fees, at the same level the payer would cover these services if performed by a physician or advanced-practice nurse
3	Restricts payers from requiring prior authorization or step-therapy to clients accessing HIV-prevention services at the pharmacy level
4	Authorizes prescribing and dispensing of preexposure and postexposure (nonoccupational) prophylaxis for prevention of HIV acquisition and the ordering of lab tests in conjunction with prescribing or dispensing the drugs

HIV BASIC SCIENCE FOR THE PHARMACIST

Therapeutic Interventions in the HIV Viral Life Cycle

HIV targets and replicates within CD4 T-lymphocytes (T helper cells)—cells that are critical to adaptive immune responses—leading to CD4 destruction and, thereby, decreasing the functionality of the immune system and increasing the risk of opportunistic infections.[40,41]

The HIV life cycle (**Figure 4**) consists of 7 stages, 5 of which inform the mechanisms of action of current ARTs (**Table 2**).[42] The first stage is *binding* (or *attachment*): HIV binds to receptors on the surface of a CD4 cell. The second stage is *fusion*: upon attachment, the viral envelope fuses with the CD4 cell membrane, allowing HIV to enter the host cell and release viral components. Stage 3 is *reverse transcription*: inside the CD4 cell, HIV releases a reverse transcriptase enzyme to convert HIV RNA (ribonucleic acid) into HIV DNA (deoxyribonucleic acid). HIV DNA then enters the nucleus and proceeds to *integration* (stage 4), during which HIV releases integrase, an enzyme that integrates viral DNA into the DNA of the host CD4 cell. In stage 5, *replication*, the machinery of the host CD4 cell produces long chains of HIV proteins (building blocks for more HIV); while in stage 6, *assembly*, new HIV proteins and HIV RNA move to the surface of the cell and combine as immature (noninfectious) HIV. The seventh and final step in the HIV life cycle is *budding*, wherein newly formed immature HIV pushes itself out of the host CD4 cell. Protease, an HIV enzyme released from the new HIV, breaks up long protein chains in the immature virus, creating a new and mature (infectious) virus.[42]

FIGURE 4. The HIV Life Cycle[42]

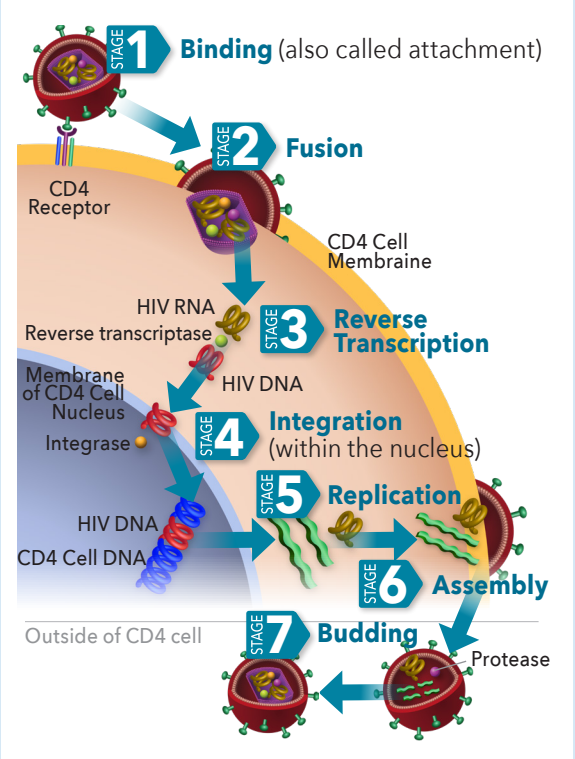


TABLE 2. HIV Life-Cycle Stages and Antiretroviral Classes That Target Them[42]

Stage	Description	Antiretroviral Class
1	Binding (attachment)	Entry inhibitors
2	Fusion	Fusion inhibitors
3	Reverse transcription	Nucleoside/nonnucleoside reverse transcriptase inhibitors
4	Integration	Integrase strand transfer inhibitors
5	Replication	None
6	Assembly	None
7	Budding	Protease inhibitors

The Immunologic Basis for HIV Testing

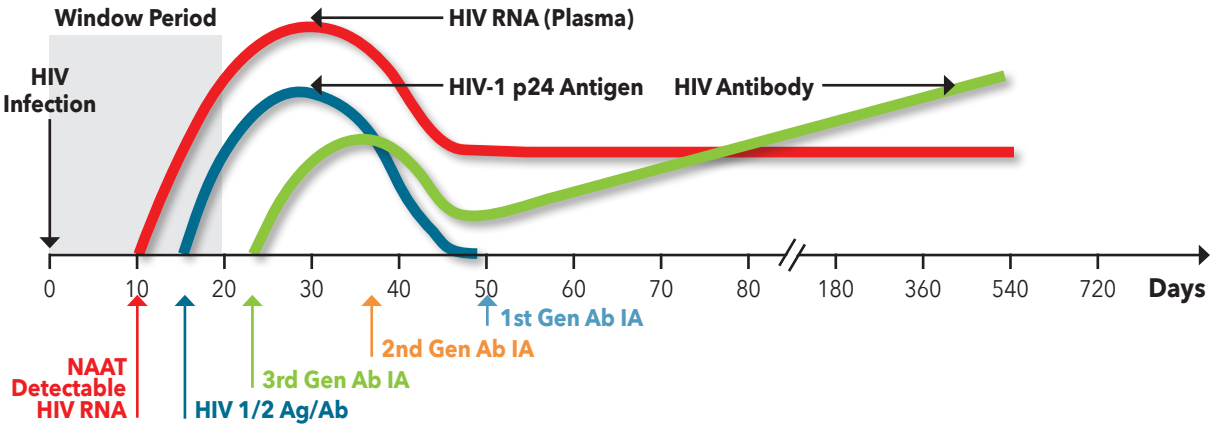
Following release of mature HIV from the CD4 cell, the viral RNA is initially present in the plasma without recognition of the host immune system. By approximately day 17, the HIV p24 antigen is present. The body recognizes this viral protein as foreign, thereby eliciting an immune response with production of specific anti-HIV antibodies. During this initial 17-day period, neither HIV antigen (Ag) nor anti-HIV antibodies (Ab) are detectable with HIV tests used most commonly in the community setting. Yet HIV RNA may be detectable as early as day 10 after acquiring HIV with more highly specialized nucleic acid amplification testing (NAAT). That is, during this *window period*, a person infected with HIV may have an HIV-negative test result (**Figure 5**).[43,44]

PREP 101

What Is PrEP?

PrEP is the use of specific antiretroviral agents to reduce the risk of HIV infection. It is intended for HIV-negative individuals who are at risk of infection through sexual intercourse or injection drug use, including sexually active MSM, heterosexual men and women, and transgender persons. PrEP is also an alternative prevention strategy for individuals receiving PEP who continue to engage in high-risk behavior or who have

FIGURE 5. Window of Detection of HIV Markers in Early HIV Infection[43,44]



Ab, antibody; Ag, antigen; Gen, generation; IA, immunoassay; IgG, immunoglobulin G; IgM, immunoglobulin M; NAAT, nucleic acid amplification testing; RNA, ribonucleic acid.

First-gen and second-gen immunoassays detect IgG HIV antibodies. Third-gen immunoassays detect IgG and IgM HIV antibodies. Third-gen tests are still used, often as disposable point-of-care methods.

received multiple courses of PEP. Sexually active adults and adolescents are defined as people engaging in anal or vaginal sex in the past 6 months.[45] At the time of this publication, CDC guidelines recognize 3 drug regimens for use as PrEP.[45]

2021 CDC Updated PrEP Clinical Practice Guidelines

In 2021, the CDC published updated clinical practice guidelines to prevent HIV and provide PrEP services. While the basic process for initiating PrEP has not really changed, there are 3 important updates[45,46]:

- It is now recommended that clinicians inform all sexually active teens and adults about PrEP
- PrEP should be offered and provided to anyone who requests it (following a brief history), even if they don't report specific HIV risk behaviors or appear "at high risk" of acquiring HIV
- Three US Food & Drug Administration (FDA)-approved medications are now available for PrEP
  - Oral daily dosing tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC)
  - Oral daily dosing tenofovir alafenamide (TAF)/FTC
  - Cabotegravir (CAB) long-acting injectable (LAI)

Efficacy and Safety of Available PrEP Options

Oral PrEP: TDF/FTC and TAF/FTC

Key clinical trials involving TDF/FTC used as PrEP–included:

- **iPrEx** (Iniciativa Profilaxis Pre-Exposición [Preexposure Prophylaxis Initiative])
- **Partners PrEP** (Partners Pre-Exposure Prophylaxis Study)
- **FEM-PrEP** (Preexposure Prophylaxis Trial for HIV Prevention Among African Women)
- **TDF2** (Botswana TDF/FTC Oral HIV Prophylaxis trial)
- **IPERGAY** (Intervention Préventive de l'Exposition aux Risques avec et pour les Gays)

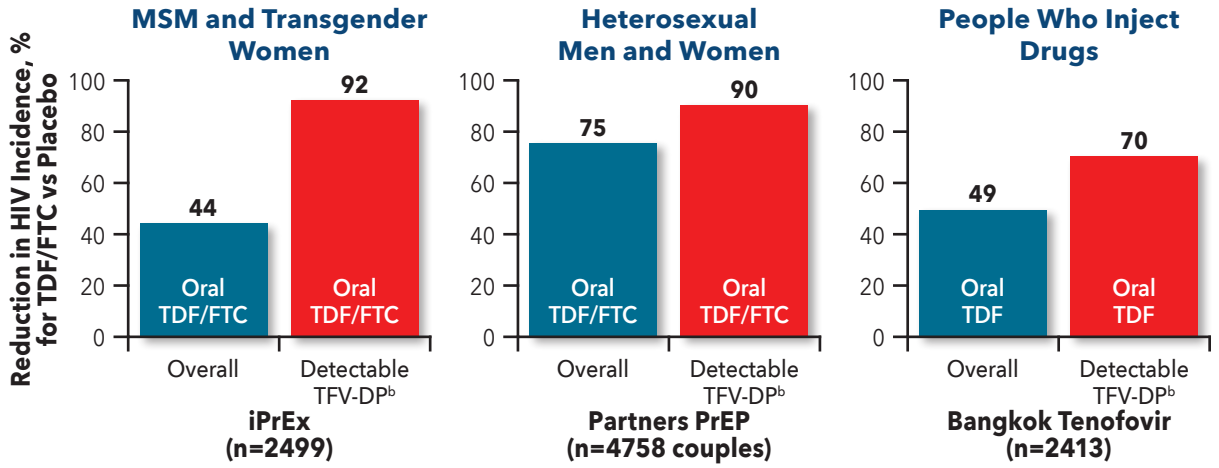
Demonstrated safety and efficacy of the combined use of these 2 nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) as PrEP across all at-risk populations (**Figure 6**), including[22,47-49,50-52]:

- MSM
- Heterosexual HIV-discordant couples
- Heterosexual men and women
- People who inject drugs (PWID)

As noted in **Table 2** and **Figure 4** above, TDF and FTC target reverse transcription, stage 3 in the HIV life cycle. Once phosphorylated intracellularly, creating diphosphate and triphosphate metabolites, respectively, these nucleotide/nucleoside analogs inhibit HIV reverse transcriptase by competing with viral substrates, thereby causing DNA chain termination and preventing viral RNA conversion.[53] Whereas older NRTIs were characterized by serious toxicities (including bone marrow suppression, peripheral neuropathy, lactic acidosis, and pancreatitis) secondary to their effects on human cellular mitochondrial DNA, these newer NRTIs are weaker inhibitors of mitochondrial DNA and are less likely to result in significant toxicities.[54]

TDF/FTC remained the sole FDA-approved antiretroviral regimen for use as PrEP from its approval in 2012 until October 2019. The randomized, double-blind, active-controlled DISCOVER trial evaluated the efficacy and safety of TAF/FTC vs TDF/FTC in high-risk cisgender MSM and transgender women who have sex with men (in North America and Europe). Eligible patients (N=5387)

FIGURE 6. TDF/FTC Prevents HIV Infections: Results From the 3 Principal Clinical Trials[22,47,48]



TDF/FTC, tenofovir disoproxil fumarate/emtricitabine; TFV-DP, tenofovir diphosphate.

had engaged in ≥2 episodes of condomless anal sex in the preceding 12 weeks or received the diagnosis of rectal gonorrhea/ chlamydia or syphilis in the preceding 24 weeks. The primary endpoint was the rate of HIV infection per 100 person-years (PY) when 50% of patients had completed 96 weeks of PrEP use.[55] Longer term results, reported once all participants completed 96 weeks, showed that just 23 HIV diagnoses occurred during the study period—an infection rate of 0.16/100 PY for TAF/FTC vs 0.30/100 PY for TDF/FTC (**Figure 7**).[56]

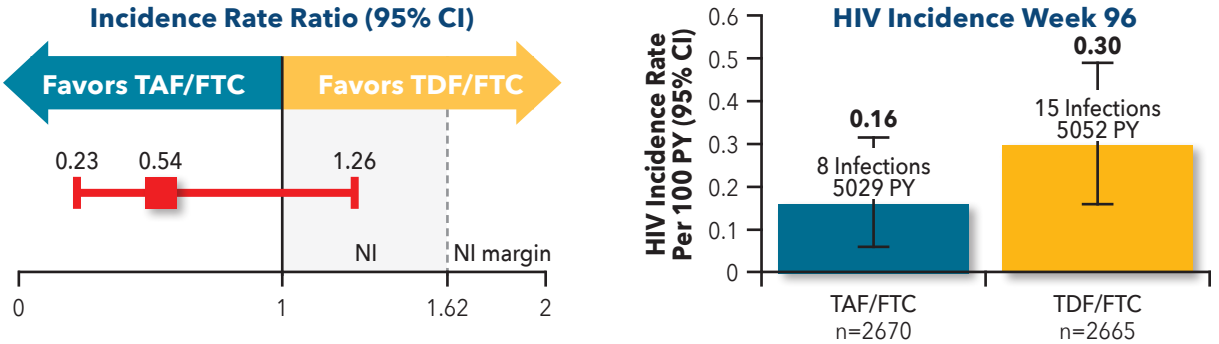
Safety Profiles/Side Effects

TAF/FTC was associated with superior bone and renal safety profiles compared with TDF/FTC, although both combinations were well-tolerated and associated with low rates of discontinuation due to adverse events. Combination TAF/FTC was considered noninferior to TDF/FTC in preventing HIV infection, thereby leading to expanded PrEP medication options for persons at risk of HIV acquisition, except for those at risk through receptive vaginal sex or injection drug use.[56,57]

Both TDF and FTC are primarily excreted through the kidneys; therefore, patients with impaired renal function—based on estimated creatinine clearance (eCrCl), as calculated using the Cockcroft-Gault equation—are at risk.[58] Use of TDF/FTC as PrEP is not recommended for persons with eCrCl <60 mL/min/1.73 m^2. Further, reduced-dosing strategies for TDF/FTC as PrEP have not been developed.[45]

In contrast, TAF is metabolized by the lysosomal multifunctional enzyme cathepsin A and can be used in patients with more compromised renal function (eCrCl ≥15 mL/min/1.73 m^2) or patients on hemodialysis. Note, however: the FTC component of TAF/FTC is not recommended for patients with eCrCl <30 mL/min/1.73 m^2 and, therefore, TAF/FTC for PrEP is not recommended for patients with eCrCl <30 mL/min/1.73 m^2).[57] The serum half-life of TAF is 0.5 hours, with an intracellular half-life of 150–180 hours. In contrast, the serum half-life of TDF is 17 hours, with an intracellular half-life of >60 hours.[57] The bone- and renal-related adverse effects associated with TDF are less likely to occur with

FIGURE 7. DISCOVER Trial Efficacy Results: TAF/FTC vs TDF/FTC[56]



CI, confidence interval; NI, noninferiority; PY, person-years; TAF/FTC, tenofovir alafenamide/emtricitabine.

TAF due to this lower plasma exposure.[59] Of note, in the context of HIV treatment (ie, not PrEP), switching patients who show a decline in bone mineral density from TDF-containing to alternative ART regimens was shown to increase bone mineral density, but the clinical significance of this increase remains unknown.[60]

While TAF/FTC appears to have safer kidney and bone toxicity profiles than TDF/FTC, TDF/FTC is associated with lower lipid levels and weight loss.[45,53,57,61] However, the CDC PrEP guidelines do not provide further parameters for consideration when choosing between these 2 PrEP regimens.[19] Other, less significant or transient adverse effects of TDF/FTC include asthenia, headache, nausea, vomiting, diarrhea, flatulence, minor decreases in high-density lipoprotein (HDL), low-density lipoprotein (LDL), and total cholesterol, and minor weight loss.[53] TAF/FTC may be associated with headache, nausea, diarrhea, minor increases in LDL cholesterol and triglycerides, and minor weight gain (**Table 3**).[57]

Drug-Drug Interactions

Potential drug-drug interactions (DDIs) with TDF/FTC or TAF/FTC are listed in **Table 4**.[36,37,50] As the incidence of hepatitis C virus (HCV) is increased in populations at risk of HIV acquisition, first-line HCV direct-acting antiviral (DAA) regimens are included, even those with no potential DDIs.

The *start-up syndrome* of headache, nausea, and flatulence occurring in the first month of TDF/FTC use as PrEP occurs in a minority of patients and typically resolves within 3 months, sooner for many patients. Patients should be forewarned of this possibility, instructed on the use of over-the-counter medications for symptom management, and educated regarding more serious signs and symptoms—such as those of acute HIV infection—that should be reported on an urgent basis.[42,67]

CAB LAI

In December 2021, the US FDA approved injectable CAB as the first long-acting injectable for HIV PrEP, representing a major change in the treatment landscape.[68] This agent is administered as an intramuscular (IM) injection every 2 months after 2 initial injections that are given 1 month apart.[66] It is indicated for at-risk adults and adolescents weighing at

TABLE 3. Comparison of TDF/FTC and TAF/FTC Side Effects/Adverse Effects[53,57,61]

TDF/FTC	TAF/FTC
Renal[45,53,62] • Contraindicated if eCrCl <60 mL/min/1.73 m^2 • Small decrease in eGFR (-2.0 mL/min/1.73 m^2)	**Renal[57]** • Not recommended if eCrCl <30 mL/min/1.73 m^2 • Small increase in eGFR (2.0 mL/min/1.73 m^2)
Bone Mineral Density[45,53] • Mean decreases from baseline ranged from -0.4% to -1.0% across total hip, spine, femoral neck, and trochanter • DEXA scans to monitor bone mineral density are not indicated for routine care • Consider discussing impact upon bone density with young people who are still growing	**Bone Mineral Density[57]** • Mean increases from baseline to week 48 of 0.5% at lumbar spine and 0.2% at hip
Lipids[57] • Lowered LDL cholesterol and triglyceride levels	**Lipids[45,57]** • Increased triglyceride and LDL cholesterol levels • Monitor triglyceride and cholesterol levels every 12 months • Lipid-lowering medications should be prescribed when indicated
Mean Body Weight[63,64] • Asthenia, headache	**Mean Body Weight[63,64]** • Mean increase 1.1 kg • Although weight gain has been reported in PrEP clinical trials, these results suggest that TDF has a weight suppressive effect, which drives differences when comparing TDF with other agents such as TAF

ART, antiretroviral therapy; DEXA, dual-energy X-ray absorptiometry; eCrCl, estimated creatinine clearance; eGFR, estimated glomerular filtration rate; LDL, low-density lipoprotein.

TABLE 4. Potential DDIs Involving TDF/FTC, TAF/FTC, or CAB[53,57,65,66]

PrEP	Drug Class or Characteristic	Recommendation
TDF/FTC[36]	Drugs that could potentially reduce renal function or compete for active renal tubular secretion: • Acyclovir • Valacyclovir • Cidofovir • Ganciclovir • Valganciclovir • Aminoglycosides • High-dose or multiple NSAIDs	• Caution • Monitor for dose-related renal toxicities
	First-line HCV direct-acting antivirals[45]	• EBR/GZR: No interactions expected • GLE/PIB: No interactions expected • SOF/LDV: Serum concentrations of TDF may be increased; monitor for toxicities • SOF/VEL: Serum concentrations of TDF may be increased; monitor for toxicities
TAF/FTC[57]	Anticonvulsants: • Carbamazepine • Oxcarbazepine • Phenobarbital • Phenytoin	• Reduced TAF concentration • Alternate anticonvulsant advised
	Antimycobacterials: • Rifabutin • Rifampin • Rifapentine	• Reduced TAF concentration • TAF/FTC coadministration not advised
	Herbal products: • St. John's wort	• Reduced TAF concentration • TAF/FTC coadministration not advised
	First-line HCV DAAs[56]	• EBR/GZR: No interactions expected • GLE/PIB: No interactions expected • SOF/LDV: No interactions expected • SOF/VEL: No interactions expected
CAB[66]	Anticonvulsants: • Carbamazepine • Oxcarbazepine • Phenobarbital • Phenytoin Antibiotics: • Rifampin • Rifapentine	• Do not coadminister with CAB
	Antibiotic: • Rifabutin	• When started before or concomitantly with 1st CAB injection, the recommended dose of CAB is a 600 mg injection, and 2 weeks later a 2nd 600 mg injection, and monthly thereafter while on rifabutin • When started at time of 2nd injection or later, the recommended dosing of CAB is 600 mg monthly while on rifabutin

CAB, cabotegravir; DAA, direct-acting antiviral; DDI, drug-drug interaction; EBR/GZR, elbasvir/grazoprevir; GLE/PIB, glecaprevir/pibrentasvir; HCV, hepatitis C virus; NSAID, nonsteroidal anti-inflammatory drug; SOF/LDV, sofosbuvir/ledipasvir; SOF/VEL, sofosbuvir/velpatasvir.

least 35 kg.[66] This LAI may be critical in aiding high-risk individuals for whom adherence to daily medications poses a major challenge.[45]

Results of the HIV Prevention Trials Network 083 (HPTN 083) study of the efficacy of the integrase inhibitor CAB as an LAI for HIV prevention yielded encouraging findings. This National Institutes of Health (NIH)-funded multisite

study of 4566 cisgender MSM and trans women who have sex with men randomized participants to receive CAB as a long-acting injectable every 8 weeks or daily oral TDF/FTC. HPTN 083 was terminated in early 2020 after the CAB group was shown to have statistically superior outcomes when compared with the TDF/FTC group, with the CAB group showing 66% lower risk of HIV infection. It should be noted that both study groups received highly effective HIV-prevention regimens: incidence rates of HIV infection were 0.41% in the cabotegravir group, and 1.22% in the TDF/FTC group (**Figure 8**).[69]

HPTN 084 was a phase 3 trial designed to track roughly 3200 women of childbearing age in sub-Saharan Africa over a 4.5-year period.[70] While both methods were highly effective—HIV incidence of 0.21% (95% CI 0.06%–0.54%) in the CAB group and 1.79% (95% CI 1.24%–2.51%) in the TDF/FTC group— long-acting CAB was 89% (95% CI 68%-96%) more effective than TDF/FTC.[70,71] The study was terminated early (November 2020) because of this demonstration of CAB's statistically based superiority.[71] No dosage adjustment is necessary for patients on CAB who have reduced renal function.[66] **Table 4** lists potentially significant drug interactions; note the lack of interactions between CAB and polyvalent cations, which interact with oral INSTIs.

In the HPTN 083 and 084 trials, injection-site reactions (eg, pain, tenderness, induration) were the most frequent adverse effects associated with CAB (82%). These reactions occurred most frequently after the first 2 or 3 injections. According to the CDC, patients should be instructed to take an over-the-counter pain medication within a couple of hours before or after the injection and continue as needed for 1 to 2 days. Also, the patient may apply a warm compress or heating pad to the injection site for 15 to 20 minutes after the injection.[45]

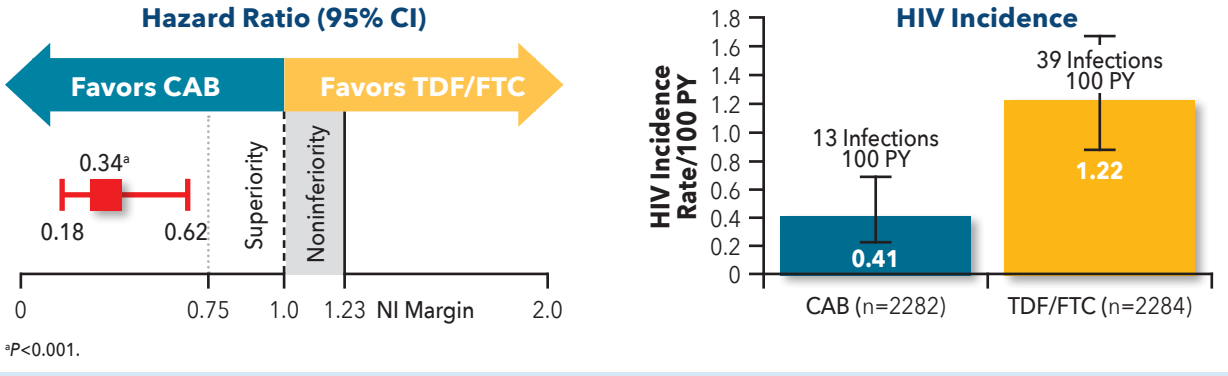
Determining PrEP Eligibility[45]

The CDC now recommends that all sexually active adult and adolescent patients be informed about HIV PrEP and that PrEP should not be withheld from HIV-uninfected patients who request it.[45] In light of this expanded approach, the updated 2021 *CDC Clinical Practice Guidelines* provide criteria for determining how to identify sexually active teens, adults, and PWID at substantial risk of acquiring HIV infection. They also delineate who is clinically eligible for daily oral PrEP and for long-acting injection for PrEP (**Table 5**). Clinicians should:

- Conduct a comprehensive behavioral risk assessment (sexual; injection drug use) to identify appropriate PrEP candidates. (See also *Embracing Sexual Wellness: Sexual Health, Well-being, and Trauma-Informed Care*, page 27)
  - **Figures 9** and **10** are 2 algorithms to help assess whether patients should merely be told about PrEP or it should be prescribed
  - The behavioral assessment may reveal additional needs for in-depth education, risk-reduction counseling, and community-based patient-support services
- Assess the patient for common signs and symptoms suggestive of acute HIV infection (**Table 6**)
- Document evidence of HIV-negative status with use of
  - An FDA-approved blood test, or CLIA-waived rapid point-of-care fingerstick blood test performed within 7 days of therapy initiation (CLIA-waived indicates that under the Clinical Laboratory Improvement Amendments, a laboratory test can be conducted without the need for more stringent standards)
  - This is for both oral PrEP and CAB

The CDC now recommends that all sexually active adults and adolescents should receive information about PrEP, and PrEP should not be withheld from HIV-uninfected patients who request it.[45] While this recommendation may seem simple, it could have a dramatic impact on ending the HIV epidemic if fully implemented by clinicians.

FIGURE 8. Results of the HIV Prevention Trials Network 083 Comparing CAB To TDF/FTC in Cisgender Men and TGW[69]



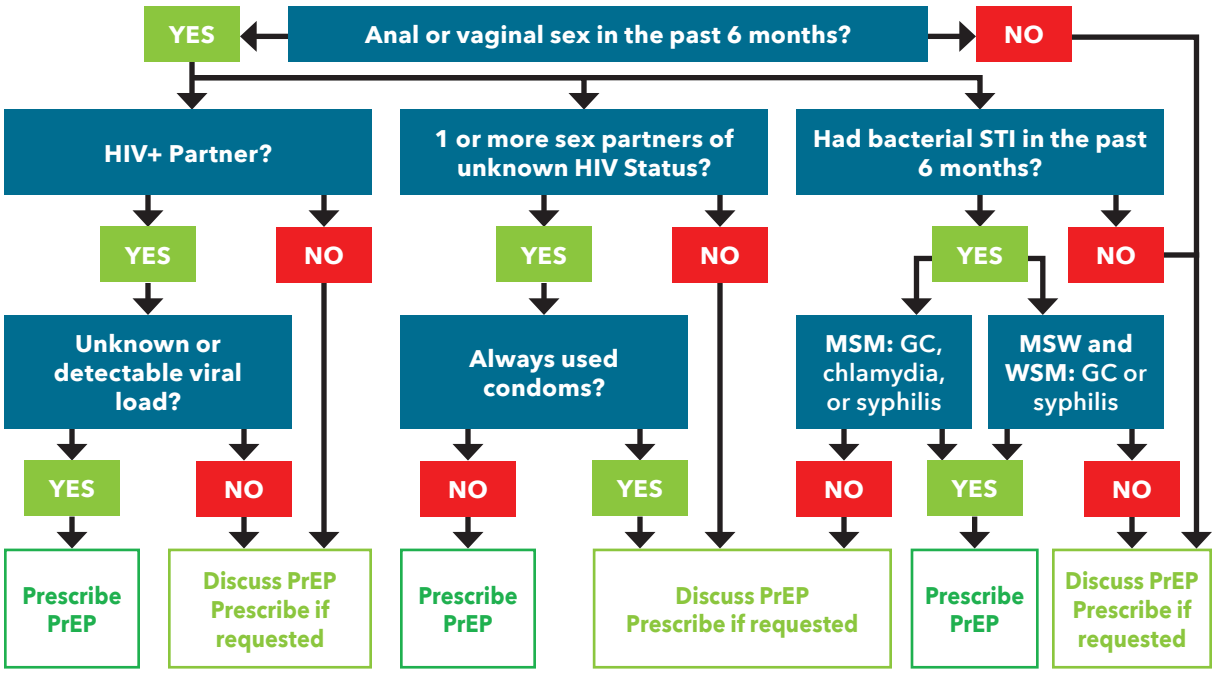
aP<0.001.

- Document evidence of HIV-negative status with use of an HIV-1 RNA assay
  - If initiating CAB
  - If initiating oral PrEP AND there has been a recent exposure with someone in a high incidence population, or there are signs/symptoms of acute or primary HIV
  - Guidelines state, however, that you may initiate PrEP if you are waiting for the RNA assay results, as long as you have the documented negative HIV Ag/Ab
- Perform baseline (pretreatment) laboratory assessment

TABLE 5. Clinical Guidance for Identifying Risk of HIV Infection and Determining Clinical Eligibility for PrEP[45]

	Sexually Active Adults and Adolescents	PWID
Substantial Risk of Acquiring HIV Infection	Anal or vaginal sex in past 6 months AND any of the following: • HIV-positive sexual partner • Bacterial STI in past 6 months (gonorrhea, chlamydia, or syphilis) • History of inconsistent or no condom use with sexual partners	• HIV-positive injecting partner **OR** • Sharing injection equipment
Clinical Eligibility for Oral PreP	All of the following: • Negative HIV Ag/Ab test result within 1 week before initially prescribing oral PrEP • No signs/symptoms of acute HIV infection • Estimated creatinine clearance ≥30 mL/min/1.73 m^2 • No contraindicated medications or conditions	
Clinical Eligibility for CAB LAI	All of the following: • Negative HIV Ag/Ab test result within 1 week before initially prescribing oral PrEP • Negative HIV-1 RNA assay • No signs/symptoms of acute HIV infection • No contraindicated medications or conditions	

FIGURE 9. Assessing PrEP Eligibility in Sexually Active Teens and Adults[45]



GC, gonorrhea; MSW, men who have sex with women; WSM, women who have sex with men.

FIGURE 10. Assessing PrEP Eligibility In PWID[45]

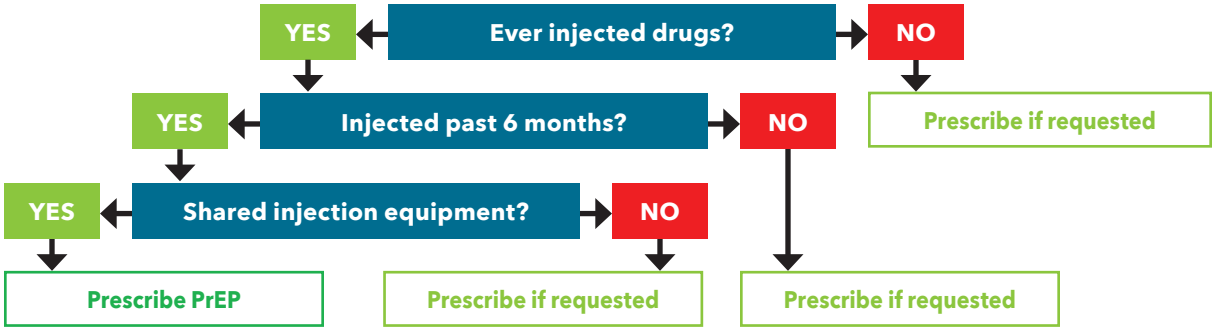


TABLE 6. Signs and Symptoms Associated With Acute HIV Infection[45]

• Fever	• Myalgia/arthralgia	• Adenopathy: cervical, axillary, inguinal
• Rash	• Headache	• Night sweats
• Fatigue	• Pharyngitis/tonsillitis	• Diarrhea

Confirming HIV-Negative Status

HIV testing is required to confirm that patients do not have HIV infection when they start taking PrEP. Based on the latest updated 2021 CDC guidelines, required testing differs for patients who have or do not have recent antiretroviral PrEP use. Recent use is defined as taking oral PrEP in the last 3 months or taking long-acting injectable (LAI) PrEP in the past 12 months. For individuals who are starting or restarting PrEP after a long period without treatment, the clinician should test using a laboratory-based HIV 1/2 Ag/Ab test. For patients who are taking or have recently taken oral or LAI PrEP, the patient should be tested using an HIV Ag/Ab test and an HIV-1 RNA test.[45]

A negative HIV test following a high-risk exposure should always be clinically correlated with any signs or symptoms of acute HIV infection and repeat testing after the window period is advised.[43,44] **Figure 11** illustrates the HIV testing guidance that should be used to determine PrEP eligibility. Ag/Ab tests utilizing blood from a vein can usually detect HIV infection 18–45 days after an exposure, whereas rapid Ag/Ab tests with finger-prick blood may detect HIV 18–90 days after exposure (**Figure 5**).[43,44,72] Other HIV tests are recognized and allowed, but it is crucial to remember the limitations of Ab-only tests. CDC-approved, CLIA-waived rapid HIV tests, suitable for use in nonclinical settings, and involving fingerstick or venous whole blood, include but are not limited to the following:

- Chembio SURE CHECK® HIV 1/2 Assay
- Clearview® HIV 1/2 STAT-PAK®
- Alere Determine™ HIV-1/2 Ag/Ab Combined Test
- INSTI® HIV-1/HIV-2 Ab Test
- Uni-Gold™ Recombigen® HIV- 1/2 Ab Test

Only the Alere Determine™ test is an HIV 1/2 Ag/Ab assay; all others listed test only for antibodies to HIV-1 and HIV-2.[73]

The following may be performed using oral-fluid swab (or fingerstick or venous whole blood). Note, however, oral-fluid swabbing should *not* be used to document HIV status.

- Chembio DPP® HIV-1/2 Assay (oral test; not acceptable for confirmation of HIV status)
- OraQuick ADVANCE® Rapid HIV-1/2 Ab Test[73]

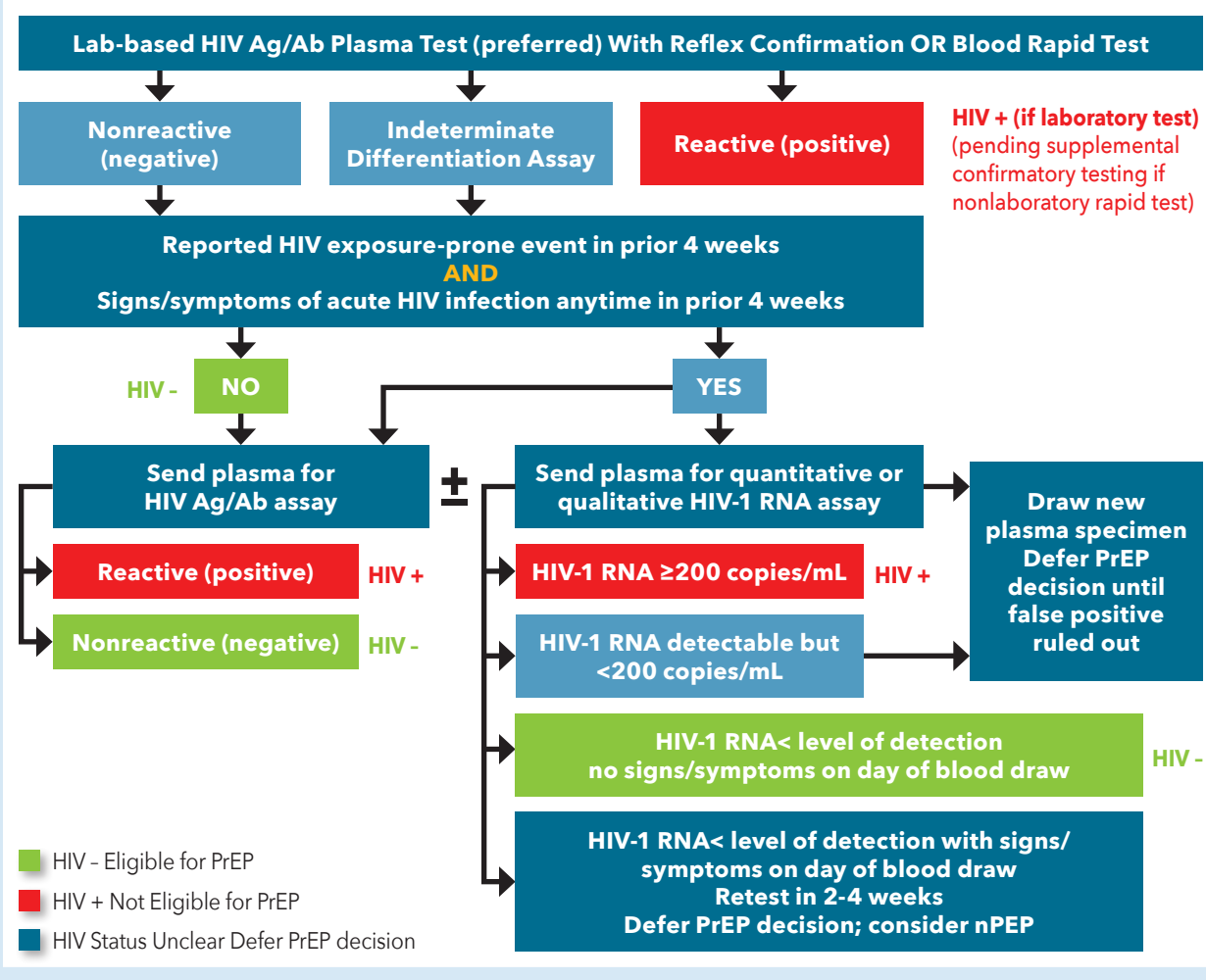
Rapid tests using finger-prick or venous whole blood can yield results in approximately 10 minutes. Oral HIV tests are not recommended in these clinical scenarios.[42] The CDC provides a website listing FDA-approved HIV diagnostic tests including a list of CLIA-waived tests: https://www.cdc.gov/hiv/testing/ laboratorytests.html.

The 2021 CDC Update requires that patients also have an HIV-1 RNA assay in the following situations as it may detect HIV infection early enough to avoid or limit integrase inhibitor resistance should CAB LAI fail to prevent infection:[74]

- Prior to initiating CAB
- Prior to initiating oral PrEP AND there has been a recent exposure with someone in a high incidence population, or there are signs/symptoms of acute or primary HIV

Guidelines state, however, that you may initiate PrEP if you are waiting for the RNA assay results, as long

FIGURE 11. HIV Testing Algorithm[45]



as you have the documented negative HIV Ag/Ab. Positive HIV tests must be confirmed with more specific conventional blood tests, with results available in <1 hour to several days.

Initiating and Managing Oral PrEP

Pre-PrEP Laboratory Testing, Screening, and Dosing

Besides confirming that the patient is HIV-negative, there are a number of other laboratory tests that should be completed prior to initiating oral PrEP (**Table 7**) The most critical is the estimated creatinine clearance (as calculated using the Cockcroft-Gault equation):

- If eCrCl <60 mL/min/1.73 m^2, TDF/FTC is not recommended; reduced-dosing strategies for TDF/FTC as PrEP have not been developed[45]
- If eCrCl 15 to <30 mL/min/1.73 m^2, TAF/FTC is not recommended[57]
- If eCrCl <15 mL/min1.73 m^2 TAF/FTC is not recommended unless receiving chronic hemodialysis (on days of hemodialysis, administer the daily dose of TAF/FTC after completion of hemodialysis treatment[57]

Pretreatment evaluation of hepatitis B (HBV) serology is equally important. Although HBV infection is not a contraindication to the use of PrEP, HBV status must be known and documented prior to PrEP initiation, as discontinuation of PrEP may be associated with acute exacerbation of HBV. Patients positive for hepatitis B surface antigen (HBsAg) should be referred to an appropriate clinician for evaluation for HBV treatment.[45]

Although TDF/FTC is a safe and effective HIV-prevention strategy for women who are at substantial risk of HIV acquisition including during conception, pregnancy, and the postpartum period, a pregnancy test is recommended for any woman of childbearing potential. Note: TAF/FTC is not approved in those having receptive vaginal sex. Continuing TDF/ FTC during breastfeeding may be beneficial for some women; however, the long-term safety of infant exposure to TDF/FTC has not been determined. TDF/FTC does not reduce the effectiveness of oral contraceptives.[45]

All patients should be screened for STIs and those considering TAF/FTC should have a lipid screen.

TABLE 7. Getting Started With Oral PrEP: Lab Testing, Screening, and Prescribing[45]

Test/Prescribe	Oral PrEP Initiation
HIV Status	• HIV Ag/Ab test (lab preferred)
Renal Status (eCrCl)	• >60 mL/min/1.73 m^2 (TDF/FTC or TAF/FTC) • >30 mL/min/1.73 m^2 (TAF/FTC)
STI Status	• Syphilis serology for all • Rectal, urinary, pharyngeal for all – Neisseria gonorrhoeae (GC) – Chlamydia trachomatis (CT)
Lipid Screen	• Only for persons prescribed TAF/FTC
Hepatitis Screen	• Hepatitis B surface antigen/antibody • Hepatitis C Ab test
Pregnancy Test	• For women of childbearing potential
Prescribe	• 90-day supply TDF/FTC **OR** • 90-day supply TAF/FTC (for MSM and TGW only) **OR** • 30-day supply TDF/FTC for On-Demand regimen (for MSM and TGW only)

TGW, transgender woman.

Patient Counseling

Having established the patient's eligibility for oral PrEP, the following actions should be taken[45]:

- Educate patients about the PrEP medications and available regimens to maximize safe use
- Decide which therapy/mode of administration will be prescribed
- Provide counseling and effective contraception to women on PrEP who do not wish to become pregnant (only TDF/FTC can be used in those having vaginal sex)
- Provide other patient-centered counseling regarding the following:
  - Medication adherence to achieve and maintain protective tissue levels
  - HIV risk reduction; including discussion/provision of prevention-services referrals
- Review PrEP discontinuation and resumption requirements and how to switch from daily to on-demand and vice versa

Selecting and Dosing Daily Oral TDF/FTC or TAF/FTC

Once the patient's eligibility is established, consider the following when selecting TDF/FTC or TAF/FTC[45,57]:

- Renal function: TDF/FTC should not be prescribed for individuals whose eCrCl is <60 mL/min/1.73 m^2, because of TDF's renal clearance
- Bone density (especially if the patient is over 50 years of age)
- Cholesterol
- Weight change
- Mode of sexual exposure may influence PrEP regimen selection: as mentioned previously, TAF has not been approved for those at risk through receptive vaginal sex[19]
- Potential for drug-drug interactions should be assessed based on all currently taken medications

In real-world clinical practice, selection of PrEP regimen may come down to the practical concerns of insurance coverage and cost.[26] A generic formulation for TDF/FTC became available as of October 2020, but TAF/FTC is available only in brand form.[28]

Dosing

- TDF/FTC: one 300 mg (TDF) /200 mg (FTC) tablet once daily with or without food, in individuals weighing at least 35 kg[45]
- TAF/FTC: one 25 mg (TAF)/200 mg (FTC) tablet once daily with or without food, in individuals weighing at least 35 kg[57]

Selecting and Dosing On-Demand/2-1-1 Oral PrEP

While not CDC-recommended or FDA-approved, evidence-based on-demand or event-driven protocols for TDF/FTC are endorsed by other organizations. For example, 2-1-1 (also known as event-driven, intermittent, or on-demand), is a PrEP dosing protocol specifically

recommended for MSM engaging in anal sex without condoms (not for vaginal sex) by the International Antiviral Society–USA (IAS–USA) and the World Health Organization (WHO).[75,76] Named on the basis of the number and timing of PrEP tablets taken, 2-1-1 provides the following recommendations (**Figure 12**)[45,52]:

- A loading dose of 2 TDF/FTC tablets is taken 2–24 hours before anal sex
- A third tablet is taken 24 hours after the first dose
- A fourth tablet is taken 24 hours later
- If there is another sexual exposure within 7 days of the last dose, 1 tablet is taken 2–24 hours before anal sex, 1 tablet 24 hours after the first dose, then 1 tablet 24 hours after the second dose
- The efficacy of this dosing protocol was demonstrated in the IPERGAY study, the scope of which was limited to TDF/FTC. The preceding 2-1-1 recommendations do not apply to TAF/FTC[45,52,75]

Initiating and Managing CAB LAI PrEP

Pre-PrEP Laboratory Testing, Screening, and Dosing

In addition to the 2 oral PrEP therapies, an IM LAI is now available. The FDA approved CAB LAI for at-risk adults and adolescents weighing at least 35 kg[66] who report sexual behaviors that place them at substantial risk of HIV exposure and acquisition.[45] Any sexually active adult or adolescent can use CAB.

As with the oral treatments, the first step is confirming that the patient is HIV-negative; other laboratory tests include STI screening prior to initiating CAB LAI (**Table 8**).[45]

Screening for PrEP Patients Receiving CAB

Patients must be tested for HIV-1 infection prior to both initial and subsequent injections of CAB using a test approved by the FDA for the diagnosis of HIV-1 infection.[66] HIV-1 RNA assay is not required at baseline but is recommended at 1 month and subsequent visits when CAB is the PrEP medication. Ideally, this testing should be conducted within 1 week prior to the initiation visit.[45] If clinicians want to administer the first injection at the initial PrEP evaluation visit based on findings of a rapid combined Ag/Ab assay, blood should always be subsequently drawn for laboratory confirmatory testing that encompasses an HIV RNA assay.[45]

Dosing

Interestingly, clinicians may initiate with CAB oral lead-in therapy prior to IM injections or may proceed directly to IM injections (600 mg [3 mL injection, gluteal only]) without oral lead-in.

FIGURE 12. On-Demand/2:1:1 PrEP Dosing With TDF/FTC[45]

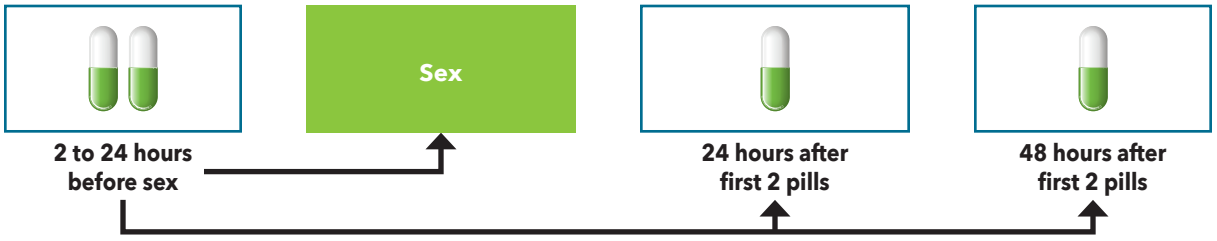


TABLE 8. Getting Started With CAB LAI: Lab Testing, Screening, and Prescribing[45]

Test/Prescribe	Oral PrEP Initiation
HIV Status	• HIV Ag/Ab test • HIV-1 RNA assay
STI Status	• Syphilis serology for all • Rectal, urinary, pharyngeal GC/CT
Pregnancy Test	• For women of childbearing potential
Prescribe	• Provide CAB injection at initiation visit and again 1 month later **OR** • Provide CAB daily oral lead-in for 4 weeks at initiation visit, injection 1 month later, another injection 1 month later • Thereafter, injections are given every 2 months

Without oral lead-in: CAB is administered every 2 months after 2 initial injections that are given 1 month apart.[66] That is:

- 1st injection at the initiation visit
- 2nd injection at the first follow-up visit 1 month later
- 3rd injection at the next follow-up visit 2 months later; all subsequent injections are given every 2 months (as long as the patient is HIV-negative)

With oral lead-in: Approved dosing for the oral lead-in therapy is 30 mg once daily for approximately 1 month. At the time of this publication, oral CAB is only available through 1 specialty pharmacy (Theracom). The injection should then be administered on the last day of oral lead-in, or within 3 days after.[66] That is:

- Oral daily CAB prescription (for 4 weeks) is given at initiation visit
- 1st injection at the first follow-up visit 1 month later on the last day or within 3 days of last oral lead-in
- 2nd injection at the next follow-up 1 month later
- 3rd injection at the next follow-up visit 2 months later; all subsequent injections are given every 2 months (as long as the patient is HIV-negative)

Missed Doses With CAB

Adherence to the CAB injection dosing schedule is strongly encouraged. Patients who miss a scheduled dose of CAB should be clinically reassessed to ensure that resumption of CAB remains appropriate.[66] Refer to **Table 9** for dosing recommendations after missed injections.

If a patient plans to miss a scheduled every-2-month continuation injection of CAB by more than 7 days, the pharmacist should instruct the individual to take daily oral CAB for up to 2 months to replace 1 missed scheduled every-2-month injection. The recommended oral daily dose of CAB is 30 mg daily. The initial dose of oral CAB should be taken approximately 2 months after the last injection of CAB. The patient should restart injection with CAB on or within 3 days of the day oral dosing ends.[66]

Pharmacist-Led Administration of CAB

Community pharmacists can administer the optional oral lead-in dosing for CAB but are not able to give the intramuscular injection; adjustments are required in pharmacies and provider offices to establish workflow processes that are safe and efficient for providing these injections.[77]

Monitoring and Counseling Patients on PrEP

Time to Protection

Time to maximum HIV prevention varies with mode of sexual exposure and type of PrEP taken. **Table 10** presents the time to maximum HIV protection when using oral PrEP. Time to protection with CAB LAI is currently unknown.[78] Patients should be advised that condom use is critical while tissue concentrations remain low, and that ongoing, consistent use of condoms is necessary for the prevention of both HIV and other STIs.[45]

Effective HIV prevention requires a high level of daily adherence to the PrEP medication, but there is some leeway for missed doses. The STRAND trial showed that 6 to 7 doses of oral PrEP per week are necessary to maintain protective vaginal tissue concentration; fewer doses per week may be adequate to maintain colorectal tissue concentrations. Nonetheless, daily adherence

TABLE 9. Injection Dosing Recommendations of CAB After Missed Injections[66]

	Time Since Last Injection	Recommendation
If second injection is missed and time since first injection is:	**≤2 months**	• Administer a 600-mg injection of CAB as soon as possible, then resume the every-2-month injection dosing schedule
	>2 months	• Restart with a 600-mg CAB injection, followed by a second 600-mg injection 1 month later. Then, continue to follow the every-2-month injection dosing schedule thereafter
If third or subsequent injection is missed and time since prior injection is:	**≤3 months**	• Administer a 600-mg injection of CAB as soon as possible, then continue with the every-2-month injection dosing schedule
	>3 months	• Restart with a 600-mg injection of CAB, followed by the second 600-mg initiation injection dose 1 month after. Then, continue with the every-2-month injection dosing schedule thereafter

TABLE 10. Time to Maximum HIV Protection (Tissue Concentration) With Oral PrEP, by Mode of HIV Exposure[78]

HIV-Exposure Mode	Approximate Time to Maximum Protection[a]
Receptive anal sex	7 days
Receptive vaginal sex	21 days
Injection drug use	21 days
Insertive anal sex	Unknown
Insertive vaginal sex	Unknown

[a]The times above only refer to use of oral PrEP as the time to protection is currently unknown with CAB LAI.

should be stressed for all persons on oral PrEP. Should a patient report missing a dose, instruct the patient to take the single missed dose as soon as it is remembered. If, however, it is nearly time for the next dose, the patient should proceed with the regular dosing schedule.[45]

Supporting the Patient's PrEP Adherence

Key tactics for successful medication-adherence counseling include the following:

- Simplified education and explanations, eg, dosage schedule, impact of adherence on PrEP efficacy
- Strategies that address patient-specific adherence barriers; eg, substance use
- Nonjudgmental adherence monitoring; eg, normalizing occasional missed doses, reinforcing success, encouraging condom use

PrEP adherence is supported by effective HIV risk-reduction education. Counseling should include information about substance use and protection from STIs with consistent condom use.[45,78] Whether recreational and/or associated with injection practices, psychotropic substances may decrease inhibitions, increase risk tolerance, and reduce self-efficacy with regard to risk-reduction practices.[79] Patients also should be reminded that PrEP does not protect against other STIs. Such personal risk-reduction practices—with emphasis on consistent condom use—remain critical, even when one is using PrEP. Adherence should also include:

- Acknowledgment of the effort required for behavior change
- Reinforcement of success
- Assistance with turning around any missteps along the way[45]

As adverse effects may impact PrEP adherence, pharmacists should counsel patients regarding the following concerns[45]:

- Common side effects for oral PrEP (headache, nausea, and flatulence) typically resolve within the first month of taking PrEP (start-up syndrome) using over-the-counter medications for symptom management
- Common side effects for CAB include mild to moderate injection-site reaction; in clinical trials 4% reported diarrhea, nausea, pyrexia, and fatigue.
- Signs or symptoms of acute HIV infection or acute renal injury, both of which require urgent intervention

Patient Monitoring: Oral PrEP

The following table provides a comprehensive look at CDC guidelines for oral on-PrEP interval laboratory testing and patient monitoring (**Table 11**).[45]

Stopping and Restarting Oral PrEP

Patients should receive specific counseling on how to safely discontinue and restart PrEP. Discontinuation may be prompted by the individual's personal choice, changed life circumstances, non-tolerated side effects, toxicities, chronic nonadherence, or acute HIV infection (AHI). The protection provided by PrEP wanes over the 7–10 days following discontinuation; therefore, alternative methods to reduce risk of HIV acquisition should be discussed, including the emergent use of PEP in the event of a high-risk exposure.[45]

Per CDC guidelines, PrEP discontinuation for any reason should be documented by the PrEP provider. This should include HIV status at the time of discontinuation, reason for discontinuation, recent PrEP adherence, and reported sexual risk behavior. Should the patient choose to restart oral PrEP, screening and prepresscription evaluation are the same as for someone newly beginning oral PrEP. The PrEP provider should engage the patient in an open discussion regarding change in personal circumstances and commitment to PrEP adherence.[45]

Patient Monitoring: CAB LAI PrEP

The following table provides a comprehensive look at CDC guidelines for CAB LAI interval laboratory testing and patient monitoring (**Table 12**).[45]

Stopping CAB LAI

CAB has a long "tail" of gradually declining drug levels when discontinuing the injections. At some point during this "tail" phase, it's possible CAB levels will fall below a protective threshold and persist for some time at nonprotective levels, exposing the patient to the risk of HIV acquisition. In the HPTN 077 trial, the median time to undetectable CAB plasma levels was 44 weeks for men and 67 weeks for women with a wide range for both sexes. While there is a risk of developing a drug-resistant strain if HIV infection is acquired during that time, this has not been borne out in the small number of tail-phase incident HIV infections observed. Therefore:

- Remind patients of the importance of keeping their follow-up appointments if they decide to discontinue CAB for PrEP

TABLE 11. Baseline Assessment, Laboratory Testing, and Monitoring for Oral PrEP[45]

Test	Initiation	Every 3 months	Every 6 months	Every 12 Months
HIV Assessment • Signs/symptoms of AHI • Discuss whether continued need for PrEP; adherence, side effects, barriers, etc	X	X	X	X
HIV Status • HIV Ag/Ab test (lab preferred) • HIV-1 qualitative RNA	X	X		
Hepatitis B and C screens	X	X (if not done at initiation)		
STI Screen • For MSM/TGW	X	X	X	X
STI Screen • For heterosexually active men and women	X		X	X (CT only every 12 months)
Renal Status: eCrCl • >60 mL/min/1.73 m^2 (TDF/FTC or TAF/FTC) • >30 mL/min/1.73 m^2 (TAF/FTC)	X			X
Renal Status • If at baseline age >50 years **OR** • eCrCl <90 mL/min/1.73 m^2 (TAF/FTC or TDF/FTC)	X		X	X
Lipid Screen • Only for person prescribed TAF/FTC	X			X
Pregnancy Test • For women of childbearing potential; suggested, but no longer in guidelines	X	X	X	X

AHI, acute HIV infection.

- Initiate an individualized discussion about ongoing HIV prevention if a patient no longer wants to receive CAB LAI, but remains at-risk for HIV infection
  - This may include oral PrEP options in combination with other effective HIV prevention behavioral changes, including universal condom use
  - Patients who want to switch to oral PrEP may do so within 8 weeks of last CAB injection
- Perform all screening as if new to therapy prior to restarting if a patient wishes to resume PrEP therapy with CAB
- The US FDA recommends quarterly HIV RNA testing over 1 year after the last injection.[45]

Tear-Out Inserts of the CDC Clinical Guidelines Summary Tables

For your convenience we have included the full tables provided in the CDC updated guidelines for both oral and CAB PrEP (**Table 13; Table 14**)

PrEP in Adolescents

In the US, TDF/FTC is approved by the FDA for use as PrEP in adolescent patients who weigh at least 35 kg.[53] TAF/FTC is also approved for use as PrEP in adolescent patients who weigh at least 35 kg and do not engage in receptive vaginal sex.[57] Moreover, CAB is also indicated for use as PrEP in adolescents.[66] Young MSM are at particularly high risk for acquiring HIV.[80,81] Among MSM aged 13 to 24 years, the rate of new infections increased by 43% from 2003 to 2014.[81]

The Adolescent Trials Network (ATN) studied daily TDF/FTC PrEP in 78 patients 15 to 17 years of age. TDF/FTC was well tolerated among those who took their medication; however, adherence was suboptimal for many of the youth (protective levels of tenofovir were found in approximately 50% at 12 weeks when they were being seen every 4 weeks, but only in 22% at 48 weeks when visits were quarterly).[82] The findings from this study suggest that potential barriers to adherence

TABLE 12. Baseline Assessment, Laboratory Testing, and Monitoring for CAB LAI[45]

Test	Initiation	1 Month Visit	Every 2 Months	Every 4 Months	Every 6 Months	Every 12 Months	When Stopping CAB
HIV Assessment • Signs/symptoms of AHI • Discuss whether continued need for PrEP; adherence, side effects, barriers, etc	X		X	X	X	X	
HIV Status • HIV Ag/Ab test (lab preferred) • HIV-1 qualitative RNA	X (HIV-1 RNA assay is not needed at initiation)	X	X	X	X	X	X
STI Screen • For MSM/TGW	X		X	CT Only	X	X	
STI Screen • For heterosexually active men and women	X				X (GT/ Syphilis only)	X (CT only every 12 months)	
Pregnancy Test • For women of childbearing potential; suggested, but no longer in guidelines	X					X	

should be identified and addressed. Furthermore, for younger MSM, more frequent pharmacy-patient contact may be important.

In addition to addressing adherence, pharmacists must weigh the potential risk of bone effects with the relative risk of acquiring HIV. The bone loss seen with TDF may pose additional risks in adolescents, however, data indicate that any effects are reversed upon discontinuation of TDF.[45,83]

Laws and regulations that may be relevant for PrEP-related services provided to adolescent minors by pharmacists differ by jurisdiction. Pharmacists considering providing PrEP to a patient <18 years old must be aware of applicable local laws, regulations, and policies. The following website from the CDC outlines the differences among states in the US: https://www.cdc.gov/hiv/policies/law/states/minors.html. Pharmacists should discuss any limits of confidentiality based on these local laws, regulations, and policies.[45]

PrEP Resistance or Failures: Transitioning From PrEP to HIV Treatment

Patients taking PrEP may become HIV-positive for various reasons. If detected at the first follow-up visit after PrEP initiation, it may be due to the patient having had undetectable acute infection at the time of pre-PrEP HIV testing (ie, within the window period). If detected at a later follow-up visit, this may indicate adherence issues.[45] Rarely, some patients become HIV-positive despite good PrEP adherence: risk of HIV acquisition is not completely eliminated by high levels of adherence and may be due to drug-resistant viral strains.[84]

Among patients who become infected with HIV while receiving PrEP, most are unlikely to develop drug-resistant virus.[47,48,50,51] In a meta-analysis that evaluated drug resistance in 6 clinical trials, drug resistance was identified in 6 of the 533 patients who became infected with HIV after enrollment, and 8 of the 44 patients who had undiagnosed acute HIV infection at study entry.[85]

In patients who develop drug-resistant virus while taking PrEP, the M184V mutation is most likely to emerge since the genetic barrier to emtricitabine is low.[86] Exposure to study drug was believed to cause drug resistance in 4 of the 33 females in the Fem-PrEP trial and in 2 of the 51 patients in the Partners PrEP study.[50,87] Among those who developed resistance, the M184V emtricitabine resistance mutation arose most frequently.[50,87]

Individuals receiving PrEP may be infected with drug-resistant HIV. In a case report, a patient became infected with HIV that contained drug resistance mutations for several classes of agents, including tenofovir and emtricitabine.[88] Transmission occurred despite tenofovir levels that were consistent with recent administration of the drug and long-term adherence.[88]

TABLE 13. TEAR-OUT PAGE OF GUIDELINES FOR ORAL PrEP[45]

	Sexually-Active Adults and Adolescents[1]	Persons Who Inject Drugs[2]
Identifying substantial risk of acquiring HIV infection	Anal or vaginal sex in past 6 months AND any of the following: • HIV-positive sexual partner (especially if partner has an unknown or detectable viral load) • Bacterial STI in past 6 months[3] • History of inconsistent or no condom use with sexual partner(s)	• HIV-positive injecting partner **OR** • Sharing injection equipment
Clinically eligible	**ALL OF THE FOLLOWING CONDITIONS ARE MET:** • Documented negative HIV Ag/Ab test result within 1 week before initially prescribing PrEP • No signs/symptoms of acute HIV infection • Estimated creatinine clearance ≥30 mL/min/1.73 m^2 [4] • No contraindicated medications	
Dosage	• Daily, continuing, oral doses of TDF/FTC (Truvada®), ≤90-day supply **OR** • For men and transgender women at risk for sexual acquisition of HIV; daily, continuing, oral doses of TAF/FTC (Descovy®), ≤90-day supply	
Follow-up care	**Follow-up visits at least every 3 months to provide the following:** • HIV Ag/Ab test and HIV-1 RNA assay, medication adherence and behavioral risk reduction support • Bacterial STI screening for MSM and transgender women who have sex with men[3] – oral, rectal, urine, blood • Access to clean needles/syringes and drug treatment services for PWID **Follow-up visits every 6 months to provide the following:** • Assess renal function for patients aged ≥50 years or who have an eCrCl <90 mL/min/1.73 m^2 at PrEP initiation • Bacterial STI screening for all sexually-active patients[3] – [vaginal, oral, rectal, urine- as indicated], blood **Follow-up visits every 12 months to provide the following:** • Assess renal function for all patients • Chlamydia screening for heterosexually active women and men – vaginal, urine • For patients on TAF/FTC, assess weight, triglyceride, and cholesterol levels	

1. Adolescents weighing at least 35 kg (77 lb);

2. Because most PWID are also sexually active, they should be assessed for sexual risk and provided the option of CAB for PrEP when indicated;

3. Sexually transmitted infection (STI): Gonorrhea, chlamydia, and syphilis for MSM and transgender women who have sex with men including those who inject drugs; Gonorrhea and syphilis for heterosexual women and men including persons who inject drugs;

4. Estimated creatine clearance (eCrCl) by Cockcroft Gault formula ≥60 ml/min for TDF/FTC use, ≥30 ml/min for TAF/FTC use.

TABLE 14. TEAR-OUT PAGE OF GUIDELINES FOR CAB LAI PrEP[45]

	Sexually Active Adults and Adolescents	Persons Who Inject Drugs[1]
Identifying substantial risk of acquiring HIV infection	Anal or vaginal sex in past 6 months AND any of the following: • HIV-positive sexual partner (especially if partner has an unknown or detectable viral load) • Bacterial STI in past 6 months[2] • History of inconsistent or no condom use with sexual partner(s)	• HIV-positive injecting partner **OR** • Sharing injection equipment
Clinically eligible	**ALL OF THE FOLLOWING CONDITIONS ARE MET:** • Documented negative HIV Ag/Ab test result within 1 week before initial cabotegravir injection • No signs/symptoms of acute HIV infection • No contraindicated medications or conditions	
Dosage	• 600 mg cabotegravir (Apretude®) administered as one 3 mL intramuscular injection in the gluteal muscle – Initial dose – Second dose 4 weeks after first dose (month 1 follow-up visit) – Every 8 weeks thereafter (month 3, 5, 7, follow-up visits etc)	
Follow-up care	**At follow-up visit 1 month after first injection** • HIV Ag/Ab test and HIV-1 RNA assay **At follow-up visits every 2 months (beginning with the third injection–month 3) provide the following:** • HIV Ag/Ab test and HIV-1 RNA assay • Access to clean needles/syringes and drug treatment services for PWID **At follow-up visits every 4 months (beginning with the third injection- month 3) provide the following:** • Bacterial STI screening[2] for MSM and transgender women who have sex with men[2]– oral, rectal, urine, blood **At follow-up visits every 6 months (beginning with the fifth injection–month 7) provide the following:** • Bacterial STI screening[1] for all heterosexually active women and men – [vaginal, rectal, urine - as indicated], blood **At follow-up visits at least every 12 months (after the first injection) provide the following:** • Assess desire to continue injections for PrEP • Chlamydia screening for heterosexually active women and men–vaginal, urine **At follow-up visits when discontinuing cabotegravir injections provide the following:** • Re-educate patients about the "tail" and the risks during declining CAB levels • Assess ongoing HIV risk and prevention plans • If PrEP is indicated, prescribe daily oral TDF/FTC or TAF/FTC beginning within 8 weeks after last injection • Continue follow-up visits with HIV testing quarterly for 12 months	

1. Because most PWID are also sexually active, they should be assessed for sexual risk and provided the option of CAB for PrEP when indicated;

2. Sexually transmitted infection (STI): Gonorrhea, chlamydia, and syphilis for MSM and transgender women who have sex with men including those who inject drugs; Gonorrhea and syphilis for heterosexual women and men including persons who inject drugs.

Transitioning From PrEP to HIV Treatment as Prevention

US Department of Health and Human Services (DHHS) HIV/AIDS treatment guidelines recommend that upon laboratory confirmation of HIV infection in an individual on PrEP, the patient should transition from PrEP to comprehensive HIV treatment.[61] Using a shared decision-making approach, an HIV provider and the patient should both be involved in determining ART selection and initiating therapy. Under guidelines for rapid ART initiation (which can be used in all patients; rapid/immediate ART; rapid/immediate start), there is no need to wait for additional laboratory results prior to starting treatment. However, baseline laboratory data should be drawn at the visit in which ART is initiated. Rapid initiation refers to initiating ART within 14 days of HIV diagnosis, while immediate initiation refers to starting ART on the same day as diagnosis.[89] The goal of a rapid/immediate start strategy is to accelerate the time from HIV diagnosis to engagement in care, ART uptake, and, ultimately, viral suppression. Current guidelines call for ART initiation on the day of diagnosis (or as close as possible).[61] Patients should be counseled regarding the benefits of early/continuous viral suppression for both themselves and their partners, with emphasis on undetectable=untransmittable (U=U). That is, maintenance of viral suppression (an undetectable viral load on ART), helps prevent the transmission of HIV to others. This is the basis of HIV treatment as prevention.[90,91]

PEP 101

PEP: Pharmacologic Considerations: Efficacy and Safety

HIV postexposure prophylaxis (PEP) utilizes specific combinations of antiretroviral agents to prevent infection in appropriately identified and evaluated HIV-negative people who have had a single high-risk HIV exposure.[19,92] Prescribing PEP should be considered an emergency intervention: PEP is not a substitute for appropriate, continuous use of PrEP in conjunction with behavioral risk reduction. It can be thought of as similar to dispensing the morning-after contraceptive pill. PEP is most effective when initiated as soon as possible—no more than 72 hours—after a potential HIV exposure.[92]

- ***Occupational*** HIV exposure refers to high-risk events occurring in a health care setting
- ***Nonoccupational*** HIV exposure refers to an isolated exposure to potentially infectious body fluids that occurs outside of a health care setting, most commonly through sexual activity or injection drug use

This discussion addresses nonoccupational PEP (nPEP) only.[92]

Although TDF and FTC are used in PEP, the clinical/pharmacologic concerns—and intensity of treatment—are more similar to treatment of established HIV infection than to PrEP. PEP requires the use of either an integrase strand transfer inhibitor (INSTI) or a boosted protease inhibitor (PI) in combination with both TDF and FTC. Current CDC PEP guidelines do not include use of TAF or CAB as a PEP-regimen component. [92]

PEP is usually prescribed as a 28-day course of treatment. Currently recommended (preferred) ART regimens for use as PEP in HIV-negative adults and adolescents include the following[92]:

- TDF 300 mg with FTC 200 mg once daily ***PLUS***
- Raltegravir (RAL) 400 mg twice daily

OR

- TDF 300 mg with FTC 200 mg once daily ***PLUS***
- Dolutegravir (DTG) 50 mg once daily

The following regimen is recommended as an ***alternative***:

- TDF 300 mg with FTC 200 mg once daily ***PLUS***
- Darunavir (DRV) 800 mg and ritonavir (RTV) 100 mg once daily

The CDC PEP guidelines do not in general recommend one INSTI over the other (ie, DTG vs RAL), however, DTG may be preferred for its once-daily dosing.[92-94] Note that use of DTG should be avoided in the periconception period because of the risk of neural tube defects linked to drug exposure during the first 28 days of gestation. There are no data to suggest that DTG has any teratogenic signal after the periconception period.[95] Among deliveries in which the mother was taking DTG at conception, neural tube defects were found in 0.30% of cases, versus 0.10% where the mother was taking a non-DTG drug at conception, and 0.08% in HIV-uninfected mothers.[95] Similarly, nonpregnant women of childbearing potential who are sexually active or have been sexually assaulted and are not using effective birth control should not receive DTG.[94] In either clinical scenario, patients should be prescribed RAL. Additional pharmacologic considerations when prescribing RAL or DTG as PEP are outlined in **Table 15**.[61,93,94]

RAL and DTG are both associated with adverse events that include headache, insomnia, and weight gain. [61,93,94] Both agents are also rarely associated with depression and suicidal ideation, although this usually occurs in patients who have preexisting psychiatric conditions. RAL may additionally cause fever, nausea, and diarrhea, and may be associated with more severe conditions, including Stevens-Johnson syndrome, toxic epidermal necrolysis, and rhabdomyolysis.[93,94]

DTG is associated with additional adverse effects that include hepatotoxicity, hypersensitivity reactions (including rash, constitutional symptoms, organ dysfunction, and liver injury) and, as noted, potential for increased risk of neural tube defects in infants born to patients treated with DTG surrounding the time of conception (**Table 16**).[94]

TABLE 15. Pharmacologic Considerations When Prescribing Raltegravir or Dolutegravir[61,93,94]

	Raltegravir	Dolutegravir
Antiretroviral class	• INSTI	• INSTI
Serum half-life	• Approximately 9 hours	• Approximately 13 hours
Absorption concerns	• Absorption affected by cation-containing (magnesium, aluminum, iron, calcium, or zinc) medications and products; eg, antacids, laxatives	• Same as raltegravir
Dosing adaptation	• Take ≥2 hours before or ≥6 hours after taking cation-containing medications or products	• Same as raltegravir, except it can be coadministered with calcium-containing antacids
Contraindication or caution		• Risk of neural tube defects • Contraindicated with dofetilide (class III antiarrhythmic) • Interaction with higher dosages of metformin

INSTI, integrase strand transfer inhibitor.

TABLE 16. Adverse Events Associated With Raltegravir or Dolutegravir[58,93,94]

	Raltegravir	Dolutegravir
Neurologic	• Headache, insomnia	• Headache, insomnia
Psychiatric (usually with preexisting conditions)	• Depression • Suicidal ideation	• Depression • Suicidal ideation
Musculoskeletal	• Elevated creatine phosphokinase • Muscle weakness • Rhabdomyolysis	
Gastrointestinal/ Hepatic	• Nausea, diarrhea	• Hepatotoxicity
Obstetric		• Neural tube defects in infants born to patients treated with dolutegravir around the time of conception
Immunologic	• Stevens-Johnson syndrome • Hypersensitivity reactions • Toxic epidermal necrolysis	• Hypersensitivity reactions: – Rash – Constitutional symptoms – Organ dysfunction, including liver injury
Metabolic	• Weight gain	• Weight gain

Pretreatment Determination of PEP Eligibility[92]

As with HIV PrEP, HIV PEP prescribing is associated with several pretreatment requirements:

- Conduct a comprehensive behavioral-risk assessment (sexual; injection-drug use) and identify individuals at substantial risk of HIV acquisition
- Confirm HIV-negative status: select preferred HIV tests and/or accurately interpret HIV test results
  - If a rapid test is not available and nPEP is otherwise indicated, therapy should still be initiated
- Order appropriate laboratory tests to assess PEP-associated risks
- Screen for drug/drug interactions

As PEP is most effective when initiated as soon as possible—no more than 72 hours—after a potential HIV exposure, these pretreatment evaluations should be performed immediately. In addition, PEP is not indicated if the patient has been consistently adherent to PrEP. [92]

Comprehensive Sexual (and Injection Drug Use) Risk Assessment[92]

During the initial postexposure evaluation, the pharmacist should determine the following:

- Route/source of the potential HIV exposure
- Timing and characteristics of the exposure, including sexual assault
- Frequency of potential HIV exposures
- Risk of other STIs (gonorrhea, chlamydia, syphilis), HBV, or HCV
- Potential for current pregnancy (with pregnancy testing)

Needle-sharing during injection drug use and receptive anal intercourse are considered the highest per-act risks for nonoccupational HIV transmission. Insertive anal intercourse, insertive penile-vaginal intercourse, and oral sex carry relatively lower risks.[92] **Figure 13** is an algorithm for determining HIV exposure and whether nPEP is recommended.

Confirmation of HIV-Negative Status[92]

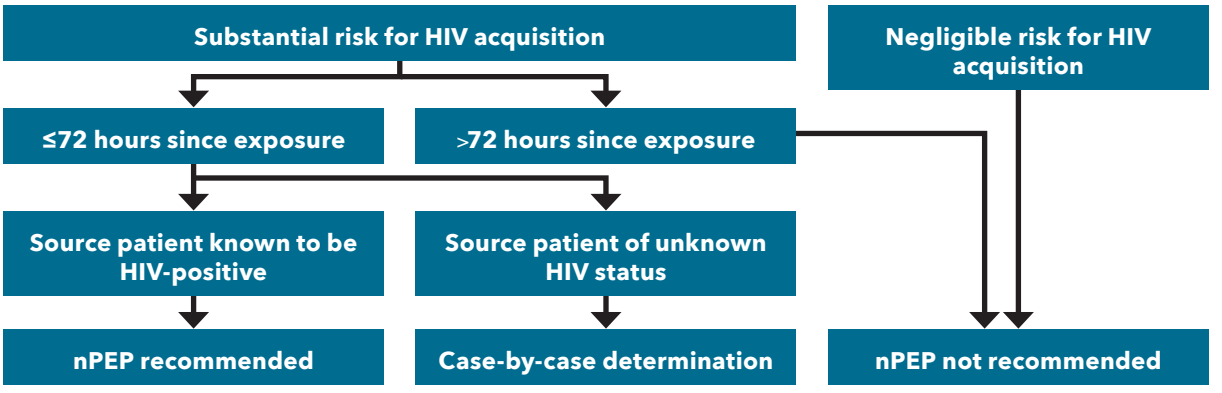
HIV-testing considerations, as outlined for pre-PrEP assessment–*Determining PrEP Eligibility, Confirming HIV-Negative Status (pg 13)*–also pertain to pre-PEP assessment. Special emphasis should be placed on clinical correlation of HIV-testing results and screening for signs and symptoms suggestive of acute/primary HIV infection. Importantly, if HIV test results are unavailable during the initial evaluation, initiation of PEP should be determined on the initial assumption that the potentially exposed patient is not infected. When the HIV status of the potential source of exposure is unknown–if possible–that individual should consent to clinical evaluation and HIV testing using an HIV 1/2 Ag/Ab test. PEP may be considered and prescribed if an HIV test is not available or if the HIV status of the source is unknown.

Other Baseline Labs and Assessment for PEP-Associated Risks

As with HIV PrEP, pre-PEP laboratory assessment must be performed prior to treatment initiation. Again, critical labs include estimated creatinine clearance (eCrCl), HBV serology, and pregnancy testing. Additionally, if indicated by the comprehensive risk assessment, patients considered for PEP should be referred for timely STI testing and treatment. When appropriate, the patient should be offered routine prophylaxis for gonorrhea, chlamydia, or trichomoniasis. This is also an opportunity to address the need for vaccinations for HBV, HCV, and human papillomavirus (HPV).[92]

DHHS guidelines for pre-PEP (baseline) and follow-up laboratory testing largely replicate those for PrEP initiation and continuation. Differences include the addition of liver function evaluation (alanine

FIGURE 13. Algorigthm for Evaluation and Treatment of Possible Nonoccupational HIV Exposure (nPEP)[92]



Substantial risk for HIV acquisition

Exposure of vagina, rectum, eye, mouth, or other mucous membrane, nonintact skin, or percutaneous contact

With blood, semen, vaginal secretion, rectal secretion, breast milk, or any body fluid that is **visibly** contaminated with blood

When the source is known to be HIV-positive

Negligible risk for HIV acquisition

Exposure of vagina, rectum, eye, mouth, or other mucous membrane, intact or nonintact skin, or percutaneous contact

With urine, nasal secretion, saliva, sweat, or tears if **not visibly** contaminated with blood

Regardless of the known or suspected HIV status of the source

GC, gonorrhea.

aminotransferase [ALT] and aspartate aminotransferase [AST]) and test-specific requirements for postexposure follow-up testing (**Table 17**). [92]

Patient-Centered PEP: Regimen Selection and Pretreatment Counseling[92]

Having established the patient's PEP eligibility—or having done so to the pharmacist's satisfaction, if HIV results are not immediately available—the PEP provider's additional pre-PEP requirements include the following clinical activities. **Table 18** provides a full summary of initial PEP evaluation, medication prescribed, and management.[58]

- Prescribe safe and effective PEP regimens for eligible persons without HIV infection
- Educate patients about the selected PEP regimen to optimize safe use
- Provide counseling and effective contraception to women initiating PEP who do not wish to become pregnant
  - Discuss emergency contraception with women of reproductive potential
  - Refer immediately for assessment of any reported sexual assault
- Provide other patient-centered counseling regarding the following:
  - Medication-adherence to achieve and maintain protective tissue levels
  - HIV risk reduction; including discussion and provision of prevention services referrals
  - PEP medication safety during pregnancy and breastfeeding, if indicated

Basic medication-education components include the following:

- Which PEP medication is being prescribed? How is it taken? What is the dosing schedule?
- How to manage missed doses
- Common signs and symptoms suggestive of acute HIV infection (**Table 6**)
- Common side effects associated with raltegravir and dolutegravir (**Table 16**)
- What quantity will be dispensed?

A 28-day course of an INSTI-based 3-drug antiretroviral regimen should be prescribed for all persons requiring PEP. To optimize adherence, consideration should be given to patient-specific characteristics, number of doses per day and/or pills per dose, and minimization of side effects. Providing an entire 28-day course of the PEP regimen and scheduling an early follow-up visit may increase the likelihood of treatment adherence, especially if patients cannot return for multiple follow-up visits.

- Follow-up visits allow pharmacists to provide further patient-centered evaluation, education, and counseling:
- Discuss baseline blood test results (including HIV results, if a rapid test was not available at the time of initial assessment)
- Assess for adherence and adverse effects, or change the PEP regimen, if indicated
- Recommend medications for symptomatic relief of side effects (eg, antiemetics)
- Recommend pill boxes or other medication adherence aids (including smartphone apps)

TABLE 17. DHHS PEP Guidelines: Baseline and Follow-up Laboratory Testing[92]

Test	Frequency	Other
HIV: combined antigen/antibody test preferred	• Baseline and at 4–6 weeks, 3 months, and 6 months after exposure	• If positive, refer
Serum creatinine for calculation of estimated creatinine clearance	• Baseline and at 4–6 weeks	
ALT; AST	• Baseline and at 4–6 weeks	
HBV serology	• Baseline and at 6 months after exposure	• If positive, refer • If negative and appropriate, vaccinate
HCV serology	• Baseline and at 6 months after exposure	• If positive, refer
STIs: syphilis serology	• Baseline, at 4–6 weeks, and at 6 months after exposure	• If positive, refer for STI care
STIs: chlamydia; gonorrhea	• Baseline and at 4–6 weeks after exposure	• If positive, refer for STI care
Pregnancy	• Baseline and at 4–6 weeks	• Pregnancy is not a contraindication for use of PEP

ALT, alanine aminotransferase; AST, aspartate aminotransferase; HBV, hepatitis B virus; HCV, hepatitis C virus; STI, sexually transmitted infection.

TABLE 18. Summary of Initial PEP Evaluation and Management[92]

Obtain history of potential exposure event	• HIV status of exposed person and exposure source (if available) • Timing of most recent potential exposure • Type of exposure event and risk for HIV acquisition
Determine if PEP is indicated, as based on history	
If PEP is indicated, conduct laboratory testing	• HIV blood test: rapid combined antigen/antibody test preferred • eCrCl, HBV and HCV serology, STI screening, pregnancy testing
Prescribe a 28-day PEP course	• TDF 300 mg with FTC 200 mg once daily plus RAL 400 mg twice daily **OR** • TDF 300 mg with FTC 200 mg once daily plus DTG 50 mg daily • Educate patient about potential regimen-specific adverse effects
Furnish prescription and provide medication counseling	• Dosage, duration, how supplied • Adherence • Adverse effects • Patient-assistance programs
For all PEP-eligible patients	• Provide patient-centered counseling on behavioral risk reduction and HIV prevention strategies • Document sexual-assault findings and fulfill reporting requirements[56] • Conduct confidential reporting of newly diagnosed STIs and HIV infection to the health department • Link HIV-infected patients to relevant medical care and psychosocial support services • Consider transition to PrEP for appropriately identified patients

eCrCl, estimated creatinine clearance; DTG, dolutegravir; FTC, emtricitabine; HBV, hepatitis B virus; HCV, hepatitis C virus; PEP, postexposure prophylaxis; PrEP, preexposure prophylaxis; RAL, raltegravir; STI, sexually transmitted infection; TDF, tenofovir disoproxil fumarate.

- Identify strategies for dosing in line with a patient's daily schedule
- Ensure means for patient-pharmacist contact during PEP treatment

Patients should be counseled repeatedly on the importance of PEP-regimen adherence and treatment completion to optimize prevention of HIV infection.[92]

Transitioning From PEP to PrEP (PEP2PrEP)

PEP is indicated only for patients with ≥1 known or suspected high-risk, unprotected HIV exposure who are HIV-negative at initial PEP evaluation. Patients with documented HIV-negative status (preferably using an HIV 1/2 Ag/Ab test) upon completion of a 28-day course of PEP, can be transitioned from PEP to PrEP without any gap in treatment.[45,92] Patients who are at frequent, recurrent risk of HIV exposure, or require sequential or near-continuous courses of PEP, should be offered one of the 3 FDA-approved PrEP regimens that best meets their needs, in conjunction with behavioral risk-reduction counseling and interventions. Patients should receive full PrEP education and be reassessed and counseled regarding medication adherence—despite their successful completion of PEP.[92]

PEP Failure and Transitioning From PEP to HIV Treatment as Prevention[92]

If use of PEP fails to prevent HIV infection, patients may experience signs and symptoms of acute/primary, or early, HIV.[44] Patients should be instructed during the initial PEP evaluation about such manifestations, as listed in **Table 6**. Should any signs and symptoms related to acute HIV infection occur during the 28-day PEP course or anytime within 1 month after PEP completion, patients should return for further evaluation and referral to an HIV treatment specialist, if indicated. If a patient is taking 3-agent PEP ART at the time of detected infection, ART should be continued until patient evaluation and treatment planning with an experienced HIV treatment specialist are completed.

EMBRACING SEXUAL WELLNESS: SEXUAL HEALTH, WELL-BEING, AND TRAUMA-INFORMED CARE

Trauma-Informed Care

SAMHSA (Substance Abuse and Mental Health Services Administration) defines trauma as events or circumstances experienced by an individual as

physically or emotionally harmful or life-threatening, which result in adverse effects on a person's functioning and well-being.[117] Trauma is very prevalent in PLWH in the United States: 30% experience childhood physical and/or sexual abuse before age 13; 68% to 95% of women living with HIV experience intimate partner violence (IPV), as do 68% to 77% of men and 93% of people who identify as transgender. Trauma is associated with psychosocial impairment (including posttraumatic stress disorder [PTSD]); panic, phobic, or generalized anxiety disorders; depression; increases in alcohol or substance use; and an increased likelihood of factors associated with increased risk for HIV, such as inconsistent condom use and multiple sex partners. In addition, poverty, race/ethnicity, sexual orientation, and gender may increase the risk of exposure to potentially traumatic events, thereby compounding HIV risk.[118] One study of young MSM (74% African American) found that childhood trauma and generalized anxiety were associated with decreased PrEP adherence.[121]

Being trauma-informed is an approach to care and prevention that acknowledges that traumas may have occurred or may even be an active part in a patient's life, and that those traumas may manifest physically, mentally and/or behaviorally.[124] A number of states have included the concept of a trauma-informed approach (TIA) to care, or trauma-informed care (TIC) in their board of pharmacy PrEP/PEP protocols. TIC recognizes that health care providers and organizations must have a complete picture of a patient's life story in order to effectively provide health care services with a healing approach. This may improve adherence, patient engagement, health outcomes, and provider wellness. SAMHSA's TIA is based on the following 4 "R" assumptions, whereby TIC seeks to[117,119]:

- **Realize** the widespread impact of trauma and understand paths for recovery
- **Recognize** the signs and symptoms of trauma in patients, families, and staff
- **Respond** by fully integrating knowledge about trauma policies, procedures, and practices
- **Resist retraumatization** of patients and staff

In a TIA, providers and staff at all levels of the organization have a basic understanding of trauma and how it may affect individuals, families, and communities. It is generally accepted that trauma plays a role in mental and substance use disorders (SUD) and needs to be addressed in prevention, treatment, and recovery.

In addition, there are 6 key principles of a TIA[117,119,124]:

- **Physical and Emotional Safety**: throughout the organization, pharmacy, and clinic, where patients and staff feel physically and psychologically safe
  - Create a safe and welcoming environment
  - Ensure privacy and confidentiality
  - Be consistent and predictable, nonshaming, nonblaming
- **Trustworthiness and Transparency**: decisions are made with transparency, with the goal of building and maintaining trust
  - Maintain professional boundaries
  - Keep roles clear, maintaining transparent policies and processes (including informed consent and grievance process)
- **Peer Support**: individuals with shared experiences are integrated into the organization and viewed as intrinsic to service delivery. Peer support and mutual self-help can:
  - Establish safety and hope
  - Build trust
  - Enhance collaboration
  - Promote recovery and healing
- **Collaboration**: importance is placed on partnering and leveling of existing power differences between staff and patients, and among staff; it recognizes that everyone has a role to play (ie, "you don't have to be a therapist to be therapeutic")
  - Ensure respect, connection, and hope
  - Recognize that healing occurs in the context of the interpersonal relationship
  - Share in decision-making (ie, doing "with" rather than "to" or "for")
- **Empowerment, Voice, and Choice**: patient and staff strengths are recognized, built upon, and validated; this includes the belief in resilience and the ability to heal from trauma
  - Use strengths to build and enhance healthy coping skills
  - Understand past coping mechanisms and the normalcy of the response to a not-normal situation
  - Value and ensure individual control and autonomy
  - Frame experiences as survivorship, not victimization
- **Cultural, Historical, and Gender Issues**: biases, stigma, stereotypes, and historical trauma are recognized and addressed
  - Actively move past stereotypes and biases based on race, ethnicity, sexual orientation, age, religion, gender, geography, etc
  - Provide gender-responsive services
  - Utilize the healing value of traditional cultural connections

Here are some examples of what pharmacists can do to promote TIC:

Among heterosexual women, unprotected condomless vaginal and/or anal sex with a male partner is the most common mode of HIV transmission. IPV constrains women's access to and use of HIV prevention methods. PrEP is a positive intervention for women, as it does not require the same interpersonal negotiation with a partner that condoms do. Further, for patients who may not have control over their sexual encounters, PrEP confers control over HIV acquisition. Ensure that patients who have experienced IPV have alone clinic time to communicate freely and privately.[120]

When a patient presents as a victim of sexual assault, one of the most urgent needs (as well as safety and criminal justice concerns) surrounds risk of HIV and PEP initiation. It is very common for individuals who have experienced sexual assault to have delayed presentation for care. If they present within the 72-hour time frame for PEP, a risk assessment must be done quickly, and the patient given a trauma-informed explanation regarding their risk of HIV acquisition and offered PEP. Discuss the 28-day regimen, laboratory tests and follow-up care and referrals. In rural, low HIV-incidence communities, PEP may not be readily available; stock the medication (or consider stocking "starter" PEP packs until the individual can access the full supply) and let other pharmacies, clinics, and organizations know that you have it available and can be a referral for care.[122] Make sure to take a nonjudgmental approach to someone who is requesting multiple courses of PEP, especially in situations involving sexual assaults, or in those who are sex workers.

A TIA to caring for adolescents will increase a teen's safety and autonomy. This can include brief counseling about healthy relationships in general and may promote healthy adolescent sexual relationships. Make sure teens know about resources for relationship abuse and sexual violence and facilitate referrals to advocates who assist survivors of abuse.[125]

A substantial number of LGBTQ individuals are victims of IPV, hate crimes, and other forms of trauma. Because of the prevalence of trauma over the course of the lives of these individuals, clinicians must always use TIC with this population. Antecedent violence should be considered if the patient presents with injuries, depression, substance use, or PTSD. In those who report violence, pharmacists can provide TIC and support by expressing empathy, ensuring safety, and addressing health consequences, including HIV prevention (as well as referring to medical assistance or helping them get care for their injuries).[123]

The Sexual Health Assessment

Comprehensive sexual health assessment is critical to determining an individual's need for PrEP, as HIV risk may be associated with numerous personal, partner, relationship, social, cultural, network, and community factors.[45] Many health care providers do not ask about same-sex behaviors because of personal discomfort or anticipated patient discomfort. Further, patients often do not disclose sexual behaviors because of perception of stigma or fear of judgment. Frank, nonjudgmental questions about sexual behavior, alcohol use, and illicit drug use should be asked.[45] The CDC's sexually transmitted diseases treatment guidelines recommend the following risk-behavior questions, known as *The 5 Ps*[96]:

- **Partners**: In the past month, with how many partners have you had sex? Are they men, women, transgender women, and/or transgender men?
- **Practices**: What body parts do you use for sex? Based on what body parts you use, that's where we test for sexually transmitted infections (STIs)
- **History of STIs**: Have you ever had an STI? When? Have any of your partners had an STI?
- **Protection from STIs**: How often do you use condoms? What do you do to protect yourself from HIV and STIs?
- **Pregnancy plans**: Do you wish to prevent pregnancy? Are you using contraception; if so, what type?

Clinicians can enhance their history-taking skills by making patients feel more comfortable and, therefore, potentially more open: use neutral and inclusive terms; avoid assumptions based on age, appearance, marital status, or other factors; and ensure that patients share an understanding of the terms used.[97-99]

Before starting, consider informing the patient about the routine nature of conducting a sexual-health assessment with the following statement: These questions can make people feel uncomfortable. But I ask to get a better assessment of your risk and to work with you to reduce this risk specific to your life. Everything you tell me is confidential, as part of our patient-provider relationship. If my questions are triggering, please let me know. Is it okay if I begin your sexual health assessment? Do you have any questions before we start?" If patients want to know the reasons/importance of a sexual health assessment, consider using the following statements[100]:

- Sexual health is important for overall emotional and physical health
- We ask these questions every year because it is common for people's sexual behaviors and partners to change over time
- As you may know, sexual activity without protection can lead to STIs. These diseases—especially syphilis, gonorrhea, and chlamydia—are very common and often do not cause any symptoms. If we do not catch and treat these diseases, they can affect general health and well-being
- These questions can also help guide our conversation about how you can protect yourself from STIs, unwanted pregnancy, or other issues that may concern you. It will also give you an opportunity to talk about problems with, or changes in, sexual desire and functioning
- Our discussion may help us identify other health needs (eg, additional laboratory testing; vaccinations) or resources you may need as part of your lifestyle (sexual or otherwise)

Communicating With LGBTQIA Persons

In addition to the empathy and respect that you show all patients participating in sexual-history discussions, there may be special considerations when taking sexual histories with LGBTQIA persons. It's important to remember that people who are transgender are high-risk and underrepresented among PrEP users and may

require particular sensitivity. The following points taken from the National LGBTQIA+ Health Education Center may be helpful when taking sexual histories, especially with regard to gender pronouns.[97]

- Make sure you have established a good rapport with the patient before asking about sexual practices (or doing a physical exam)
- Be sure to use the patient's preferred name during conversations and ask what the patient's pronouns are
  - This will not necessarily be the name that appears on insurance and medical records, and some people change their personal pronoun preference
  - Ensure that pronouns are very visible in the patient's chart and any documentation that the patient would read in MyChart would reflect chosen name and pronouns
  - Many people who are transgender want you to use the pronoun that matches their gender identity. For example, a transgender female may like you to use "she/her/hers"
  - Some people who are transgender or gender-nonconforming may ask you to use "ze" or "they," or to try to avoid using any pronouns
  - When in doubt, use the patient's name or the gender neutral "they"
  - Instead of assigning gender to partners, just ask the patient what body part(s) they use for sex, in order to guide your STI testing and your risk-reduction conversation
- If possible, use affirming language when discussing a patient's body parts. The easiest way to accomplish this is to ask the patients what words they use to describe their genitals and body. Mirroring a patient's language can lead to improved health goals and outcomes

Discussing Risk of HIV Acquisition Through Injection-Drug Practices

The US Preventive Services Task Force recommends that all health care providers be aware of signs and symptoms associated with injection drug use. Brief risk-behavior assessment questions that address this concern include the following[45]:

- Have you ever injected drugs that were not prescribed to you by a clinician?
- If yes, when did you last inject nonprescribed drugs?
- In the past 6 months, have you injected using needles, syringes, or other drug-preparation equipment that had already been used by another person?
- In the past 6 months, have you been in a methadone or other medication-assisted substance use disorder treatment program?

Answers from these questions may help you determine if additional resources are needed for patients who inject drugs or have other high-risk substance-use related concerns or behaviors. Such resources include harm-reduction (behavioral risk-reduction) programs and services, including the National Harm Reduction Coalition (https://harmreduction.org/), medication-assisted treatment (eg, buprenorphine), inpatient or residential drug-treatment programs, or relapse-prevention services (eg, 12-step programs or mental health/behavioral support programs). In addition, be able to offer naloxone or know where to refer people for it.[45,101] The website for SAMHSA (https://www.samhsa.gov) is a valuable resource for locating substance use disorder treatment facilities and programs and behavioral and mental health services.[102]

HELPING YOUR PATIENT NAVIGATE BEYOND PHARMACY-BASED HIV PREVENTIVE CARE: REFERRAL, ADVOCACY, & RESOURCES

When to Refer to Primary Care or Specialist Providers

A positive HIV screen should prompt immediate linkage to the patient's PCP or HIV specialist for confirmatory testing and subsequent initiation of comprehensive ART, if positive.

Further, if acute HIV is suspected (based on symptoms)—or a patient tests positive for HBV, becomes pregnant, or has symptoms or laboratory findings of acute renal injury—a referral to a PCP or other appropriate provider should be made and the patient should cease participation in the statewide protocol. A positive STI screen or considerations pertaining to usual care are not necessarily reasons to terminate a patient's participation.

Developing relationships with physicians and advanced practice nurses in your area who are experienced in HIV care and prevention will expedite the referral process and ease patient concerns. The individual patient's records, along with full documentation of pharmacist-provided PrEP services, should be transferred to the patient's PCP, whenever a referral is necessary.

Patients who do not have a PCP experienced in PrEP provision can be referred to the American Academy of HIV Medicine database to locate a PrEP provider in their area[103]: https://providers.aahivm.org/referral-link-search?reload=timezone.

Keep in mind that patients who initially request PrEP or PEP from their pharmacist—not their PCP—may have a higher level of comfort with and/or do not perceive stigma/discrimination on the part of the pharmacist. This trusted patient-pharmacist relationship should be maintained to support the patient's well-being.

Your Patient's Advocate:

Financial-Assistance Resources

For patients who lack prescription drug coverage, several resources are available. Ready, Set, PrEP is a nationwide program launched by the CDC in December

2019 to make PrEP available at no cost to individuals who meet the following requirements[21]:

- Test negative for HIV **AND**
- Have a valid prescription from a health care provider **AND**
- Do not have health insurance coverage for outpatient prescription drugs

Although Ready, Set, PrEP ensures access to PrEP for qualifying individuals, it also stipulates that the costs for necessary clinic visits and laboratory testing may vary based on income.[21] Gilead's Advancing Access® program is another patient assistance program available for both insured and uninsured patients that offers a copay coupon program and patient support: http://www.gileadadvancingaccess.com. There is also a program sponsored by ViiV, called ViiVConnect to help patients with financial and insurance issues and providers with tools, resources, and individual assistance with benefits verification, prior authorizations, or medication reimbursement: https://www.viivconnect.com/

In addition, some states in the US have PrEP-specific financial assistance programs that cover medication, clinical care, or both. This information is available from the National Alliance of State and Territorial AIDS Directors (NASTAD) (**Table 19**).[104]

Pharmacist Resources

The CDC has created tools to help pharmacists and other providers keep track of important patient and provider steps before PrEP is prescribed[101]:

- https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-provider-supplement-2021.pdf

Establishing a safe and supportive environment in which to discuss a patient's personal health issues—one that also promotes confidentiality—is an important consideration for pharmacists who are starting to build a PrEP/PEP-provider practice.[105] Several resources are available to help pharmacists develop a comprehensive and supportive sexual-history dialogue with patients:

- Centers for Disease Control and Prevention. A Guide to Taking a Sexual History[105] https://www.cdc.gov/std/treatment/sexual-history.htm
- National LGBTQIA+ Health Education Center. Taking Routine Histories of Sexual Health: A System-Wide Approach for Health Centers[97] https://www.lgbthealtheducation.org/publication/taking-routine-histories-of-sexual-health-a-system-wide-approach-for-health-centers/
- TargetHIV. Sexual History Taking Toolkit[98] https://targethiv.org/library/sexual-history-taking-toolkit

TABLE 19. NASTAD Table of State PrEP Financial Assistance Programs[104]

State	Copay Assistance	Medication Assistance	Clinical Visits and Lab Test Assistance	Patient Income Limit
California	Yes	Yes	Any participating provider	Up to 500%
Colorado	Yes	Yes	Any participating provider	Below 500%
District of Columbia	Yes	No	Local health department clinics	Up to 500%
Florida	No	Yes	Local health department clinics	No threshold
Illinois	Yes	No	Select grantees	No threshold
Indiana	Yes	No	Contracted providers	400%
Iowa	Yes	No	Sub-recipients	No threshold
Massachusetts	Yes	No	Select grantees	Up to 500%
New Mexico	Yes	Yes	Contracted providers	No threshold
New York State	No	No	Any participating provider	Up to 435%
Ohio	Yes	No	Any participating provider	Up to 500%
Oklahoma	Yes	Yes	Contracted providers	No threshold
Virginia	No	Yes	Local health departments and contracted providers	No threshold
Washington State	Yes	Yes	Any participating provider	No threshold

NASTAD, National Alliance of State and Territorial AIDS Directors.

ADDRESSING PRACTICAL CHALLENGES OF PREP/PEP IMPLEMENTATION

Legislation in states such as California and Colorado allow any qualified pharmacist in the state to offer PrEP/PEP services independent of physician authorization and is intended to help fill gaps in care, especially in urgent situations in which a PCP is not established.[29,39] There are a number of other models/examples across the country:

- Mission Wellness Pharmacy is a one-stop PrEP program that allows pharmacists to initiate and furnish PrEP directly to patients as part of a demonstration project with the San Francisco Department of Public Health.[106]
- Other models in the US utilize a collaborative practice agreement (CPA) (also called a collaborative drug therapy agreement [CDTA]) that reflects an established and formal relationship among providers (eg, pharmacists, physicians, and advanced practice nurses) and generally requires a referral. This allows pharmacists to order labs and initiate PrEP.
  - Kelley-Ross Pharmacy in Seattle is able to offer pharmacist-driven PrEP provision and HIV-prevention services through not only CPAs, but also through Washington State legislation allowing pharmacists to bill for patient-care services, including monthly patient evaluations, without a limit on length of time the patient can remain under the care of a pharmacist.[107]
- CPAs can include a variety of different elements. The key elements are ensuring that everybody who is a stakeholder has a voice within the process of developing the agreement and that there is an understanding of how the different practice types will be integrated for the best interest of the patient. Promoting mutual trust and respect is crucial for fostering communication and good team building to maintain these structures over time to have a productive relationship among pharmacists and other members of the multidisciplinary team.[108,109]
  - There are many CPA/CDTA templates that can be used and modified to fit the unique needs of each agency. Here are a few areas to consider when creating a CDTA:
    - Confirm that there is malpractice insurance for the pharmacist and the medical director
    - Include STI testing and not just PrEP/HIV, since these two go hand-in-hand in PrEP services
    - Review the rules about notifying the health department with STI/HIV-positive results
    - Work in consultation when needed
    - Develop a regular review process to maintain communication and improve the coordination between the medical-license provider and pharmacist(s)
    - CPAs will likely not allow administration of CAB for PrEP in pharmacies, which will probably remain oral at this time
- Collaborative practice agreements are often embedded into existing pharmacy infrastructure, which makes it easier to implement these types of programs. Rather than creating a new independent service line, it is contained within existing services. It is intended to generate meaningful outcome measures, as it lends itself to programmatic evaluation and quality improvement efforts. Such collaborative practice agreements can reduce costs by improving efficiencies among diverse components of the care team.[108,109]
- **Table 20** outlines the barriers and opportunities associated with collaborative practice agreements in pharmacy for HIV PrEP.
- Different types of technology, including electronic medical records, can be vital to supporting the efforts of a collaborative practice agreement and ensuring that anybody on the care team can confirm the status of patients who are being cared for. The language should be simple and empowering so that everybody has a clear understanding of the expectations. It often will include algorithmic guidance as well as clear delineations regarding when other parts of the team should be involved if there are specific questions.[108,109]

TABLE 20. Collaborative Practice Agreements: Common Barriers and Opportunities[4]

Barriers	Opportunities
• Fitting additional services into already busy workflow	• Medication therapy management: reimbursement tied to accepted interventions
• Designating dedicated physical space for confidential consultation	• Reduced cost overall
• Securing reimbursement or funding from other sources	• Improve patient access to preventive care
• Building relationships and establishing trust with prescribers	

Building In-Pharmacy Infrastructure and Capacity

A commentary in the Journal of the American Pharmacists Association (2020) provides recommendations for implementing a community-based PrEP program, one reflecting the previously discussed San Francisco and Seattle models. That publication also provides recommendations for how community pharmacies can integrate PrEP/PEP implementation with their existing services infrastructure[4]:

- Set up logistics for on-site laboratory testing or for sending out specimens
  - Provide designated physical space (including restrooms) within the pharmacy for laboratory specimen collection
  - Order CLIA-waived rapid HIV tests
  - Utilize mail-in lab kits
  - Train staff regarding on-site ("one-stop PrEP") and/or off-site specimen collection and handling
  - Consider use of an on-site phlebotomist
  - Establish a relationship with an external lab; using a single lab can help streamline staff training and administrative burden
  - Work with your lab of choice to discuss the feasibility of its providing designated staff at your collection site. Many labs with significant capacity can offer this service
  - Train staff on self-collection (patient) techniques and post instructions with visual aids in the restroom. If on-site specimen collection is not an option for your practice location, work with a single lab with several specimen collection locations
- Manage laboratory test results
  - Adapt pharmacy workflow
  - Encourage an appointment-based model for protocol-based assessment, laboratory specimen collection, and prescription pickup
  - Establish private/confidential spaces for discussion of test results
  - Consider installing modular-ready private counseling rooms
  - Assign specific pharmacy staff to accommodate walk-in requests for lab results
- Establish communication protocols and methods
  - Determine how confidential information will be shared among team members, patients, referring providers, or health departments in accordance with Health Insurance Portability and Accountability Act (HIPAA) requirements[110]
  - Set up online portals with secure access for e-mail, text messages, apps, and shared electronic medical records (EMRs); this can save both time and staff resources
  - Utilize secure lab-based online portals for accessing test results; access eligibility may vary
  - Create a standardized referral mechanism for positive screens or abnormal laboratory results
- Provide and monitor pharmacist education and hands-on training, including training of pertinent auxiliary pharmacy staff
  - Require pharmacists to demonstrate competency in delivering PrEP and PEP per state and national guidelines, inclusive of sexual-health counseling, comprehensive risk-appropriate prevention strategies, laboratory testing and interpretation, and navigation of insurance benefits and patient-assistance programs
  - Set realistic time frames for implementation of new work processes and attainment of target number of patient visits
  - Provide ongoing pharmacist and staff feedback, training, and monitoring
  - Designate a pharmacy staff member to disseminate PrEP/PEP guideline changes

The approval of CAB LAI for PrEP has created additional implementation issues, which were discussed with Faculty Member, Melissa Badowski, PharmD, from the University of Illinois at Chicago, College of Pharmacy[111]:

- In Illinois, Dr. Badowski is not able to administer the IM injection; only the nursing staff may do so. However, another faculty member from Nevada was able to receive additional training to give CAB gluteal IM injections. Therefore, the ability to obtain training to provide gluteal IM injections will vary by state and between state boards of pharmacy
- Currently, the CPA at Dr. Badowski's facility only includes oral PrEP (based on current insurance coverage), but it will be updated to include recommendations regarding CAB initiation. This will still follow the same baseline and routine monitoring as outlined by the 2021 CDC Updated Guidelines.
- CAB does require refrigeration, and this is their process: "Once the patient shows up, that is when it is removed/picked up from the on-site pharmacy, and we wait approximately 15 minutes for CAB to come to room temperature. If it's left out more than 2 hours in a syringe, the CAB injection needs to be discarded."
- Clinics need to make sure that they can store the medication, which may be an issue for some sites. A pharmacy may deliver the medication to a clinic (after dispensing), but a staff member needs to accept it (ie, it can't arrive on a weekend or after hours and be left unrefrigerated). On-site pharmacies in clinical settings may not have these issues.

TelePrEP/Telehealth

Starting in the mid-20th century, telemedicine programs began to emerge as a novel option to provide remote clinical examination and maintenance health support.[112,113] Since that time, the use of telemedicine, particularly video visits, has expanded to include telehealth and mobile health applications.[114] Telehealth is different from telemedicine. Telemedicine refers specifically to remote clinical services. Telehealth is

a broader scope of remote health care services and may include clinical services and nonclinical services, such as provider training, administrative meetings, and continuing education.[115]

During the SARS-CoV-2 (COVID-19) pandemic, the use of telehealth dramatically increased, and it is anticipated that telehealth will remain a frequently utilized modality for patient encounters. Telehealth is very helpful for chronic disease management (eg, patient taking HIV PrEP) by allowing continuity of care for high-risk populations while maintaining social distancing and reducing the risk for exposure to infection.[116] As such, pharmacists providing HIV PrEP services to patients must gain competence in applying telehealth to their practices. The CDC guidelines list recommendations for adequately implementing the following procedures for care related to HIV PrEP[45]:

- Conduct PrEP screening, initiation, and follow-up visits by phone or web-based consultation with clinicians
- Obtain specimens for HIV and STI laboratory tests by:
  - Laboratory visits for specimen collection only
  - Order home specimen collection kits for specified tests
    - Specimen kits are sent to the patient's home and contain supplies to collect blood from a fingerstick or other appropriate method
    - The kit is then mailed back to the laboratory with results returned to the clinician who acts on results accordingly and promptly
- When an HIV-negative test is confirmed, provide a prescription for a 3-month supply of oral PrEP medication as opposed to a 1-month supply to minimize trips to the pharmacy

CONCLUDING COMMENTS

HIV Prevention: The Pharmacist as Educator, Provider, and Advocate

This monograph has outlined the pharmacist's role in the provision of HIV PrEP and PEP. A comprehensive nationwide protocol allowing pharmacists to provide nationally endorsed public health preventive care is a win for patient access to care, and a strike against the spread of HIV. As such, it may bring the United States one step closer to ending the HIV epidemic.

The pharmacy setting is an ideal entry point for people at risk of HIV acquisition to initiate pre- or postexposure HIV prophylaxis. The pharmacist's role as HIV-prevention educator, PrEP/PEP provider, and patient advocate has the potential to grow into a greater presence within the local public health sphere. This expansion of the pharmacist's scope of practice can potentially help build strong relationships with patients, PCPs, and community-based patient-support services, while establishing the pharmacist as an essential and reliable resource. Provision of PrEP and PEP services by well-trained and well-placed pharmacists can be a driving force in attaining the goal of zero new HIV infections.

LIST OF ABBREVIATIONS

Ab	antibody
Ag	antigen
AHI	acute HIV infection
AIDS	acquired immunodeficiency syndrome
ALT	alanine aminotransferase
AST	aspartate aminotransferase
ART	antiretroviral therapy
CAB	cabotegravir
CDC	Centers for Disease Control and Prevention
CDPHE	Colorado Department of Public Health & Environment
CI	confidence interval
CLIA	Clinical Laboratory Improvement Amendments
CT	chlamydia trachomatis
DAA	direct-acting antiviral
DDI	drug-drug interaction
DEXA	dual-energy X-ray absorptiometry
DHHS	US Department of Health and Human Services
DNA	deoxyribonucleic acid
DRV	darunavir
DTG	dolutegravir
EBR/GZR	elbasvir/grazoprevir
eCrCl	estimated creatinine clearance
eGFR	estimated glomerular filtration rate
EMR	electronic medical record

GC	gonorrhea
GLE/PIB	glecaprevir/pibrentasvir
FDA	US Food and Drug Administration
FEM-PrEP	Preexposure Prophylaxis Trial for HIV Prevention Among African Women
FTC	emtricitabine
Gen	generation
HAV	hepatitis A virus
HBV	hepatitis B virus
HCV	hepatitis C virus
HDL	high-density lipoprotein
HIPAA	Health Insurance Portability and Accountability Act
HIV	human immunodeficiency virus
HPV	human papillomavirus
IA	immunoassay
IgG	immunoglobulin G
IgM	immunoglobulin M
IAS-USA	International Antiviral Society-USA
IDU	injection drug use
iPrEx	Iniciativa Profilaxis Pre-Exposición [Preexposure Prophylaxis Initiative]
INSTI	integrase strand transfer inhibitor
IPV	intimate partner violence
IRR	incidence rate ratio
LAI	long-acting injection
LDL	low-density lipoprotein
LGBTQIA	lesbian, gay, bisexual, transgender, queer, intersex, asexual
MSM	men who have sex with men
NAAT	nucleic acid amplification testing
NNRTI	nonnucleoside reverse transcriptase inhibitor
NRTI	nucleoside reverse transcriptase inhibitor
NSAID	nonsteroidal anti-inflammatory drug
NI	noninferiority
NIH	National Institutes of Health
nPEP	nonoccupational PEP
PCP	primary care provider
PCR	polymerase chain reaction
PEP	postexposure prophylaxis
PI	protease inhibitor
PWH/PLWH	people with HIV/people living with HIV
PrEP	preexposure prophylaxis
PTSD	posttraumatic stress disorder
PY	person-years
PWID	people who inject drugs
RAL	raltegravir
RNA	ribonucleic acid
RTV	ritonavir
SAMHSA	Substance Abuse and Mental Health Services Administration
SBOP	State Board of Pharmacy
SOF/LDV	sofosbuvir/ledipasvir
SOF/VEL	sofosbuvir/velpatasvir
STI	sexually transmitted infection
SUD	substance use disorder
TAF	tenofovir alafenamide
TDF	tenofovir disoproxil fumarate
TDF2	Botswana TDF/FTC Oral HIV Prophylaxis trial
TFV-DP	tenofovir diphosphate.
TGW	transgender women
TIA	trauma-informed approach
TIC	trauma-informed care
WHO	World Health Organization

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CALLING ALL PHARMACISTS FROM NEVADA, OREGON, AND VIRGINIA! CHECK OUT THESE STATE PRIMERS!

Among the states that have recently expanded pharmacy practice to include PrEP/PEP initiation and management are Nevada, Oregon, and Virginia. These state primers (also available for CE) provide an overview of the requirements set out by their Boards of Pharmacy that are specific to those states and not covered in the Monograph.

Nevada: www.ExchangeCME.com/PrEPpharmNV
Oregon: www.ExchangeCME.com/PrEPpharmOR
Virginia: www.ExchangeCME.com/PrEPpharmVA