

POINT OF CARE  
301

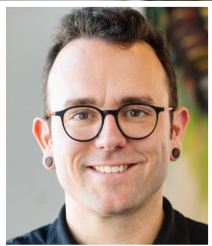
POWER-PAK CE®  
ONLINE MONOGRAPH

EARN  
2.0  
CPE CREDITS

This ACPE educational program has been developed to fulfill the educational requirements of Statewide Protocols in Colorado State Board of Pharmacy Rule 17.00.50.\*

# EXPANDING HIV PREVENTION IN COLORADO— AND NATIONWIDE

## A PEP/PrEP TRAINING GUIDE FOR PHARMACISTS



### PRIMARY AUTHOR

**Dan Scales,  
PharmD,  
AAHIVP**

Director of Pharmacy  
Collaborative Care  
Vivent Health  
Denver, Colorado



### FACULTY REVIEWER

**Emily Zadvorny,  
PharmD, BCPS**

Executive Director  
Colorado Pharmacists Society  
Clinical Associate Professor  
University of Colorado  
Skaggs School of Pharmacy  
Denver, Colorado

## 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 [ExchangeCME.com/PrEPforCOPharmacists](https://ExchangeCME.com/PrEPforCOPharmacists).

Estimated time to complete this activity is 2 hours.

This activity fulfills Colorado State Board of Pharmacy training requirements under Colorado State House Bill 20-1061 (CO HB20-1061).\* Participants who successfully complete this activity will receive a certificate confirming they have fulfilled the requirements laid out by the Colorado State Board of Pharmacy under CO HB20-1061.



Postgraduate Institute  
for Medicine



INTEGRITAS  
COMMUNICATIONS

Jointly provided by the Postgraduate Institute for Medicine and Integritas Communications.

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



Developed in collaboration with the American Academy of HIV Medicine and the Colorado Pharmacists Society.

## TARGET AUDIENCE

This activity is intended for clinical and community pharmacists involved in the care of patients at risk for human immunodeficiency virus (HIV) infection.

## LEARNING OBJECTIVES

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

- Assess patients' risk of HIV acquisition based on the type of exposure
- Determine patients' preexposure prophylaxis (PrEP) eligibility through HIV testing, sexual history-taking, and appropriate laboratory testing
- Implement guideline-driven postexposure prophylaxis (PEP)- and PrEP-prescribing principles with regard to treatment initiation and monitoring
- Select appropriate antiretroviral regimens for PEP or PrEP to prevent HIV infection
- Apply rules from the Colorado State Board of Pharmacy for pharmacist-prescribed and dispensed PrEP and PEP regimens

## PROGRAM DESCRIPTION

This in-depth electronic monograph for pharmacists provides guideline-based clinical information and resources to support those whose scope of practice now allows for direct provision of HIV preexposure and postexposure prophylaxis (PrEP and PEP). This "301"-level activity specifically supports the needs of Colorado pharmacists now challenged to come up to speed on PEP/PrEP guidelines as they relate to their expanded scope of practice under Colorado State House Bill (HB) 20-1061 and the Colorado State Board of Pharmacy Statewide Protocols (Rule 17, Appendix C). It also offers a synthesis of best practices and real-world considerations and serves as a model for expansion and optimization of PEP/PrEP care across pharmacy practice nationwide. This activity will provide Colorado pharmacists with clinical information for initiating and monitoring PrEP and PEP treatment in a pharmacy setting. In addition, the activity discusses policy updates and includes all content necessary to fulfill the training requirements, as determined by the Colorado Board of Pharmacy Licensing Committee, for pharmacists wishing to become PrEP and PEP providers, such as:

- HIV epidemiology and burden of disease
- Pharmacology of HIV medications used for PEP and PrEP as well as their efficacy and safety
- Pretreatment determination of PrEP/PEP eligibility: eligibility criteria, screening, and labs
- Assessment of sexual health and HIV risk
- Patient-centered medication selection: assessing advantages and disadvantages of approved medications for individual patients
- Monitoring considerations and potential adverse events
- Patient counseling and adherence
- Testing for HIV and sexually transmitted infections (STIs)
- Helping the patient navigate beyond pharmacy-based care: referral, advocacy, and resources
- In-pharmacy PEP/PrEP implementation
- Resources for pharmacists

Although the focus of this activity will be the Colorado scope of practice, it may also inform pharmacists nationwide of evolving practice protocols, so they may be prepared—and advocate—for future opportunities in their areas.

The monograph also contains an electronic **Q&A Forum** in which learners can pose questions to the program faculty as they prepare to implement PEP and PrEP services in their pharmacy practices.

## JOINT ACCREDITATION STATEMENT



JOINTLY ACCREDITED PROVIDER  
INTERPROFESSIONAL CONTINUING EDUCATION

In support of improving patient care, this activity has been planned and implemented by the Postgraduate Institute for Medicine (PIM) and Integritas Communications. PIM is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the health care team.

## CONTINUING PHARMACY EDUCATION



PIM designates this continuing education activity for 2.0 contact hours (0.2 CEUs) of the Accreditation Council for Pharmacy Education. (Universal Activity Number – JA4008162-9999-21-2557-H01-P)

This is a knowledge-based activity.

## DISCLOSURE OF CONFLICTS OF INTEREST

PIM requires instructors, planners, managers, and other individuals who are in a position to control the content of this activity to disclose any real or apparent conflicts of interest (COIs) they may have as related to the content of this activity. All identified COIs are thoroughly vetted and resolved according to PIM policy. PIM is committed to providing its learners with high quality activities and related materials that promote improvements or quality in health care and not a specific proprietary business interest of a commercial interest.

**Dan Scales, PharmD, AAHIVP** Nothing to disclose

**Emily Zadvorny, PharmD, BCPS** Nothing to disclose

## PLANNERS AND MANAGERS

The PIM planners and managers have nothing to disclose. The Integritas Communications planners and managers have nothing to disclose.

## DISCLOSURE OF UNLABELED USE

This educational activity may contain discussion of published and/or investigational uses of agents that are not indicated by the US Food and Drug Administration. The planners of this activity do not recommend the use of any agent outside of the labeled indications. The opinions expressed in the educational activity are those of the faculty and do not necessarily represent the views of the planners. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications, and warnings.

## DISCLAIMER

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 or suggested in this activity should not be used by clinicians without evaluation of their patients' conditions and possible contraindications and/or dangers in use, review of any applicable manufacturer's product information, and comparison with recommendations of other authorities.

## INSTRUCTIONS TO RECEIVE CREDIT

To receive credit for this activity, participants must complete the preactivity questionnaire, complete and receive a minimum score of 70% on the posttest, and complete the program evaluation.

## COLORADO STATE BOARD OF PHARMACY TRAINING REQUIREMENTS

This activity fulfills Colorado State Board of Pharmacy training requirements under CO HB20-1061. This legislation stipulates that you are responsible for retaining a record of completing this training for at least 3 years from the date of completion. In order to prescribe PrEP and provide ongoing management of these patients you must also: 1) hold a current license to practice in Colorado; 2) be engaged in the practice of pharmacy; 3) have a PharmD degree or at least 5 years of experience as a licensed pharmacist; and 4) carry adequate liability insurance (at least \$1,000,000 per incident and at least \$3,000,000 in aggregate). If you need more information about liability insurance, go to <https://www.copharm.org/professional-liability-insurance>.

## FEE INFORMATION & REFUND/CANCELLATION POLICY

There is no fee for this educational activity.

## CPE QUESTIONS – PIM CONTACT INFORMATION

For information about the accreditation of this program, please contact PIM via email at [inquiries@pimed.com](mailto:inquiries@pimed.com) or at <http://www.pimed.com/>.

## INTEGRITAS CONTACT INFORMATION

For all other questions regarding this monograph, please contact Integritas via email at [info@exchangeccme.com](mailto:info@exchangeccme.com).

## INTRODUCTION: PHARMACIST'S EXPANDING ROLE IN HIV PREVENTION

Addressing the national call to action to reduce the incidence of human immunodeficiency virus (HIV) infection—especially in high-risk, yet underserved populations—Colorado has proactively led the way as one of the first states to allow pharmacists, via a statewide protocol, to prescribe HIV preexposure prophylaxis (PrEP) and postexposure prophylaxis (PEP) for appropriately identified candidates. Pioneering legislation—Colorado (CO) House Bill 20-1061 and subsequent authorization under CO State Board of Pharmacy Rule 17 Appendix C (SBOP Rule 17)<sup>1,2</sup>—has made the expanded scope of pharmacy practice possible. This continuing education and training monograph will address the legislation's provisions and regulations and provide a foundation for HIV prevention services: current clinical guidelines for PrEP and PEP provision, key pharmacologic considerations, pharmacist/patient communication, and practice-management strategies. Rule 17 specifies that all HIV-prevention care will be provided in accordance with current guidelines of the US Centers for Disease Control and Prevention (CDC) and the United States Preventive Services Task Force (USPSTF). In some instances, however, Colorado requirements may differ. These differences will be noted throughout this educational activity. Participants are also reminded to reference applicable regulations pertaining to all statewide protocols in Rule 17.<sup>2</sup>

### HIV Epidemiology and the Burden of Disease

Approximately 1.2 million people in the United States are living with HIV today, with 1 in 7 HIV-infected individuals unaware of their infection. Latest estimates from the CDC indicate that there were 36,400 new HIV infections in the United States in 2018. Populations including men who have sex with men (MSM),

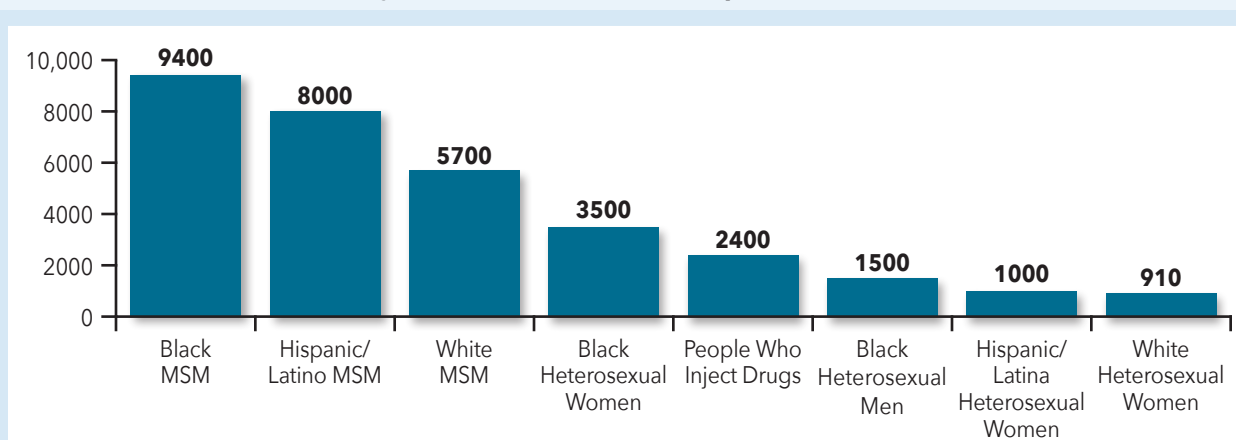
transgender persons, and black and Hispanic/Latinx individuals continue to be disproportionately affected. While new annual infections in the United States have been reduced by more than two thirds since the mid-1980s when HIV initially emerged, black and Hispanic/Latinx populations are among those that continue to have high rates of undiagnosed infections (**Figure 1**).<sup>3,4</sup>

The burden of HIV 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.<sup>5,6</sup> 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 antiretroviral therapy (ART), and proven prevention strategies and tactics.<sup>7</sup>

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.<sup>8</sup> ART has also given rise to modalities designed to limit HIV acquisition in HIV-negative individuals—namely, specific antiretroviral drug combinations used as PrEP and 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.<sup>9</sup>

Despite 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.<sup>10-12</sup> High risk populations with the lowest rates of PrEP uptake include young MSM, racial or ethnic minority groups, and individuals living

**FIGURE 1. New HIV Infections by Race and Transmission Group, 2018<sup>3</sup>**



HIV, human immunodeficiency virus; MSM, men who have sex with men.

in the South or Southeast regions of the United States. Without preventive efforts, 1 in 2 black MSM and 1 in 5 Hispanic/Latino MSM will contract HIV in their lifetimes.<sup>13,14</sup> The majority of PrEP uptake (75%) has been among white gay and bisexual men, predominantly those living in the Northeast or on the West Coast.<sup>15</sup> As of 2017, the PrEP-to-need ratio (ie, the number of PrEP users divided by new HIV diagnoses) was lowest among individuals age ≤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 2**).<sup>17</sup>

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.<sup>18</sup>

Further, clinicians may be unfamiliar with how to monitor patients on PrEP, and may not realize that a less costly generic PrEP formulation is now available.<sup>19</sup> In many locales, required preauthorization has been one of the most common barriers to prescribing PrEP, according to primary care and HIV-treatment providers.<sup>13</sup> 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, (see page 22, *Your Patient’s Advocate: Coordination of Care and Access to Financial-Assistance Resources*) cost may be a barrier for young black and Latino MSM and transgender women—many of whom are likely to be uninsured or underinsured—and who may benefit the most from PrEP.<sup>15</sup>

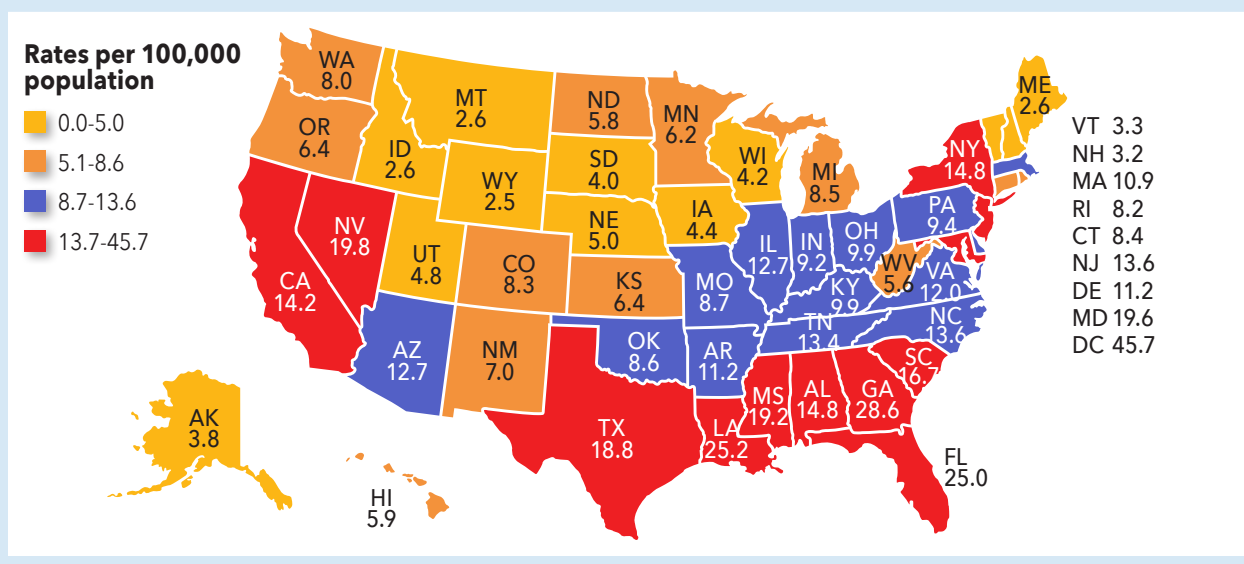
### Building Upon an Established Practice Foundation

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.<sup>1,14</sup> Many states, in an effort to curb the soaring rates of drug overdose, now allow pharmacists to dispense naloxone without a prescription.<sup>15,20</sup> Frequently, pharmacists in patient-centered medical homes lead medication-management services; help patients meet clinical-management goals as diverse as control of glycosylated hemoglobin (HbA1c), systolic blood pressure, and serum lipids; and increase vaccination rates and medication adherence.<sup>21</sup> In certain states, including Colorado, 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.<sup>1,13</sup> 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).<sup>21</sup>

Within the realm of HIV disease management, pharmacists have already demonstrated high levels of success in increasing ART adherence through comprehensive means: identification of patient-specific barriers (eg, health literacy, cognitive factors, mental-health and substance-use comorbidities, economic factors); detection of therapy-related barriers (eg, adverse effects, drug-drug interactions); and recognition of service-delivery barriers (eg, patient-provider relationships, providers’ cultural competencies).<sup>22</sup>

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

**FIGURE 2. Rates of New HIV Diagnoses in United States, 2018<sup>17</sup>**



of chronic-disease medication management, and knowledgeable of HIV pharmacology, the pharmacist can play an essential role in HIV prevention across diverse practice venues.<sup>23-25</sup>

### The Evolving Scope of Pharmacy Practice: The Future of HIV Prevention Is Here<sup>25</sup>

Despite Colorado’s relatively low HIV incidence—an estimated 470 new cases in 2019 per fourth-quarter estimates of the Colorado Department of Public Health and Environment (CDPHE)—there is an upward trend. The 2019 estimate reflects an approximate 13% increase over cases reported in 2018.<sup>26</sup> This contrasts with overall US HIV incidence rates, which remained stable or showed slight decreases between 2014 and 2018.<sup>27</sup>

Responding to this public health imperative, to reduce HIV incidence in Colorado, Senator Alex Valdez and Representative Leslie Herod, along with 45 bipartisan State Senate and House cosponsors drafted and introduced legislation to expand PrEP and PEP access through inclusion of pharmacists as providers of HIV-prevention care. In June 2020, Colorado’s House Bill (HB) 20-1061 passed both the State Senate and House with striking majorities (30-3 and 47-17, respectively). HB 20-1061 Section 4 amends the Colorado Revised Statutes 12-280-103 to include prescribing and dispensing of preexposure and postexposure (nonoccupational) prophylaxis for the prevention of HIV acquisition and ordering of lab tests in conjunction with prescribing or dispensing the drugs (Table 1).<sup>1,28</sup>

Moreover, HB 20-1061 Section 2 mandates coverage of the pharmacy-based clinical or administrative service, 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. Section 3 restricts payers from requiring prior authorization or step-therapy for clients accessing HIV-prevention services at the pharmacy level. As these mandates are Colorado-specific, they do not apply to large, nationwide employer-based health plans or Medicaid- or Medicare-backed plans.<sup>1</sup>

## BASIC-SCIENCE ESSENTIALS FOR THE PHARMACIST

### Therapeutic Interventions in the HIV Viral Life Cycle

**H**IV 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.<sup>29,30</sup>

The HIV life cycle (Figure 3) consists of 7 stages, 5 of which inform the mechanisms of action of current ARTs (Table 2).<sup>31</sup> The first stage is *binding* (or *attachment*): HIV binds to receptors on the surface of a CD4 cell. The second stage is called *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 and uses 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.<sup>31</sup>

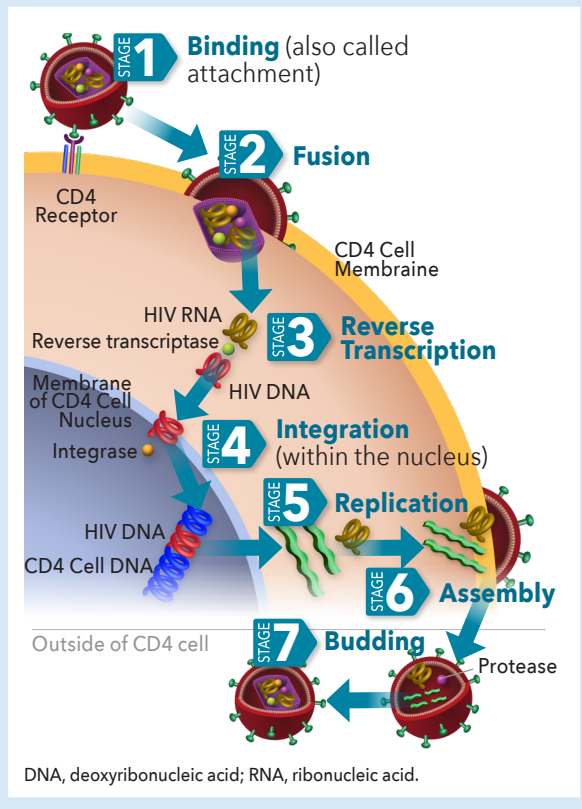
### Understanding the Immunologic Basis for HIV Testing

Following release of mature HIV from the CD4 cell, the viral RNA is initially present in the plasma without recognition by the host immune system. By approximately day 17, the HIV *p24 antigen* is present. The body recognizes

**TABLE 1. Summary of Updates to the Definition of Practice of Pharmacy per Colorado Revised Statutes<sup>1</sup>**

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 for 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

**FIGURE 3. The HIV Life Cycle<sup>31</sup>**



**TABLE 2. HIV Life-Cycle Stages and Antiretroviral Classes That Target Them<sup>31</sup>**

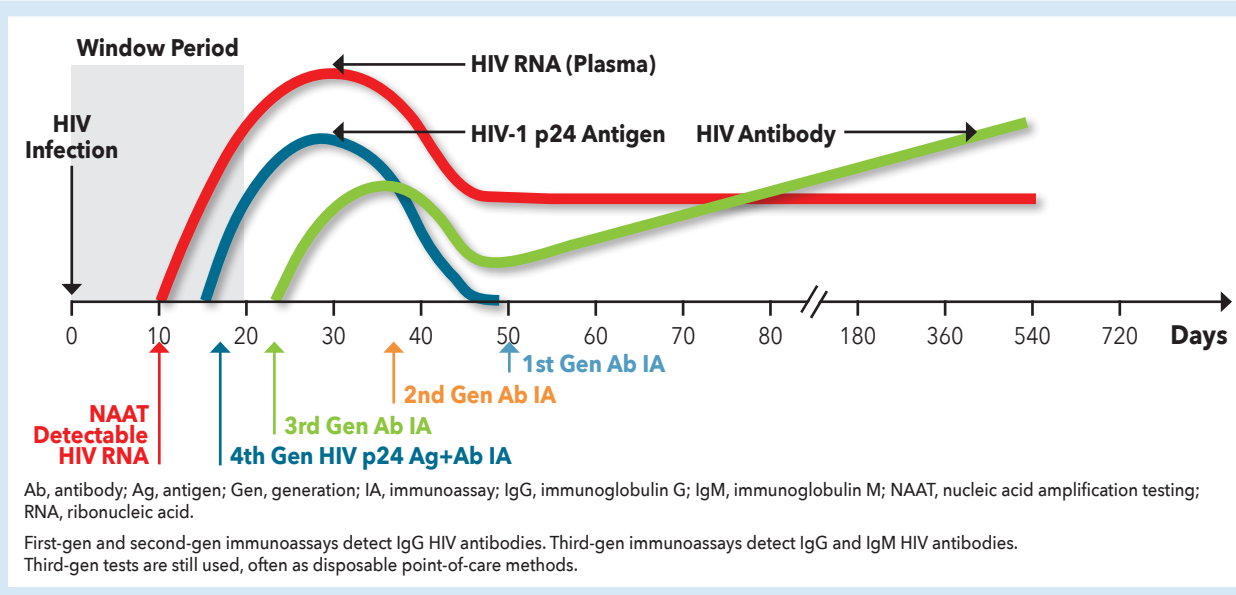
Stage	Description	Antiretroviral Class
1	Binding (attachment)	Entry inhibitors
2	Fusion	Fusion inhibitors
3	Reverse transcription	Nucleoside/nonnucleoside reverse transcriptase inhibitors
4	Integration	Integrase strand transfer inhibitors
5	Replication	None
6	Assembly	None
7	Budding	Protease inhibitors

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 with more highly specialized nucleic acid amplification testing (NAAT). That is, during this *window period*, an HIV-infected person may have an HIV-negative test result (Figure 4).<sup>32,33</sup>

Use of 4th-generation (gen) antigen/antibody (Ag/Ab) tests is the current standard of care. Usually performed in the laboratory setting, this immunoassay (IA) detects both p24 antigen and HIV-specific antibodies at approximately day 18. Third-gen IAs detect immunoglobulin G (IgG) and immunoglobulin M (IgM) HIV antibodies at about day 23. Third-gen tests are still used, often as a point-of-care testing modality.

**FIGURE 4. Window of Detection of HIV Markers in Early HIV Infection<sup>32,33</sup>**



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 should be advised.<sup>32,33</sup>

## PrEP 101

### What Is PrEP?

**P**rEP is the use of specific combinations of 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 alternate prevention strategy for individuals receiving PEP who continue to engage in high-risk behavior or who have 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.<sup>34</sup>

At the time of this publication, CDC guidelines recognize only 2 drug regimens for use as PrEP.<sup>34,35</sup>

- Tenofovir disoproxil fumarate (TDF) 300 mg/emtricitabine (FTC) 200 mg (fixed-dose combination) once daily (Truvada®, US Food and Drug Administration [FDA]-approved for treatment of chronic HIV infection in 2004 and FDA-approved for PrEP in 2012)<sup>36</sup>
  - Approved for all persons at risk of HIV acquisition
  - Currently the only PrEP regimen with an FDA-approved generic formulation (available as of October 2020)<sup>19</sup>
- Tenofovir alafenamide (TAF) 25 mg/FTC 200 mg (fixed-dose combination) once daily (Descovy®, FDA-approved for PrEP, October 2019)<sup>37</sup>
  - Indicated for all persons at risk of HIV acquisition, with the current exception (ie, has not been studied) of those at risk through receptive vaginal sex or injection drug use

### PrEP Pharmacologic Considerations: Efficacy and Safety

Key clinical trials involving TDF/FTC used as PrEP—including 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), and TDF2 (Botswana TDF/FTC Oral HIV Prophylaxis trial)—demonstrated safety and efficacy of the combined use of these 2 nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) as PrEP across all at-risk populations, including MSM, heterosexual HIV-discordant couples, heterosexual men and women, and people who inject drugs (PWID).<sup>34,38-42</sup> As noted, TDF and FTC target reverse transcription, stage 3 in the HIV life cycle (**Figure 3**). Once phosphorylated intracellularly, creating diphosphate and triphosphate

metabolites, respectively, these nucleotide/nucleoside analogs inhibit HIV reverse transcriptase by competing with viral substrates and, thereby, causing DNA chain termination and preventing viral RNA conversion.<sup>36</sup>

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.<sup>43</sup>

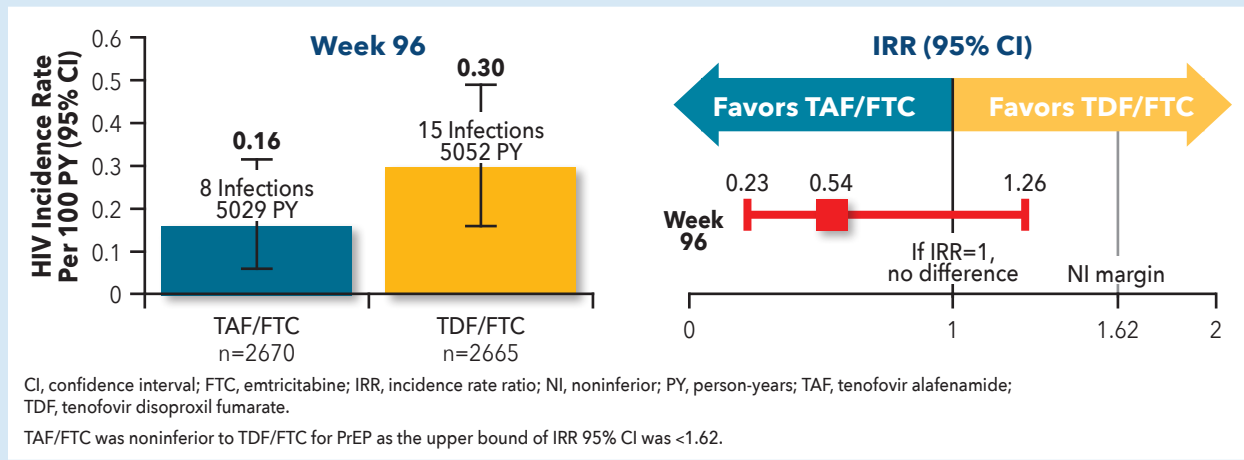
TDF/FTC remained the sole FDA-approved antiretroviral regimen for use as PrEP until October 2019. The randomized, double-blind, active-control DISCOVER trial evaluated the efficacy and safety of TAF/FTC vs TDF/FTC in high-risk cisgender MSM and transgender women (in North America and Europe).<sup>44</sup> Eligible patients (N=5387; mean age 36 years) 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. 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 5**).<sup>45</sup>

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.<sup>37,45</sup>

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.<sup>46</sup> Use of TDF/FTC as PrEP is not recommended for persons with eCrCl <60 mL/min/1.73 m<sup>2</sup>. Further, reduced-dosing strategies for TDF/FTC as PrEP have not been developed.<sup>34</sup>

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<sup>2</sup>) 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<sup>2</sup> and, therefore, TAF/FTC for PrEP is not recommended for patients with eCrCl <30 mL/min/1.73 m<sup>2</sup>.<sup>37</sup> 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. The bone- and renal-related adverse effects associated with TDF are less likely to occur with TAF due to this lower plasma exposure.<sup>47</sup> Of note, in

**FIGURE 5. DISCOVER Trial: TAF/FTC Is Noninferior to TDF/FTC for HIV Prevention<sup>45</sup>**



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.<sup>48</sup>

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.<sup>34,36,37,49</sup> However, the CDC PrEP guidelines do not provide further parameters for consideration when choosing between these 2 PrEP regimens.<sup>35</sup> 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.<sup>36</sup> TAF/FTC may be associated with headache, nausea, diarrhea, minor increases in LDL cholesterol and triglycerides, and minor weight gain (Table 3).<sup>37</sup>

Potential drug-drug interactions (DDIs) with TDF/FTC or TAF/FTC are listed in Table 4.<sup>36,37,50</sup> 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 listed, including 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—including those of acute HIV infection—that should be reported on an urgent basis.<sup>31,51</sup>

**TABLE 3. Adverse Events Associated With TDF and TAF<sup>36,37,49</sup>**

	TDF	TAF
<b>Renal</b>	<ul style="list-style-type: none"> <li>Fanconi syndrome</li> <li>Proximal renal tubulopathy</li> </ul>	
<b>Bone</b>	<ul style="list-style-type: none"> <li>Decreased bone mineral density</li> <li>Osteomalacia</li> </ul>	
<b>Hepatic</b>	<ul style="list-style-type: none"> <li>Acute exacerbation of HBV with PrEP discontinuation</li> </ul>	<ul style="list-style-type: none"> <li>Acute exacerbation of HBV with PrEP discontinuation</li> </ul>
<b>Neurologic</b>	<ul style="list-style-type: none"> <li>Asthenia, headache</li> </ul>	<ul style="list-style-type: none"> <li>Headache</li> </ul>
<b>Gastrointestinal</b>	<ul style="list-style-type: none"> <li>Nausea, vomiting, diarrhea, flatulence</li> </ul>	<ul style="list-style-type: none"> <li>Nausea, diarrhea</li> </ul>
<b>Metabolic</b>	<ul style="list-style-type: none"> <li>Minor decreases in HDL, LDL, and total cholesterol</li> </ul>	<ul style="list-style-type: none"> <li>Minor increases in LDL cholesterol and triglycerides</li> </ul>
<b>General</b>	<ul style="list-style-type: none"> <li>Minor weight loss</li> </ul>	<ul style="list-style-type: none"> <li>Minor weight gain</li> </ul>

HBV, hepatitis B virus; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PrEP, preexposure prophylaxis; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.



**TABLE 4. Potential DDIs Involving TDF/FTC or TAF/FTC**

PrEP	Drug Class or Characteristic	Recommendation
TDF/FTC <sup>36</sup>	Drugs that could potentially reduce renal function or compete for active renal tubular secretion: <ul style="list-style-type: none"> <li>• Acyclovir</li> <li>• Valacyclovir</li> <li>• Cidofovir</li> <li>• Ganciclovir</li> <li>• Valganciclovir</li> <li>• Aminoglycosides</li> <li>• High-dose or multiple NSAIDs</li> </ul>	<ul style="list-style-type: none"> <li>• Caution</li> <li>• Monitor for dose-related renal toxicities</li> </ul>
	First-line HCV DAAs <sup>50</sup>	<ul style="list-style-type: none"> <li>• EBR/GZR: No interactions expected</li> <li>• GLE/PIB: No interactions expected</li> <li>• SOF/LDV: Serum concentrations of TDF may be increased; monitor for toxicities</li> <li>• SOF/VEL: Serum concentrations of TDF may be increased; monitor for toxicities</li> </ul>
TAF/FTC <sup>37</sup>	Anticonvulsants: <ul style="list-style-type: none"> <li>• Carbamazepine</li> <li>• Oxcarbazepine</li> <li>• Phenobarbital</li> <li>• Phenytoin</li> </ul>	<ul style="list-style-type: none"> <li>• Reduced TAF concentration</li> <li>• Alternate anticonvulsant advised</li> </ul>
	Antimycobacterials: <ul style="list-style-type: none"> <li>• Rifabutin</li> <li>• Rifampin</li> <li>• Rifapentine</li> </ul>	<ul style="list-style-type: none"> <li>• Reduced TAF concentration</li> <li>• TAF/FTC coadministration not advised</li> </ul>
	Herbal products: <ul style="list-style-type: none"> <li>• St. John’s wort</li> </ul>	<ul style="list-style-type: none"> <li>• Reduced TAF concentration</li> <li>• TAF/FTC coadministration not advised</li> </ul>
	First-line HCV DAAs <sup>50</sup>	<ul style="list-style-type: none"> <li>• EBR/GZR: No interactions expected</li> <li>• GLE/PIB: No interactions expected</li> <li>• SOF/LDV: No interactions expected</li> <li>• SOF/VEL: No interactions expected</li> </ul>

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; TAF/FTC, tenofovir alafenamide/emtricitabine; TDF/FTC, tenofovir disoproxil fumarate/emtricitabine.

### Pretreatment Determination of PrEP Eligibility<sup>2,34</sup>

Determination of an individual’s eligibility for PrEP includes several required clinical components:

- Conduct a comprehensive behavioral risk assessment (sexual; injection drug use) to identify appropriate PrEP candidates
- 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 Improved Amendments, a laboratory test can be conducted without the need for more stringent standards)

- **Note:** Per SBOP Rule 17, oral swab tests and patient reports are *not* acceptable as evidence of negative HIV status
- Perform *baseline* (pretreatment) laboratory assessment (**Table 5**) and clinically correlate results

### Comprehensive Behavioral Risk Assessment (Sexual and Injection Drug Use)<sup>34</sup>

A comprehensive behavioral risk assessment (including sexual and injection drug use) is critical for identification of appropriate PrEP candidates (**Table 6**).

The behavioral assessment may also reveal additional needs for in-depth education, risk-reduction counseling, and community-based patient-support

**TABLE 5. CDC Guidelines for Minimum Baseline Laboratory Assessment<sup>34</sup>**

- HIV: rapid combined antigen/antibody test preferred
- Serum creatinine for calculation of estimated creatinine clearance
- HBV and HCV serology
- STIs: chlamydia, gonorrhea, syphilis
- Pregnancy

CDC, Centers for Disease Control and Prevention; HBV, hepatitis B virus; HCV, hepatitis C virus; STI, sexually transmitted infection.

services. *Embracing Sexual Wellness and Discussing HIV Risk: The Sexual Health Assessment* (page 20) provides a more in-depth discussion of these concerns.

**Confirmation of HIV-Negative Status**

Currently, 4th-gen combined antigen/antibody tests are both recommended and preferred. Antigen/antibody tests utilizing blood from a vein can usually detect HIV infection 18–45 days after an exposure, while rapid antigen/antibody tests with fingerprick blood may detect HIV 18–90 days after exposure (**Figure 4**).<sup>32,33,52</sup> Other HIV tests are recognized and allowed, but it is crucial to remember the limitations of antibody-only tests. As of June 2018, 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 Antigen/Antibody Combined Test
- INSTI® HIV-1/HIV-2 Antibody Test
- Uni-Gold™ Recombigen® HIV-1/2 Antibody Test

Only the Alere Determine™ test is a 4th-gen combined antigen/antibody assay; all others listed test only for antibodies to HIV-1 and HIV-2.<sup>53</sup>

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 Antibody Test<sup>53</sup>

Rapid tests using finger-prick or venous whole blood can yield results in approximately 10 minutes. No further testing is needed if test results are negative, but positive tests must be confirmed with more specific conventional blood tests, with results available in <1 hour to several days. Oral HIV tests are not recommended in these clinical scenarios.<sup>31</sup> 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>.

When interpreting HIV-test results, clinicians must keep in mind the *approximate* 18-day period (see **Figure 4**), during which time even the 4th-gen combined antigen/antibody tests may fail to detect early infection. Therefore, all patients should be questioned regarding specific signs and symptoms suggestive of or consistent with early/acute HIV (**Table 7**). Only with both negative HIV testing and negative screening for these signs and symptoms should there be further consideration of PrEP prescribing.<sup>34</sup>

**TABLE 6. Summary of Risk Factors Associated With Substantial Risk of HIV Acquisition<sup>34</sup>**

MSM	Heterosexual Women and Men	Patients With Injection Drug Use
<ul style="list-style-type: none"> <li>• HIV-positive sexual partner</li> <li>• Sexual partner with unknown HIV status</li> <li>• Recent bacterial STI (gonorrhea, chlamydia, or syphilis)</li> <li>• High number of sexual partners</li> <li>• History of inconsistent or no condom use</li> <li>• Commercial sex work</li> </ul>	<ul style="list-style-type: none"> <li>• HIV-positive sexual partner</li> <li>• Sexual partner with unknown HIV status</li> <li>• Recent bacterial STI (gonorrhea, chlamydia, or syphilis)</li> <li>• High number of sexual partners</li> <li>• History of inconsistent or no condom use</li> <li>• Commercial sex work</li> <li>• In high HIV prevalence area or network</li> </ul>	<ul style="list-style-type: none"> <li>• HIV-positive injecting partner</li> <li>• Sharing injection equipment</li> </ul>

IDU, injection drug use; MSM, men who have sex with men; STI, sexually transmitted infection.

**TABLE 7. Signs and Symptoms Associated With Acute HIV Infection<sup>34</sup>**

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

**Laboratory Assessment for PrEP-Associated Risks**

Estimated creatinine clearance (as calculated using the Cockcroft-Gault equation) is critical to determination of PrEP eligibility.

- If eCrCl <60 mL/min/1.73 m<sup>2</sup>, TDF/FTC is *not* recommended; reduced-dosing strategies for TDF/FTC as PrEP have not been developed<sup>34</sup>
- If eCrCl <30 mL/min/1.73 m<sup>2</sup>, TAF/FTC is *not* recommended<sup>37</sup>

Pretreatment evaluation of hepatitis B (HBV) serology is equally important. While HBV infection is not a contraindication to 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 and consideration for HBV treatment.<sup>34</sup>

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. **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.<sup>34</sup>

**Patient-Centered PrEP: Regimen Selection and Pretreatment Counseling**

Once the patient's eligibility is established, few considerations will impact the selection of PrEP regimen. The most critical is the patient's renal function: TDF/FTC should not be prescribed for individuals whose eCrCl is <60 mL/min/1.73 m<sup>2</sup>, because of TDF's renal clearance.<sup>34,37</sup> Bone density (especially if the patient is over 50 years of age), cholesterol, and weight change may also be considerations for the given individual.<sup>34,37</sup> 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.<sup>35</sup> Further, the patient's 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.<sup>15</sup> A generic formulation for TDF/FTC became available as of October 2020, but TAF/FTC is available only in brand form.<sup>19</sup>

Under CO HB 20-1061 and CO SBOP Rule 17, the pharmacist may prescribe and dispense the following FDA-approved PrEP regimens (**Table 8**).<sup>1,2</sup>

Having established the patient's PrEP eligibility, the PrEP provider's additional pretreatment requirements address the following clinical activities<sup>34</sup>:

- Prescribe safe and effective PrEP regimens for eligible HIV-uninfected persons
- Educate patients about the selected PrEP regimen to maximize safe use

**TABLE 8. Prescribing and Dispensing Approved PrEP Regimens Under Colorado SBOP Rule 17<sup>1,2</sup>**

Medication	Age/Weight	Frequency	Prescribing Considerations	Notes
TDF 300 mg/ FTC 200 mg (brand or generic)	≥35 kg	Once daily	<ul style="list-style-type: none"> <li>• May take with or without food</li> <li>• Not recommended for eCrCl &lt;60 mL/min/1.73 m<sup>2</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Prescription issued for 30 days with no refills if all lab requirements are not completed</li> </ul>
TAF 25 mg/ FTC 200 mg (brand only)	≥35 kg	Once daily	<ul style="list-style-type: none"> <li>• May take with or without food</li> <li>• Not recommended for eCrCl &lt;30 mL/min/1.73 m<sup>2</sup></li> <li>• Should only be used for at-risk cisgender men and transgender women</li> <li>• Pharmacist must review for potential drug-drug interaction as per package insert</li> </ul>	<ul style="list-style-type: none"> <li>• Up to 90 days if all lab requirements are completed</li> <li>• Refill quantity only until next scheduled lab follow-up</li> </ul>

eCrCl, estimated creatinine clearance; TAF/FTC, tenofovir alafenamide/emtricitabine; TDF/FTC tenofovir disoproxil fumarate/emtricitabine.

- Provide counseling and effective contraception to women on PrEP who do not wish to become pregnant
- 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

**Emerging (nonapproved) PrEP Regimens**

While **Table 8** presents TDF 300 mg/FTC 200 mg and TAF 25 mg/FTC 200 mg as the *only currently approved* PrEP regimens, SBOP Rule 17 states, “Other FDA-approved/CDC-recommended medication or regimens can be used if they become available.”<sup>1,2</sup>

Of particular note, preliminary results of the HIV Prevention Trials Network 083 (HPTN 083) study of the efficacy of the integrase inhibitor cabotegravir (CAB) as a long-acting injectable for HIV prevention were presented at the *AIDS 2020: Virtual* conference held July 6–10, 2020. 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 6**).<sup>54</sup> Approval of CAB for use as PrEP by MSM and trans women who have sex with men is anticipated in the near future.

The HIV Prevention Trials Network is currently studying the effectiveness of long-acting CAB as PrEP in HIV-uninfected women. HPTN 084 (LIFE) is a phase 3 trial

designed to track roughly 3200 women of childbearing age in sub-Saharan Africa over a 4.5-year period. 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 cabotegravir was 89% (95% CI 68%–96%) more effective than TDF/FTC. The study was terminated early (November 2020) because of this demonstration of CAB’s statistically based superiority.<sup>55</sup> Similarly, approval for CAB for use as PrEP in women of childbearing age is anticipated. This long-acting, injectable PrEP option has the potential advantage of enhanced HIV prevention without reliance on daily adherence to an oral PrEP regimen for women, as well as MSM and trans women who have sex with men.

**Alternative (nonapproved) PrEP Strategies**

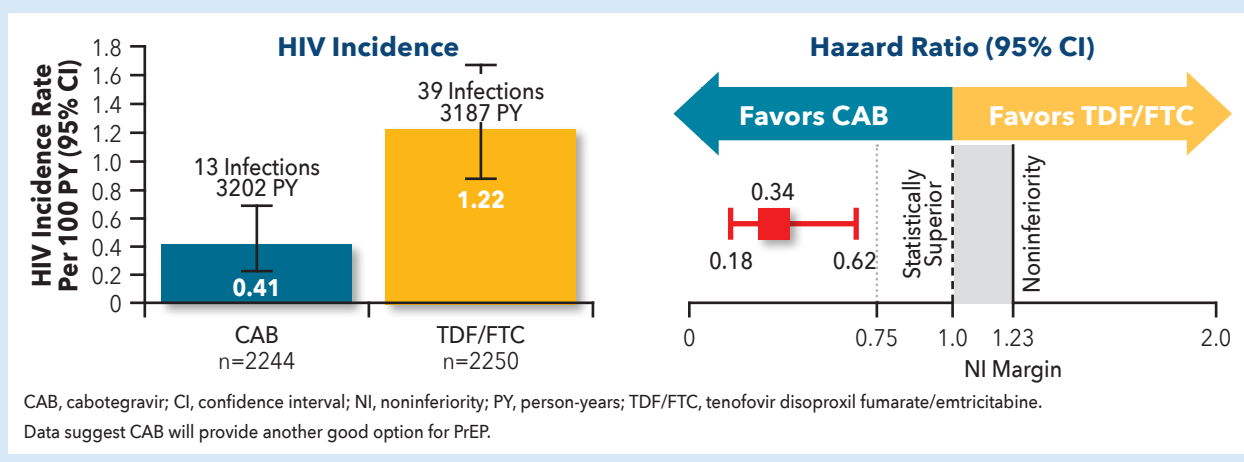
**Note:** Colorado SBPO Rule 17 does not authorize the following 2 PrEP strategies.

CDC guidelines provide for use of TDF monotherapy for PWID and for heterosexual men and women, based on prior trials demonstrating efficacy in these specific populations. There are no data supporting TDF monotherapy for MSM and, therefore, it is not recommended.<sup>34</sup>

While not CDC-recommended or FDA-approved, evidence-based *on-demand* or *event-driven* protocols are endorsed by other organizations. For example, 2-1-1 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).<sup>56,57</sup> Named on the basis of the number and timing of PrEP tablets taken, 2-1-1 provides the following recommendations<sup>58</sup>:

- 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

**FIGURE 6. HPTN 083 – HIV Incidence: CAB vs TDF/FTC<sup>54</sup>**



- 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.<sup>56,58</sup>

### On-PrEP Interval Laboratory Testing and Patient Monitoring

The following table provides a comprehensive look at CDC guidelines for on-PrEP interval laboratory testing and patient monitoring (Table 9).<sup>34</sup>

CO SBOP Rule 17 allows for the pharmacist’s continuous prescribing of approved PrEP therapies, as based on adherence to monitoring requirements. An initial 30-day supply of the selected PrEP medication can be

prescribed and dispensed by the pharmacist following confirmation of the patient’s HIV-negative status. The pharmacist may authorize PrEP refills beyond the initial 30-day prescription as long as laboratory and monitoring requirements are fulfilled.<sup>2</sup>

### Indications for Referral

If at any point in the PrEP care continuum—from baseline evaluation to long-term monitoring—acute HIV is suspected, a patient tests positive for HBV, becomes pregnant, has symptoms or laboratory findings of acute renal injury, or has a positive STI screen, referral to a PCP or appropriate provider should be made as soon as possible (Table 10).<sup>2</sup>

### Patient Education, Counseling, and Support for PrEP Adherence

Components of basic medication-related education for patients include the following:

**TABLE 9. Baseline Assessment, Laboratory Testing, and On-PrEP Interval-Monitoring Requirements<sup>34</sup>**

Test	Baseline	Every 3 Months	At Least Every 6 Months	At Least Every 12 Months	Colorado SBOP Rule 17	CDC Recommendation	Notes
<b>Provider assessment</b>	X	X				X	• Discuss adherence, side effects, barriers, etc
<b>Risk assessment/ need to continue PrEP</b>	X			X	X	X	• Consider discussing continued risk and need for PrEP at each visit
<b>HIV Screen</b>	X	X			X	X	• Consider need for HIV RNA PCR for acute HIV
<b>Hepatitis A screen</b>							• Offer vaccination if not immune
<b>Hepatitis B screen</b>	X				X	X	• Offer vaccination if not immune; if positive, refer for care
<b>Hepatitis C screen</b>	X					X	• If positive, refer for care
<b>Serum creatinine</b>	X		X			X	• Test at baseline, at 3 months and thereafter, every 6 months • If eCrCl <60 mL/min/1.73 m <sup>2</sup> , cannot use TDF/FTC • If eCrCl <30 mL/min/1.73 m <sup>2</sup> cannot use TAF/FTC
<b>3-site STI screening</b> (syphilis, gonorrhea, chlamydia)	X	X	X			X	• Test at baseline + at 3 months if symptomatic; every 6 months if asymptomatic • If positive refer for care

CDC, Centers for Disease Control & Prevention; eCrCl, estimated creatinine clearance; TAF/FTC, tenofovir alafenamide/emtricitabine; TDF/FTC, tenofovir disoproxil fumarate/emtricitabine; PCR, polymerase chain reaction; SBOP, State Board of Pharmacy; STI, sexually transmitted infection.

**TABLE 10. SBOP Rule 17: Indications for Referral to a PCP or Other Appropriate Provider<sup>2</sup>**

*A referral should be made if a patient . . .*

- Tests positive for HIV infection
- Manifests signs/symptoms of acute HIV infection
- Tests positive for HBV
- Becomes pregnant while on PrEP
- Manifests signs/symptoms of acute renal injury
- Tests positive for an STI

HBV, hepatitis B virus; PCP, primary care provider; STI, sexually transmitted infection.

- Which PrEP medication is being prescribed? How is it taken? What is the dosing schedule? (**Table 8**)
- Time to maximum HIV-prevention effectiveness, as based on exposure mode (**Table 11**)
- How to manage missed doses
- Common signs and symptoms suggestive of acute HIV infection (**Table 7**)
- Common side effects of the prescribed PrEP regimen (**Table 3**)
- What quantity will be dispensed? (**Table 8**)
- Requirement to remain under the care of the PrEP prescriber for required interval monitoring

Time to maximum HIV prevention varies with mode of sexual exposure (**Table 11**). 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.<sup>34</sup>

Effective HIV prevention requires a high level of daily adherence to the PrEP medication, but there is some

**TABLE 11. Time to Maximum HIV Protection (Tissue Concentration), by Mode of HIV Exposure<sup>59</sup>**

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

leeway for missed doses. The STRAND trial showed that 6 to 7 doses per week are required to maintain protective vaginal tissue concentration; fewer doses per week may be adequate to maintain colorectal tissue concentrations. Nonetheless, daily adherence should be stressed for all persons on PrEP. Should a patient report missing a dose, instruct the patient to take a 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.<sup>34</sup>

**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.<sup>34,59,60</sup> 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.<sup>61</sup> 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<sup>34</sup>

Additional adherence strategies can be found in the provider supplements to the CDC PrEP guidelines<sup>62</sup>; <https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-provider-supplement-2017.pdf>

As adverse effects may impact PrEP adherence, pharmacists should counsel patients regarding the following concerns<sup>34</sup>:

- Common side effects (headache, nausea, and flatulence) that typically resolve within the first month of taking PrEP (start-up syndrome) and over-the-counter medications for symptom management
- Signs or symptoms of acute HIV infection (**Table 7**) or acute renal injury, both of which require urgent intervention

**PrEP Discontinuation and Resumption**

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, nontolerated side effects, toxicities, chronic nonadherence, or acute HIV infection. 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.<sup>34</sup>

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 resume PrEP at some point after discontinuation, all pretreatment requirements must be repeated and fulfilled. The PrEP provider should engage the patient in an open discussion regarding change in personal circumstances and commitment to PrEP adherence.<sup>34</sup>

### Transitioning From PrEP to HIV Treatment as Prevention

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.<sup>34</sup> 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.<sup>63</sup>

US Department of Health and Human Services (DHHS) HIV/AIDS guidelines recommend that upon laboratory confirmation of HIV infection in an individual on PrEP, the patient should transition from PrEP to comprehensive HIV treatment. An HIV treater (specialist or PCP) should be involved in determining ART selection and initiating therapy. Under new guidelines for rapid ART initiation (*rapid ART*; *rapid start*), there is no need to wait for additional laboratory results. A rapid ART strategy seeks to accelerate the time from HIV diagnosis to engagement in care and ART uptake and, ultimately, viral suppression. Current guidelines call for ART initiation on the day of diagnosis (or as close as possible).<sup>49</sup> 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.<sup>64</sup>

### Summary of Colorado State Board of Pharmacy Statewide Protocols (Rule 17 Appendix C) Regarding PrEP

HB 20-1016 authorizes pharmacists to prescribe and dispense medications for HIV PrEP. Although the bill addresses minimal requirements for the pharmacist's participation in the statewide protocol, the bill defers implementation of specific considerations to the

Colorado State Board of Pharmacy, in conjunction with the state's medical and nursing boards. The output of this multiboard collaboration is CO SBOP Rule 17 Appendix C, a protocol that specifies assessment of HIV status and high-risk behaviors, determination of PrEP eligibility (including pretreatment laboratory testing), and selection and provision of FDA-approved/CDC-recommended oral antiretroviral agents for appropriately identified PrEP candidates.

The protocol further delineates requirements for on-PrEP monitoring (laboratory and patient assessments; **Table 9**), minimum counseling components, dispensing guidelines, and referral processes. Patient counseling must be provided at the time of each prescription refill or interval evaluation/lab work visit: counseling components include proper medication use, including dosage, schedule; possible side effects (both common and severe); and the importance of medication adherence. Signs and symptoms of acute HIV infection, consistent use of condoms, other STI prevention techniques, and primary care follow-up for usual care should also be addressed routinely.

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 at any time in the PrEP care continuum the patient tests positive for or develops signs/symptoms of any of the conditions listed in **Table 7**, appropriate referral should be made (**Table 10**).

Developing relationships with physicians and advanced practice nurses in the local area who are experienced in HIV care and prevention will expedite the referral process and ease patient concerns. If you, the pharmacist, are unaware of any appropriate providers in the local area, the following CDPHE resource may be of help: <https://cdphe.colorado.gov/living-with-hiv>.<sup>65</sup>

CO HB Bill 20-1061 and subsequent authorizations under CO State Board of Pharmacy Rule 17 Appendix C have paved the way for clinical and community pharmacists to assume active roles in HIV prevention through provision of comprehensive PrEP services (See **page 28 for Appendix C in its entirety**.)

## 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.<sup>9,66</sup> 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.<sup>66</sup>

Occupational HIV exposure refers to high-risk events occurring in a health care setting, whereas 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.<sup>66</sup>

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 as a PEP-regimen component.<sup>66</sup>

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:

- TDF 300 mg/FTC 200 mg once daily *plus* raltegravir (RAL) 400 mg twice daily
- OR**
- TDF 300 mg/FTC 200 mg once daily *plus* dolutegravir (DTG) 50 mg once daily

The following regimen is **not approved for use** under CO SBOP Rule 17, although it is included under the CDC guidelines as an alternative: TDF 300 mg/FTC 200 mg once daily plus darunavir (DRV) 800 mg and ritonavir (RTV) 100 mg once daily.<sup>2,66</sup>

The CDC PEP guidelines do not in general recommend 1 INSTI over the other (ie, DTG vs RAL), however, DTG may be preferred for its once-daily dosing.<sup>66-68</sup> Note that use of DTG should be avoided in *periconception period*

because of the risk of neural tube defects linked to drug exposure during the first 28 days of gestation, yet there are no data to suggest that DTG has any teratogenic signal after the periconception period.<sup>69</sup> 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.<sup>68</sup> In either clinical scenario, patients should be prescribed RAL. Additional pharmacologic considerations when prescribing RAL or DTG as PEP are outlined in **Table 12**.<sup>49,67,68</sup>

RAL and DTG are both associated with adverse events that include headache, insomnia, and weight gain.<sup>49,67,68</sup> 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.<sup>67,68</sup>

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 13**).<sup>68</sup>

**Pretreatment Determination of PEP Eligibility<sup>2,66</sup>**

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

**TABLE 12. Pharmacologic Considerations When Prescribing Raltegravir or Dolutegravir<sup>49,67,68</sup>**

	Raltegravir	Dolutegravir
<b>Antiretroviral class</b>	• INSTI	• INSTI
<b>Serum half-life</b>	• Approximately 9 hours	• Approximately 13 hours
<b>Absorption concerns</b>	• Absorption affected by cation-containing (magnesium, aluminum, iron, calcium, or zinc) medications and products; eg, antacids, laxatives	• Same as raltegravir
<b>Dosing adaptation</b>	• 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
<b>Contraindication or caution</b>		• Risk of neural tube defects • Contraindicated with dofetilide (class III antiarrhythmic) • Interaction with higher dosages of metformin

INSTI, integrase strand transfer inhibitor.



**TABLE 13. Adverse Events Associated With Raltegravir or Dolutegravir<sup>46,67,68</sup>**

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

- 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 for PEP-associated risks
- Screen for drug/drug interactions
- In Colorado, the patient must be 13 years of age or older

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 patient has been consistently adherent to PrEP.<sup>66</sup>

**Comprehensive Sexual (and Injection Drug Use) Risk Assessment<sup>66</sup>**

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.<sup>66</sup> **Figure 7** is an algorithm for determining substantial HIV exposure. The information obtained through the comprehensive risk assessment will inform your use of the algorithm.

**Confirmation of HIV-Negative Status<sup>2,66</sup>**

HIV-testing considerations, as outlined (see page 10) for pre-PrEP assessment—*PrEP 101, Confirmation of HIV-Negative Status*—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 (**Table 7**). 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 a 4th-gen antigen/antibody 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**

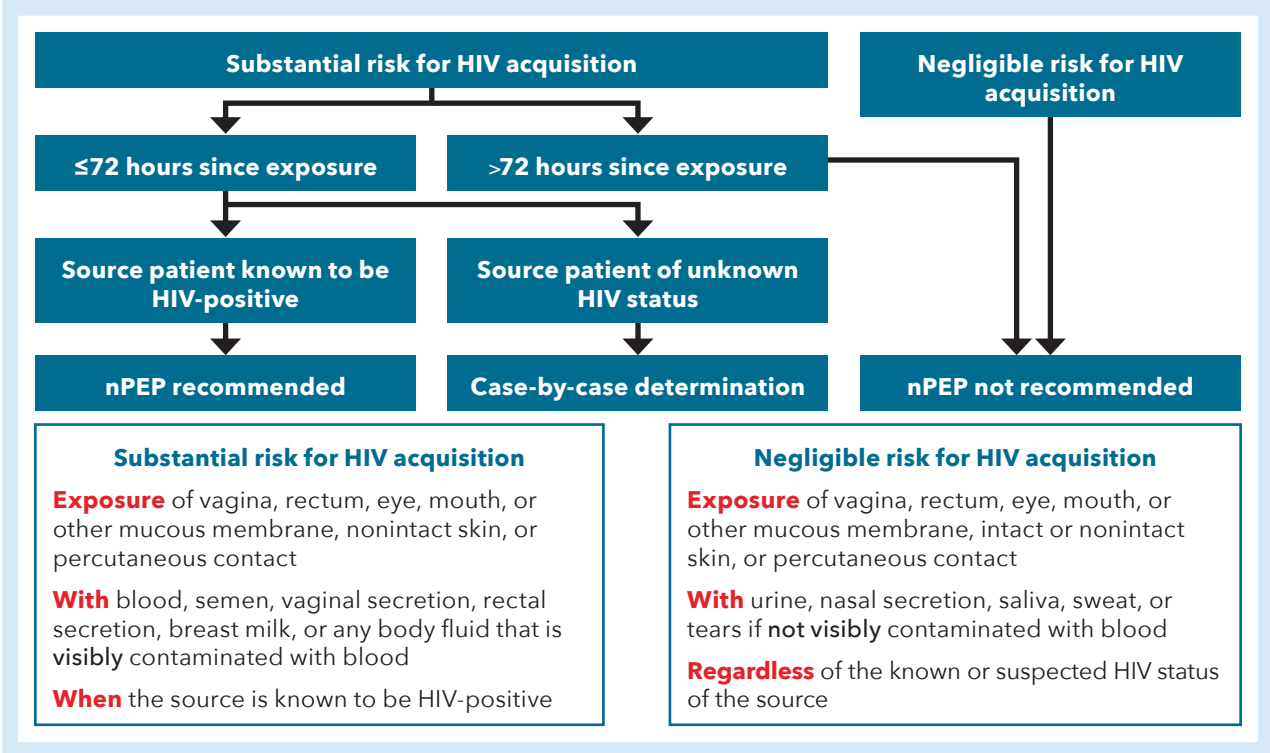
As with HIV PrEP, pre-PEP laboratory assessment must be performed prior to treatment initiation. Again, critical labs include estimated creatinine clearance (eCrCl), HBV serology, and pregnancy testing. Additionally, if indicated by the comprehensive risk assessment, patients considered for PEP should 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 routine vaccinations, eg, HAV, HBV, and human papillomavirus (HPV).<sup>66</sup>

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 aminotransferase [ALT] and aspartate aminotransferase [AST]) and test-specific requirements for postexposure follow-up testing (**Table 14**).<sup>66</sup>

**FIGURE 7. Algorithm for Evaluation and Treatment of Possible Nonoccupational HIV Exposure (nPEP)<sup>66</sup>**



**TABLE 14. DHHS PEP Guidelines: Baseline and Follow-up Laboratory Testing<sup>66</sup>**

Test	Frequency	Other
HIV: combined antigen/antibody test preferred	<ul style="list-style-type: none"> <li>Baseline and at 4–6 weeks, 3 months, and 6 months after exposure</li> </ul>	<ul style="list-style-type: none"> <li>If positive, refer</li> </ul>
Serum creatinine for calculation of estimated creatinine clearance	<ul style="list-style-type: none"> <li>Baseline and at 4–6 weeks</li> </ul>	
ALT; AST	<ul style="list-style-type: none"> <li>Baseline and at 4–6 weeks</li> </ul>	
HBV serology	<ul style="list-style-type: none"> <li>Baseline and at 6 months after exposure</li> </ul>	<ul style="list-style-type: none"> <li>If positive, refer</li> <li>If negative and appropriate, vaccinate</li> </ul>
HCV serology	<ul style="list-style-type: none"> <li>Baseline and at 6 months after exposure</li> </ul>	<ul style="list-style-type: none"> <li>If positive, refer</li> </ul>
STIs: syphilis serology	<ul style="list-style-type: none"> <li>Baseline, at 4–6 weeks, and at 6 months after exposure</li> </ul>	<ul style="list-style-type: none"> <li>If positive, refer for STI care</li> </ul>
STIs: chlamydia; gonorrhea	<ul style="list-style-type: none"> <li>Baseline and at 4–6 weeks after exposure</li> </ul>	<ul style="list-style-type: none"> <li>If positive, refer for STI care</li> </ul>
Pregnancy	<ul style="list-style-type: none"> <li>Baseline and at 4–6 weeks</li> </ul>	<ul style="list-style-type: none"> <li>Pregnancy is not a contraindication for use of PEP</li> </ul>

ALT, alanine aminotransferase; AST, aspartate aminotransferase; DHHS, Department of Health and Human Services; HBV, hepatitis B virus; HCV, hepatitis C virus; PEP, postexposure prophylaxis; STI, sexually transmitted infection.

## Patient-Centered PEP: Regimen Selection and Pretreatment Counseling<sup>6,68</sup>

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.<sup>2</sup>

- 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 7**)
- Common side effects associated with raltegravir and dolutegravir (**Table 13**)
- 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. Although 3-7-day PEP starter packs exist, *they are not an option in Colorado*.

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)

- 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.<sup>66</sup> Colorado Rule 17 requires pharmacists to make "every reasonable effort" to follow up with patients at 4-6 weeks post PEP initiation for determination of post-PEP HIV status. If negative, the patient should be advised that repeat HIV testing is recommended at 3 and 6 months. Further, the patient should be counseled regarding the availability of PrEP. Patients testing positive for HIV after the course of PEP has been completed should be referred to an HIV treatment specialist to transition to HIV treatment.<sup>2,66</sup>

### Transitioning From PEP to PrEP

PEP is indicated only for patients with  $\geq 1$  known or suspected high-risk, unprotected HIV exposure who are HIV-negative at initial PEP evaluation. If the patient has documented HIV-negative status (preferably using a 4th-gen antigen/antibody test) upon completion of a 28-day course of PEP, s/he can be transitioned from PEP to PrEP without any gap in treatment.<sup>34,66</sup> Patients who are at frequent, recurrent risk of HIV exposure, or require sequential or near-continuous courses of PEP, should be offered 1 of the 2 FDA-approved PrEP ART regimens 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.<sup>66</sup>

### PEP Failure and Transitioning From PEP to HIV Treatment as Prevention<sup>66</sup>

If use of PEP fails to prevent HIV infection, patients may experience signs and symptoms of acute/primary, or early, HIV.<sup>33</sup> Patients should be instructed during the initial PEP evaluation about such manifestations, as listed in **Table 7**. 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.

### Summary of Colorado State Board of Pharmacy Statewide Protocol (Rule 17 Appendix C) Regarding PEP<sup>2</sup>

As with PrEP, HB 20-1061 authorizes pharmacists to prescribe and dispense medications for HIV PEP. Colorado State Board of Pharmacy Statewide Protocol Rule 17 Appendix C operationalizes this authority and provides specific guidance.

Appendix C allows pharmacists to prescribe a complete 28-day course of an FDA-approved/CDC-recommended PEP antiretroviral regimen for patients meeting CDC-guideline criteria. Pharmacists must address additional patient-centered considerations beyond those assessed in the context of pre-PrEP assessment, given that high-risk HIV exposures may involve sexual abuse and/or assault.

Appendix C delineates patient assessment, laboratory testing, and counseling requirements for all phases of PEP-related care, including but not limited to pretreatment determination of PEP eligibility, PEP regimen selection, treatment adherence support, posttreatment reassessment of HIV-status, and patient-centered education regarding topics such as manifestations of acute HIV infection, availability of emergency contraception, behavioral risk mitigation, and post-PEP use of PrEP for patients remaining HIV-negative but at substantial risk of HIV acquisition. **Table 15** provides a consolidated summary of initial PEP evaluation and longitudinal management.

Hand-in-hand with Colorado-based pharmacists’ prescribing and management of HIV PrEP, the PEP protocol allows for the delivery of comprehensive HIV prevention services (See page 28 for Appendix C in its entirety.)

## EMBRACING SEXUAL WELLNESS

### The Sexual Health Assessment

A 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.<sup>34</sup> 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.<sup>34</sup> The CDC’s sexually transmitted diseases treatment guidelines recommend the following risk-behavior questions, known as *The 5 Ps*<sup>70</sup>:

- **Partners:** In the past 12 (or 3, or 6) months, with how many partners have you had sex? Are they men, women, transgender women, and/or transgender men?
- **Practices:** To understand your risks for STIs, I need to understand the kind of sex you have had recently. Do you have oral sex, vaginal sex, anal sex? For MSM: are you a *top* (insertive), *bottom* (receptive), or *versatile* (insertive or receptive)?

**TABLE 15. Summary of Initial PEP Evaluation and Management<sup>66</sup>**

<b>Obtain history of potential exposure event</b>	<ul style="list-style-type: none"> <li>• HIV status of exposed person and exposure source (if available)</li> <li>• Timing of most recent potential exposure</li> <li>• Type of exposure event and risk for HIV acquisition</li> </ul>
<b>Determine if PEP is indicated, as based on history</b>	
<b>If PEP is indicated, conduct laboratory testing</b>	<ul style="list-style-type: none"> <li>• HIV blood test: rapid combined antigen/antibody test preferred</li> <li>• eCrCl, HBV and HCV serology, STI screening, pregnancy testing</li> </ul>
<b>Prescribe a 28-day PEP course</b>	<ul style="list-style-type: none"> <li>• TDF 300 mg with FTC 200 mg once daily plus RAL 400 mg twice daily <b>OR</b></li> <li>• TDF 300 mg with FTC 200 mg once daily plus DTG 50 mg daily</li> <li>• Educate patient about potential regimen-specific adverse effects</li> </ul>
<b>Furnish prescription and provide medication counseling</b>	<ul style="list-style-type: none"> <li>• Dosage, duration, how supplied</li> <li>• Adherence</li> <li>• Adverse effects</li> <li>• Patient-assistance programs</li> </ul>
<b>For all PEP-eligible patients</b>	<ul style="list-style-type: none"> <li>• Provide patient-centered counseling on behavioral risk reduction and HIV prevention strategies</li> <li>• Document sexual-assault findings and fulfill reporting requirements<sup>56</sup></li> <li>• Conduct confidential reporting of newly diagnosed STIs and HIV infection to the health department</li> <li>• Link HIV-infected patients to relevant medical care and psychosocial support services</li> <li>• Consider transition to PrEP for appropriately identified patients</li> </ul>
<p>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.</p>	

- **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. (Figure 8).<sup>71-73</sup> For additional training on opening a sexual health dialogue, go to <https://realcme.com/learner/course/2591> or <https://realcme.com/learner/course/2508>.

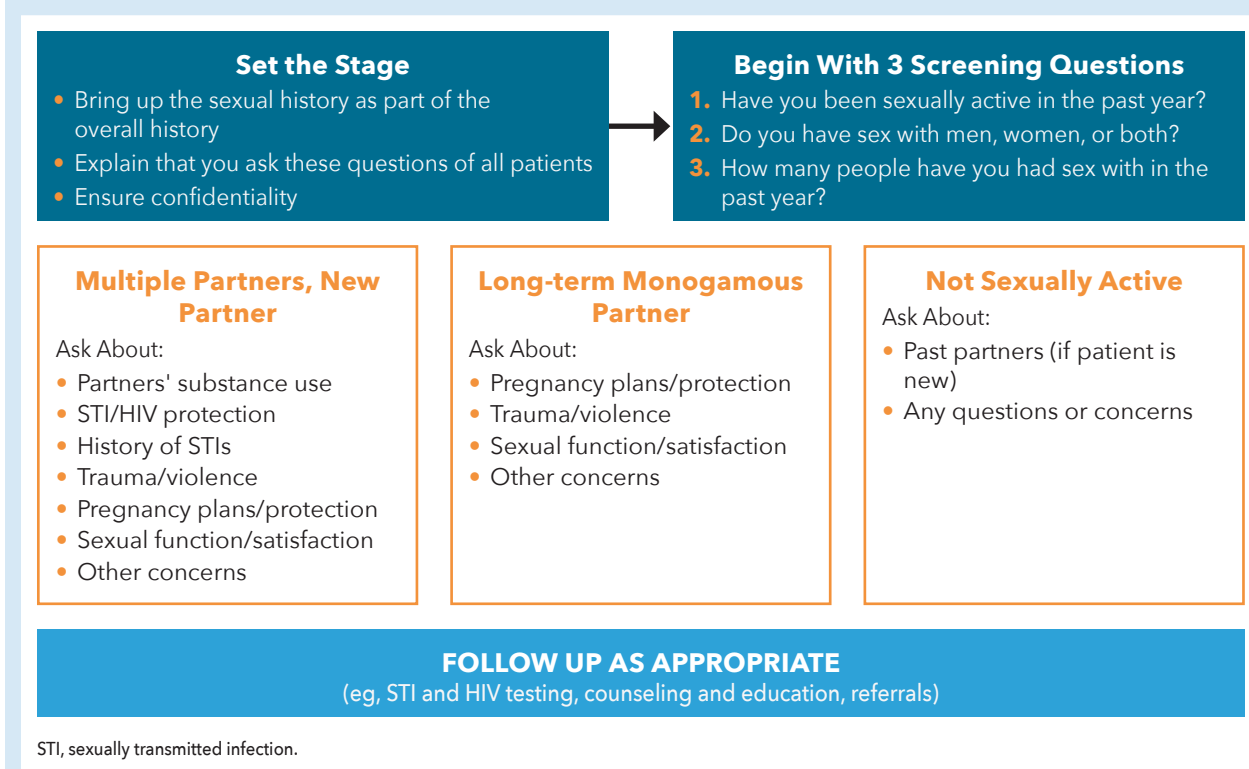
Before starting, consider informing the patient about the routine nature of conducting a sexual-health assessment with the following statement: "I am going to ask you a few questions about your sexual history. I ask these questions at least once a year of all my patients because the information is very important for your overall health. Everything you tell me is confidential, as part of our patient-provider relationship. 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<sup>74</sup>:

- 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 nonsexual-related)

### Communicating With Transgender 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 transgender people, a high-risk population that is underrepresented among PrEP users. The

**FIGURE 8. Algorithm for Conducting a Sexual History<sup>71</sup>**



following points are taken from the National LGBTQIA+ Health Education Center and may also be helpful when taking sexual histories from other individuals, especially with regard to gender pronouns.<sup>71</sup>

- 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. This will not necessarily be the name that appears on insurance and medical records
- Ask what pronoun(s) your patient prefers. This is best done on an intake form but may also be needed during the clinic visit. Some people change their personal pronoun preference
  - Many transgender people want you to use the pronoun that matches their gender identity. For example, a transgender woman would like you to use "she/her"
  - Some transgender or gender-nonconforming people may ask you to use "ze" or "they," or to try to avoid using any pronouns

### Discussing Risk of HIV Acquisition Through Injection Drug Practices

The USPSTF 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<sup>34</sup>:

- 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, 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).<sup>34,62</sup> The website for the Substance Abuse and Mental Health Services Administration (<https://www.samhsa.gov>) is a valuable resource for locating substance use disorder treatment facilities and programs and behavioral and mental health services.<sup>75</sup>

## 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<sup>76</sup>: <https://providers.aahivm.org/referral-link-search?reload=timezone>. Pharmacists can also locate appropriate providers using the following CDPHE resource: <https://cdphe.colorado.gov/living-with-hiv>.<sup>65</sup>

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

CO HB 20-1016 not only expands the pharmacist's scope of practice to include prescribing and dispensing PrEP and PEP, but also addresses equitable reimbursement by insurance carriers for all pharmacist-directed PrEP/PEP services.<sup>1</sup>

For those 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<sup>2,10</sup>:

1. Test negative for HIV **AND**
2. Have a valid prescription from a health care provider **AND**

### 3. 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.<sup>10</sup> Gilead's *Advancing Access*<sup>®</sup> program is another patient assistance program available for both insured and uninsured patients: <http://www.gileadadvancingaccess.com>.<sup>76</sup>

Uninsured/underinsured patients and providers can visit the following CDPHE webpage for additional information: <https://cdphe.colorado.gov/prep-for-hiv>.<sup>78</sup> Further, CDPHE offers guidance on reimbursement of pharmacists who do not have insurance-carrier contracts covering PrEP/PEP services: <https://cdphe.colorado.gov/public-health-intervention-program>.<sup>79</sup>

### 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<sup>62</sup>: <https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-provider-supplement-2017.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.<sup>80</sup> 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<sup>80</sup>  
<https://www.cdc.gov/std/treatment/sexualhistory.pdf>
- National LGBTQIA+ Health Education Center. Taking Routine Histories of Sexual Health: A System-Wide Approach for Health Centers<sup>71</sup>  
<https://www.lgbthealtheducation.org/publication/taking-routine-histories-of-sexual-health-a-system-wide-approach-for-health-centers/>
- TargetHIV. Sexual History Taking Toolkit<sup>72</sup>  
<https://targethiv.org/library/sexual-history-taking-toolkit>
- US Public Health Service. Preexposure Prophylaxis for the Prevention of HIV Infection in the United States - 2017 Update. Clinical Providers' Supplement<sup>62</sup>  
<https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-provider-supplement-2017.pdf>

## ADDRESSING PRACTICAL CHALLENGES OF PREP/PEP IMPLEMENTATION

The Colorado model allows any qualified pharmacist in the state to offer PrEP/PEP services independently of physician authorization and is intended to help fill gaps in care, especially in urgent situations where a PCP is not established. Colorado's HB 20-1061 protocol requires all pharmacies/pharmacists to participate

in accordance with the statewide regulations, which ensure a standard level of care across all pharmacies providing the service.<sup>1,2</sup>

Other models in the United States utilize a collaborative practice agreement that reflects an established relationship among providers (eg, pharmacists, physicians, and advanced practice nurses) and generally requires a referral. 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.<sup>81</sup> Kelley-Ross Pharmacy in Seattle is able to offer pharmacist-driven PrEP provision and HIV-prevention services through not only collaborative practice agreements, 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.<sup>82</sup>

Both models of care are beneficial to expanding preventive services and HIV prevention.

### 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<sup>83</sup>:

- 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.
- Note:** Colorado does not have a licensing body for phlebotomy or specified requirements for conducting sample collection; therefore, it is possible to train existing staff to perform this duty
- 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 onsite 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 pick-up
  - 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<sup>84</sup>
  - 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

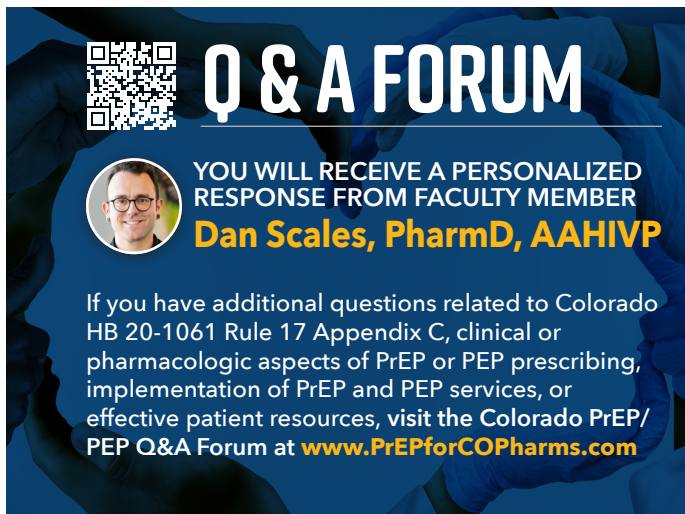
Part of ensuring successful PrEP/PEP services in the community-pharmacy setting is engaging and supporting pharmacists who can educate stakeholders, build community-based relationships and partnerships, and break down barriers to PrEP access.<sup>81,85</sup> Ultimately, instead of waiting to access PrEP, patients will be able to participate in a 45-minute conversation with the pharmacist to get the PrEP they need—when they need it.

## CONCLUDING COMMENTS

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

This monograph has outlined the Colorado pharmacist’s role in the provision of HIV PrEP and PEP, as based on CO HB 20-1061 and subsequent authorizations under CO State Board of Pharmacy Rule 17 Appendix C. A comprehensive statewide protocol allowing pharmacists to provide nationally endorsed public health preventative care is a win for patient access to care and a strike against the spread of HIV. However, success of this model of care will depend on overcoming implementation challenges. HB 20-1061 has made a significant first step to ensure sustainability of advanced-level clinical services through both direct billing and equitable reimbursement, but the full implementation of a pharmacy infrastructure that supports the provision of PrEP/PEP will remain a challenge for many.<sup>1,2</sup>

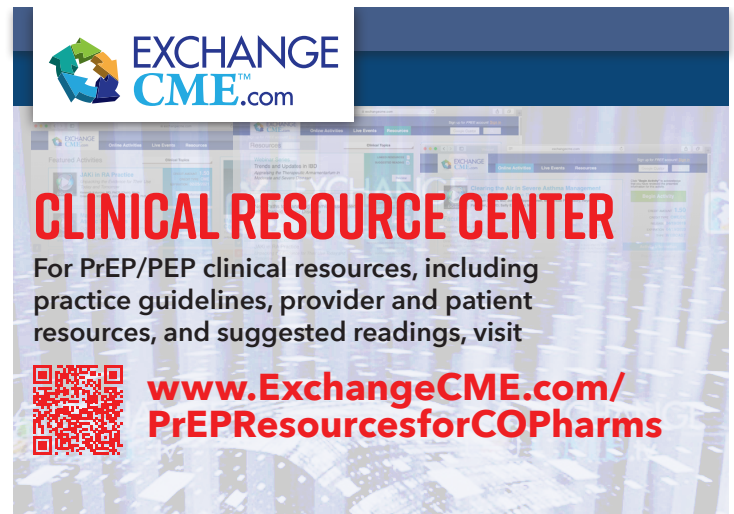
The pharmacy setting is an ideal entry point for people at risk of HIV acquisition to initiate pre- or postexposure HIV prophylaxis. The pharmacist’s role as HIV-prevention educator, PrEP/PEP provider, and patient advocate has the potential to grow into a greater presence within the local public health 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.



**Q & A FORUM**

YOU WILL RECEIVE A PERSONALIZED RESPONSE FROM FACULTY MEMBER  
**Dan Scales, PharmD, AAHIVP**

If you have additional questions related to Colorado HB 20-1061 Rule 17 Appendix C, clinical or pharmacologic aspects of PrEP or PEP prescribing, implementation of PrEP and PEP services, or effective patient resources, visit the Colorado PrEP/PEP Q&A Forum at [www.PrEPforCOPharms.com](http://www.PrEPforCOPharms.com)



**EXCHANGE CME.com**

**CLINICAL RESOURCE CENTER**

For PrEP/PEP clinical resources, including practice guidelines, provider and patient resources, and suggested readings, visit

[www.ExchangeCME.com/PrEPResourcesforCOPharms](http://www.ExchangeCME.com/PrEPResourcesforCOPharms)



## LIST OF ABBREVIATIONS

Ab	antibody	IgG	immunoglobulin G
Ag	antigen	IgM	immunoglobulin M
AIDS	acquired immunodeficiency syndrome	IAS-USA	International Antiviral Society-USA
ALT	alanine aminotransferase	IDU	injection drug use
AST	aspartate aminotransferase	iPrEx	Iniciativa Profilaxis Pre-Exposición [Preexposure Prophylaxis Initiative]
ART	antiretroviral therapy	INSTI	integrase strand transfer inhibitor
CAB	cabotegravir	IRR	incidence rate ratio
CDC	Centers for Disease Control and Prevention	LDL	low-density lipoprotein
CDPHE	Colorado Department of Public Health & Environment	MSM	men who have sex with men
CI	confidence interval	NAAT	nucleic acid amplification testing
CLIA	Clinical Laboratory Improved Amendments	NNRTI	nonnucleoside reverse transcriptase inhibitors
DAA	direct-acting antiviral	NRTI	nucleoside reverse transcriptase inhibitors
DDI	drug-drug interaction	NSAID	nonsteroidal anti-inflammatory drug
DHHS	US Department of Health and Human Services	NI	noninferiority
DNA	deoxyribonucleic acid	NIH	National Institutes of Health
DRV	darunavir	nPEP	nonoccupational PEP
DTG	dolutegravir	PCP	primary care provider
EBR/GZR	elbasvir/grazoprevir	PCR	polymerase chain reaction
eCrCl	estimated creatinine clearance	PEP	postexposure prophylaxis
EMR	electronic medical record	PI	protease inhibitor
GLE/PIB	glecaprevir/pibrentasvir	PWH/PLWH	people with HIV/people living with HIV
FDA	US Food and Drug Administration	PrEP	preexposure prophylaxis
FEM-PrEP	Preexposure Prophylaxis Trial for HIV Prevention Among African Women	PY	person-years
FTC	emtricitabine	PWID	people who inject drugs
Gen	generation	RAL	raltegravir
HAV	hepatitis A virus	RNA	ribonucleic acid
HBV	hepatitis B virus	RTV	ritonavir
HCV	hepatitis C virus	SBOP	State Board of Pharmacy
HDL	high-density lipoprotein cholesterol	SOF/LDV	sofosbuvir/ledipasvir
HIPAA	Health Insurance Portability and Accountability Act	SOF/VEL	sofosbuvir/velpatasvir
HIV	human immunodeficiency virus	STI	sexually transmitted infection
HPV	human papillomavirus	TAF	tenofovir alafenamide
IA	immunoassay	TDF	tenofovir disoproxil fumarate
		TDF2	Botswana TDF/FTC Oral HIV Prophylaxis trial
		WHO	World Health Organization

## REFERENCES

1. State of Colorado. House Bill. 20-1061. July 13, 2020. <https://leg.colorado.gov/bills/hb20-1061>. Accessed January 21, 2021.
2. Colorado Department of Regulatory Agencies. State Board of Pharmacy: Laws, Rules and Policies. Code of Colorado Regulations 3 CCR 719-1. Rule 17 Appendix C. 2021. <https://dpo.colorado.gov/Pharmacy/Laws>. Accessed January 21, 2021.
3. Centers for Disease Control and Prevention (CDC). HIV Basics: US Statistics. Updated June 30, 2020. <https://www.hiv.gov/hiv-basics/overview/data-and-trends/statistics>. Accessed January 21, 2021.
4. CDC. Policy, Planning and Strategic Communication. Dear colleagues: information from CDC's Division of HIV/AIDS Prevention. <https://www.cdc.gov/hiv/policies/dear-colleague/dcl/050720.html>. Accessed January 21, 2021.
5. Roser M, Richie H. HIV/AIDS. Last updated November 2019. <https://ourworldindata.org/hiv-aids>. Accessed January 21, 2021.
6. Kochanek KD, et al. Deaths: final data for 2017. *Natl Vital Stat Rep*. 2019;68(9):1-77.
7. US Department of Health & Human Services (DHHS). What Is Ending the HIV Epidemic: A Plan for America? October 2020. <https://www.hiv.gov/federal-response/ending-the-hiv-epidemic/overview>. Accessed January 21, 2021.
8. Oguntibeju OO. Quality of life of people living with HIV and AIDS and antiretroviral therapy. *HIV AIDS (Auckl)*. 2012;4:117-124.
9. CDC. Pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP). Updated September 2020. <https://www.cdc.gov/hiv/clinicians/prevention/prep-and-pep.html>. Accessed January 21, 2021.
10. DHHS. Ending the HIV epidemic: Ready, Set, PrEP. Updated November 2020. <https://www.hiv.gov/federal-response/ending-the-hiv-epidemic/prep-program>. Accessed January 21, 2021.
11. Choopanya K, et al. Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet*. 2013;381(9883):2083-2090.
12. Anderson PL, et al. Emtricitabine-tenofovir concentrations and pre-exposure prophylaxis efficacy in men who have sex with men. *Sci Transl Med*. 2012;4(151):151ra125.
13. Kazi DS, et al. PrEParing to end the HIV epidemic—California's route as a road map for the United States. *N Engl J Med*. 2019;381(26):2489-2491.
14. Hess KL, et al. Lifetime risk of a diagnosis of HIV infection in the United States. *Ann Epidemiol*. 2017;27(4):238-243.
15. Goldstein RH, et al. Being PrEPared—preexposure prophylaxis and HIV disparities. *N Engl J Med*. 2018;379(14):1293-1295.
16. Siegler AJ, et al. The prevalence of pre-exposure prophylaxis use and the pre-exposure prophylaxis-to-need ratio in the fourth quarter of 2017, United States. *Ann Epidemiol*. 2018;28(12):841-849.
17. CDC. HIV. Figures. Diagnoses of HIV infection in the United States and Dependent Areas, 2018—United States and 6 dependent areas. <https://www.cdc.gov/hiv/library/reports/hiv-surveillance/vol-31/content/figures.html>. Accessed January 21, 2021.
18. Cahill S, et al. Stigma, medical mistrust, and perceived racism may affect PrEP awareness and uptake in black compared to white gay and bisexual men in Jackson, Mississippi and Boston, Massachusetts. *AIDS Care*. 2017;29(11):1351-1358.
19. Highleyman L. First generic Truvada now available in the United States. *POZ Online*. October 2, 2020. <https://www.poz.com/article/first-generic-truvada-now-available-united-states>. Accessed January 21, 2021.
20. CDC. Life-saving naloxone from pharmacies. Updated August 6, 2019. <https://www.cdc.gov/vitalsigns/naloxone/index.html>. Accessed January 21, 2021.
21. Newman TV, et al. Optimizing the role of community pharmacists in managing the health of populations: barriers, facilitators, and policy recommendations. *J Manag Care Spec Pharm*. 2019;25(9):995-1000.
22. Kibicho J, Owczarzak J. Pharmacists' strategies for promoting medication adherence among patients with HIV. *J Am Pharm Assoc (2003)*. 2011;51(6):746-755.
23. Hill LA, et al. The role of the clinical pharmacist in the management of people living with HIV in the modern antiretroviral era. *AIDS Rev*. 2019;21(4):195-210.
24. Tseng A, et al. Role of the pharmacist in caring for patients with HIV/AIDS: clinical practice guidelines. *Can J Hosp Pharm*. 2012;65(2):125-145.
25. Brown J. As HIV infection rates rise in Colorado, pharmacies can now prescribe preventative pills. *The Colorado Sun*. November 18, 2020. <https://coloradosun.com/2020/11/18/as-hiv-infection-rates-rise-in-colorado-pharmacies-can-now-prescribe-preventative-pills/>. Accessed January 21, 2021.
26. Colorado Department of Public Health and Environment (CDPHE). HIV surveillance quarterly reports. <https://cdphe.colorado.gov/sexually-transmitted-infections-and-hiv/sti-hiv-data/hiv-surveillance-quarterly-reports>. Accessed January 21, 2021.
27. DHHS. U.S. statistics: fast facts. Updated June 2020. <https://www.hiv.gov/hiv-basics/overview/data-and-trends/statistics>. Accessed January 21, 2021.
28. State of Colorado. Colorado revised statutes 2019. Title 12; 12 280 103. <https://leg.colorado.gov/sites/default/files/images/olls/crs2019-title-12.pdf>. Accessed January 22, 2021.
29. Avert. The science of HIV and AIDS—overview. Last updated October 2019. <https://www.avert.org/professionals/hiv-science/overview>. Accessed January 21, 2021.
30. Cummins NW, Badley AD. Making sense of how HIV kills infected CD4 T cells: implications for HIV cure. *Mol Cell Ther*. 2014;2:20.
31. AIDSinfo. Understanding HIV/AIDS: The HIV life cycle. Updated July 1, 2019. <https://aidsinfo.nih.gov/understanding-hiv-aids/factsheets/19/73/the-hiv-life-cycle>. Accessed January 21, 2021.
32. Liu Y, Tran N. Best practices for HIV-1/2 screening: when to test and what to test. <https://blog.ucdmc.ucdavis.edu/labbestpractice/?s=best+practices+for+HIV-1%2F2+screening>. Accessed January 21, 2021.
33. Patel P, et al. Rapid HIV screening: missed opportunities for HIV diagnosis and prevention. *J Clin Virol*. 2012;54(1):42-47.
34. US Public Health Service. Preexposure Prophylaxis for the Prevention of HIV Infection in the United States—2017 Update (A Clinical Practice Guideline). March 2018. <https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf>. Accessed January 21, 2021.
35. CDC. Pre-exposure prophylaxis (PrEP). Last reviewed May 2020. <https://www.cdc.gov/hiv/clinicians/prevention/prep.html>. Accessed January 21, 2021.
36. US Food and Drug Administration (FDA). Drugs@FDA: FDA-Approved Drugs. Emtricitabine and tenofovir disoproxil fumarate (Truvada®; package insert). Last updated June 2020. [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2020/021752s0611bl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/021752s0611bl.pdf). Accessed January 21, 2021.
37. FDA. Drugs@FDA: FDA-Approved Drugs. Emtricitabine and tenofovir alafenamide (Descovy®; package insert). Last updated December 2019. [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2019/208215s0111bl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/208215s0111bl.pdf). Accessed January 21, 2021.
38. Grant RM, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med*. 2010;363(27):2587-2599.
39. Baeten JM, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. *N Engl J Med*. 2012;367(5):399-410.
40. Murnane PM, et al. Efficacy of preexposure prophylaxis for HIV-1 prevention among high-risk heterosexuals: subgroup analyses from a randomized trial. *AIDS*. 2013;27(13):2155-2160.
41. Van Damme L, et al. Preexposure prophylaxis for HIV infection among African women. *N Engl J Med*. 2012;367(5):411-422.
42. Thigpen MC, et al. Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. *N Engl J Med*. 2012;367(5):423-434.
43. Pau AK, George JM. Antiretroviral therapy: current drugs. *Infect Dis Clin North Am*. 2014;28(3):371-402.
44. Hare CB, et al. The phase 3 DISCOVER study: daily F/TAF or F/TDF for HIV preexposure prophylaxis. Presented at Conference on Retroviruses and Opportunistic Infections (CROI) 2019. March 4-7, 2019; Seattle, Washington. Abstract: O-10.

45. Ruane P, et al. Phase 3 randomized, controlled DISCOVER study of daily F/TAF or F/TDF for HIV pre-exposure prophylaxis: week 96 results. Presented at 17th European AIDS Conference (EACS). November 6-9, 2019; Basel, Switzerland. Poster: PE3/16.
46. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron*. 1976;16(1):31-41.
47. Chan L, et al. Potential kidney toxicity from the antiviral drug tenofovir: new indications, new formulations, and a new prodrug. *Curr Opin Nephrol Hypertens*. 2018;27(2):102-112.
48. Tao X, et al. Efficacy and safety of the regimens containing tenofovir alafenamide versus tenofovir disoproxil fumarate in fixed-dose single-tablet regimens for initial treatment of HIV-1 infection: a meta-analysis of randomized controlled trials. *Int J Infect Dis*. 2020;93:108-117.
49. DHHS. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. <https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/whats-new-guidelines>. Accessed January 21, 2021.
50. University of Liverpool. HEP Drug Interactions. <https://www.hep-druginteractions.org/checker>. Accessed January 21, 2021.
51. Glidden DV, et al. Symptoms, side effects and adherence in the iPrEx open-label extension. *Clin Infect Dis*. 2016;62(9):1172-1177.
52. CDC. HIV Testing. Last reviewed June 2020. <https://www.cdc.gov/hiv/testing/index.html>. Accessed January 21, 2021.
53. CDC. Rapid HIV tests suitable for use in non-clinical settings (CLIA-waived). Updated June 11, 2018. <https://www.cdc.gov/hiv/pdf/testing/rapid-hiv-tests-non-clinical.pdf>. Accessed January 21, 2021.
54. Landovitz RJ, et al. HPTN083 interim results: Pre-exposure prophylaxis (PrEP) containing long-acting injectable cabotegravir (CAB-LA) is safe and highly effective for cisgender men and transgender women who have sex with men (MSM, TGW). Presented at: 23rd International AIDS Conference (AIDS2020: Virtual). July 6-10, 2020; virtual. Abstract OAXLB0101.
55. World Health Organization. Trial results reveal that long-acting injectable cabotegravir as PrEP is highly effective in preventing HIV acquisition in women. November 9, 2020. <https://www.who.int/news/item/09-11-2020-trial-results-reveal-that-long-acting-injectable-cabotegravir-as-prep-is-highly-effective-in-preventing-hiv-acquisition-in-women>. Accessed January 21, 2021.
56. Saag MS, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2018 recommendations of the International Antiviral Society-USA Panel. *JAMA*. 2018;320(4):379-396.
57. World Health Organization (WHO). What is the 2+1+1? Event-driven oral pre-exposure prophylaxis to prevent HIV for men who have sex with men: update to WHO's recommendation on oral PrEP. July 2019. <https://www.who.int/hiv/pub/prep/211/en>. Accessed January 21, 2021.
58. Molina J-M, et al. On-demand preexposure prophylaxis in men at high risk for HIV-1 infection. *N Engl J Med*. 2015;373(23):2237-2246.
59. CDC. PrEP. Last reviewed November 2020. <https://www.cdc.gov/hiv/basics/prep.html>. Accessed January 21, 2021.
60. Harm Reduction Coalition. <https://harmreduction.org>. Accessed January 21, 2021.
61. Lambers F, et al. Changing the odds: motives for and barriers to reducing HCV-related sexual risk behavior among HIV-infected MSM previously infected with HCV. *BMC Infect Dis*. 2018;18(1):678.
62. US Public Health Service. Preexposure Prophylaxis for the Prevention of HIV Infection in the United States - 2017 Update. Clinical Providers' Supplement. <https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-provider-supplement-2017.pdf>. Accessed January 21, 2021.
63. Cairns G. Does PrEP cause more HIV drug resistance? Yes, some. NAM AIDSmap. February 2020. <https://www.aidsmap.com/news/feb-2020/does-prep-cause-more-hiv-drug-resistance-yes-some>. Accessed January 21, 2021.
64. CDC. HIV Treatment as Prevention. Last reviewed March 2020. <https://www.cdc.gov/hiv/risk/art/index.html>. Accessed January 21, 2021.
65. CDPHE. People living with HIV. <https://cdphe.colorado.gov/living-with-hiv>. Accessed January 21, 2021.
66. CDC. Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV—United States, 2016. <https://www.cdc.gov/hiv/pdf/programresources/cdc-hiv-npep-guidelines.pdf>. 2016. Accessed January 21, 2021.
67. FDA. Drugs@FDA: FDA-Approved Drugs. Raltegravir package insert. Last updated August 2013. [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2013/022145s0291bl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/022145s0291bl.pdf). Accessed January 21, 2021.
68. FDA. Drugs@FDA: FDA-Approved Drugs. Dolutegravir package insert. June 2020. [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2020/204790s0251bl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/204790s0251bl.pdf). Accessed January 21, 2021.
69. Zash R. Update on neural tube defects with antiretroviral exposure in the Tsepamo study, Botswana. Presented at: AIDS2020: Virtual. July 6-10, 2020; virtual. Abstract OAXLB0102. As reported by NAM AIDSmap. <https://www.aidsmap.com/news/jul-2020/if-we-dont-include-women-trials-we-are-not-protecting-women-dolutegravir-pregnant>. Accessed January 21, 2021.
70. CDC. Clinical Prevention Guidance. <https://www.cdc.gov/std/tg2015/clinical.htm>. Accessed January 21, 2021.
71. National Association of Community Health Centers, National LGBT Health Education Center. Taking Routine Histories of Sexual Health: A System-Wide Approach for Health Centers. February 2016. <https://www.lgbthealtheducation.org/publication/taking-routine-histories-of-sexual-health-a-system-wide-approach-for-health-centers>. Accessed January 21, 2021.
72. TargetHIV. Sexual History-Taking Toolkit. July 2020. <https://targethiv.org/library/sexual-history-taking-toolkit>. Accessed January 21, 2021.
73. CDC. Discussing sexual health with your patients. Last reviewed October 2019. <https://www.cdc.gov/hiv/clinicians/screening/discussing-sexual-health.html>. Accessed January 21, 2021.
74. Pakpreo P. Why do we take a sexual history? *Virtual Mentor*. 2005;7(10):677-682.
75. Substance Abuse and Mental Health Services Administration. <https://www.samhsa.gov>. Accessed January 21, 2021.
76. American Academy of HIV Medicine (AAHIVM). Referral Link. <https://providers.aahivm.org/referral-link-search?reload=timezone>. Accessed January 21, 2021.
77. Gilead Advancing Access. 2020. <http://www.gileadadvancingaccess.com>. Accessed January 22, 2021.
78. CDPHE. Pre-exposure prophylaxis (PrEP). <https://cdphe.colorado.gov/prep-for-hiv>. Accessed January 21, 2021.
79. CDPHE. Public health intervention program (PHIP). <https://cdphe.colorado.gov/public-health-intervention-program>. Accessed January 21, 2021.
80. CDC. A Guide to Taking a Sexual History. <https://www.cdc.gov/std/treatment/sexualhistory.pdf>. Accessed January 21, 2021.
81. Miller J. Increasing access to HIV prevention medicine: Healthforce Center at UCSF. November 19, 2019. <https://healthforce.ucsf.edu/blog-article/healthcare-policy/increasing-access-hiv-prevention-medication>. Accessed January 21, 2021.
82. Tung EL, et al. Implementation of a community pharmacy-based pre-exposure prophylaxis service: a novel model for pre-exposure prophylaxis care. *Sex Health*. 2018;15(6):556-561.
83. Lopez MI, et al. Community pharmacy delivered PrEP to STOP HIV transmission: an opportunity NOT to miss! *J Am Pharm Assoc (2003)*. 2020;60(4):e18-e24.
84. DHHS. HIPAA for Professionals. Last reviewed June 2017.. Accessed January 21, 2021.
85. Ross M. 4 findings from a successful HIV PrEP program. <https://www.pharmacytimes.com/news/4-findings-from-a-successful-hiv-prep-program>. Accessed January 21, 2021.

# COLORADO STATE BOARD OF PHARMACY STATEWIDE PROTOCOL, RULE 17, APPENDIX C

## Pre-Exposure and Post-Exposure Prophylaxis of HIV

This collaborative pharmacy practice statewide protocol authorizes qualified Colorado-licensed pharmacists (“Pharmacists”) to provide pertinent assessment of risk of HIV acquisition and prescribe pre-exposure and post-exposure prophylaxis medications for the prevention of HIV infection according to and in compliance with all applicable state and federal laws and rules.

Pharmacists may prescribe and dispense FDA approved medication(s) to eligible patients according to indications and contraindications recommended in current guidelines from the US Centers for Disease Control and Prevention (CDC)<sup>1, 3</sup> and the United States Preventive Services Task Force (USPSTF)<sup>2</sup>.

Prior to prescribing and dispensing HIV prevention medication per this protocol, the pharmacist must:

1. Hold a current license to practice in Colorado
2. Be engaged in the practice of pharmacy
3. Have earned a Doctor of Pharmacy degree or completed at least 5 years of experience as a licensed pharmacist
4. Carry adequate professional liability insurance as determined by the Board
5. Complete a training program accredited by the Accreditation Council for Pharmacy Education, or its successor entity, pursuant to the protocol (in compliance with Board Rule 17.00.50 b.2.)
6. Pharmacists must also follow all board rules for statewide protocols in section 17.00.00.

The pharmacy shall ensure that appropriate space is available to provide counseling and ensure confidentiality. Records:

- A. Pursuant to Pharmacy Board Rule 17.00.50, a process shall be in place for the pharmacist to communicate with the patient’s primary care provider and document changes to the patient’s medical record. If the patient does not have a primary care provider, or is unable to provide contact information for his or her primary care provider, the pharmacist shall provide the patient with a written record of the drugs or devices furnished, and lab test(s) ordered, and any test results.
- B. Pharmacists shall comply with all aspects of Pharmacy Board Rules 17.01.00 and 17.02.00 with respect to the maintenance of proper records.

## Pre-Exposure Prophylaxis (PrEP) Protocol

Under this protocol, Pharmacists may assess for HIV status and high-risk behaviors in which pre-exposure prophylaxis against HIV would be warranted.

The pharmacist may consider and offer the patient an oral antiretroviral agent listed in Table I according to the following criteria:

1. Evidence of HIV negative status as documented by an FDA- approved test, or rapid CLIA-waived point of care fingerstick blood test, taken within 7 days. Neither oral swab testing nor patient report of negative status are acceptable for evidence.
2. Persons who meet eligibility requirements for PrEP per CDC guidelines in the following categories:
  - a. MSM (men who have sex with men)
    - Adult man
    - Without acute or established HIV infection
    - Any male sex partners in past 6 months
    - Not in a monogamous partnership with a recently tested, HIV-negative man

AND at least one of the following:

    - any anal sex without condoms (receptive or insertive) in the past 6 months
    - A bacterial STI (syphilis, gonorrhea or chlamydia) diagnosed or reported in past 6 months
  - b. Heterosexually Active Men and Women
    - Adult person
    - Without acute or established HIV infection
    - Any sex with opposite sex partners in past 6 months
    - Not in a monogamous partnership with a recently tested HIV-negative partner

AND at least one of the following:

    - Is a man who has sex with both women and men (behaviorally bisexual)
    - Infrequently uses condoms during sex with 1 or more partners of unknown HIV status who are known to be substantial risk of HIV infection (persons who inject drugs PWID or bisexual male partner)
    - Is in an ongoing sexual relationship with an HIV-positive partner
    - A bacterial STI (syphilis, gonorrhea in women or men) diagnosed or reported in past 6 months
  - c. Persons Who Inject Drugs (PWID)
    - Adult person
    - Without acute or established HIV infection
    - Any injection of drugs not prescribed by a clinician in past 6 months

AND at least one of the following:

    - Any sharing of injection or drug preparation equipment in past 6 months
    - Risk of sexual acquisition (see above)

Patients who should NOT be prescribed PrEP under this protocol and should be referred to primary care provider for further action:

- Patients with baseline HIV tests indicating existing HIV infection
- Recent flu-like symptoms in the past month as this may suggest recent HIV infection not yet detectable (tiredness, fever, joint or muscle aches, headache, sore throat, vomiting, diarrhea, rash, night sweats, and/or enlarged lymph nodes in the neck or groin)
- CRCL < 60 ml/min

**TABLE 1 – MEDICATION OPTIONS**

Other FDA approved / CDC recommended medications or regimens can be used if they become available.

Formulations, cautions and dose adjustments for antiretroviral medications shall minimally follow the CDC guidelines and package insert information for all regimens.

Medication	Age/Weight	Frequency	Duration of Therapy	Notes
<b>FTC/TDF emtricitabine 200 mg/tenofovir disoproxil fumarate 300mg (Truvada® or generic)</b>	≥35 kg	Once daily	Prescription issued for 30 days with no refills if baseline labs not completed; or up to 90 days if baseline labs completed. Refill quantity only until next scheduled lab follow up.	May take with or without food. Not recommended for CRCL <60 ml/min.
<b>FTC/TAF emtricitabine 200mg/tenofovir alafenamide 25mg (Descovy®)</b>	≥35 kg	Once daily	Prescription issued for 30 days with no refills if baseline labs not completed; or up to 90 days if baseline labs completed. Refill quantity only until next scheduled lab follow up.	May take with or without food. Not recommended for CRCL <30 ml/min. Should only be used for at-risk cis-gender men and transgender women. Pharmacist must review drug/drug interaction considerations as per <u>package insert Table 5.</u>

**TABLE 2 – ROUTINE REQUIRED MONITORING OF TREATMENT****Labs:**

- PrEP cannot be started without a negative HIV test at baseline.
- Pharmacist is authorized to order the following labs for the patient OR can refer to another provider for ordering and accept lab results.
- PrEP refills will not be authorized past the initial 30 day supply if recommended baseline testing is not done by one of the above mechanisms.

Test	Frequency	CDC recommendations	Notes
<b>HIV</b>	Baseline + Every 3 months	<b>Required</b>	If positive, refer
<b>Three site STI screening (syphilis, gonorrhea, chlamydia)</b>	Baseline + At 3 mo if symptomatic. Every 6 months if asymptomatic	Recommended	If positive – refer for care
<b>Serum creatinine</b>	Baseline, at 3 months, and thereafter every 6 months	Recommended	If CRCL <60 ml/min, cannot use FTC/TDF If CRCL <30 ml/min cannot use FTC/TAF
<b>Hepatitis B screening</b>	Baseline	Recommended	If positive – refer for care
<b>Bone health</b>		Optional	
<b>Need to continue PrEP</b>	Annually	Recommended if at continued risk	Discuss with patient

Counseling (at minimum):

- Proper use of medication dosage, schedule and potential common and serious side effects (and how to mitigate)
- The importance of medication adherence with relation to efficacy of PrEP/nPEP
- Signs/symptoms of acute HIV infection and recommended actions
- Consistent and correct use of condoms and prevention of STIs
- The necessity of follow up care with a primary care provider for usual care
- The importance and requirement of testing for HIV, renal function, hepatitis B, and sexually transmitted diseases

Documentation:

- The pharmacist will notify the patient's primary care provider of a record of all medications prescribed. If a patient does not have a primary care provider, the pharmacist will provide the patient with a list of providers and clinics for which they may seek ongoing care.
- The pharmacist will also follow all documentation rules in Pharmacy Board Rule 17.

Referrals to primary care provider:

- If a patient tests positive for HIV infection, the pharmacist will refer/direct the patient to a primary care provider and provide a list of providers and clinics in that region for confirmatory testing and follow up care. A list of providers may be found at: <https://www.colorado.gov/pacific/cdphe/linkage-to-care>

- If a patient tests positive for an STI, the pharmacist will refer/direct the patient to a primary care provider and provide a list of providers and clinics in that region for confirmatory testing and follow up care. A list of providers may be found at: <https://www.colorado.gov/pacific/cdphe/linkage-to-care>
- If a patient tests positive for Hepatitis B, the pharmacist will refer/direct the patient to a primary care provider and provide a list of providers and clinics in that region for confirmatory testing and follow up care.
- Urgent evaluation referral for symptoms or signs of acute renal injury or acute HIV infection.
- If a female patient becomes pregnant while on PrEP
- Usual care for any other issues, stress importance of routine primary care and health maintenance.

\* What is this for?

<sup>1</sup> CDC. Preexposure prophylaxis for the prevention of HIV infection in the United States, 2017 update Clinical Practice Guideline. Available at: <https://stacks.cdc.gov/view/cdc/53509>

<sup>2</sup> USPTF. Preexposure Prophylaxis for the Prevention of HIV Infection US Preventive Services Task Force Recommendation Statement. *JAMA*. 2019;321(22):2203-2213. doi:10.1001/jama.2019.6390

### Non-Occupational Post-Exposure Prophylaxis (nPEP) Protocol

Non-Occupational Post-Exposure Prophylaxis (nPEP) is the use of antiretroviral drugs after a single high-risk event to decrease the risk of HIV seroconversion. nPEP must be started as soon as possible to be effective, and always within 72 hours of the possible exposure. This particular protocol addresses non occupational post-exposure prophylaxis (nPEP) only, those with occupational exposures are not eligible and should be referred for care.

Under this protocol, pharmacists may assess patients 13 and older for high-risk exposure to HIV and prescribe antiretroviral drugs if appropriate. Patients under 18 years of age require parental consent to access this Protocol. nPEP should only be provided for infrequent exposures.

If the pharmacy is not able to provide care to the patient, or if the patient does not qualify for care at the pharmacy, the patient should be referred to another provider. PEP providers in Colorado include the STD Clinic at Denver Public Health (303.602.3540) and local emergency departments (CDPHE to comment).

**If the following criteria are met, antiretroviral agents in Table 1 are recommended:**

- The exposure must have occurred within 72 hours
- A rapid antibody CLIA waived point of care test yields a negative result for HIV. However, if a rapid test is not available, and nPEP is otherwise indicated, therapy should still be initiated.
- Exposure to a source individual known to be HIV-positive. Exposure of:
  - o Vagina
  - o Rectum
  - o Eye



- o Mouth
- o Other mucous membranes
- o Nonintact skin
- o Percutaneous contact (e.g., injecting drugs with a contaminated needle or needle stick injury)

WITH

- o Blood
  - o Semen
  - o Vaginal secretions
  - o Rectal secretions
  - o Breast milk
  - o Any body fluid visibly contaminated with blood
- Exposure types with the highest risk of transmission of HIV are:
    - o Needle sharing during injection drug use
    - o Percutaneous needle stick
    - o Receptive anal intercourse
  - If exposure with a source in which the HIV status is not known, nPEP may be considered and antiretroviral agents in Table 1 may be prescribed. NPEP should strongly be considered after exposure in an individual who also meets the criteria for PrEP therapy (see Colorado Statewide Protocol for Pre-Exposure Prophylaxis of HIV).

**Patients who should NOT be prescribed nPEP under this protocol and should be referred to primary care provider for further action:**

- Patients younger than 13 years of age.
- Patients taking any contraindicated medications per guidelines and package insert information
- Patients with baseline rapid HIV tests indicating existing HIV infection should be referred to a primary care provider.
- Patients who have a potential exposure but have been consistently adherent to PrEP
- If a child presents to the pharmacy with a request for NPEP and is potentially a victim of child abuse, child protective services MUST be contacted.

Other Considerations:

- If the case involves a sexually assaulted person, patients should also be examined and co-managed by professionals specifically trained in assessing and counseling patients and families during these circumstances (e.g., Sexual Assault Nurse Examiner [SANE] program staff). Resources may be found at <https://www.ccasa.org/gethelp/health-related-organizations/>
- If a child presents to the pharmacy with a request for nPEP and is potentially a victim of child abuse, child protective services MUST be contacted 1-844-CO-4-KIDS.

**TABLE 1 – MEDICATION OPTIONS**

Other FDA approved / CDC recommended medications or regimens can be used if they become available. Formulations cautions and dose adjustments for antiretroviral medications shall minimally follow the CDC guidelines and package insert information for all regimens.

Medication	Age/Weight	Dose	Duration of Therapy	Notes
<b>PREFERRED REGIMEN</b>				
emtricitabine 200 mg/tenofovir disoproxil fumarate 300mg (Truvada® or generic) <b>PLUS</b> raltegravir 400mg <b>OR</b> Dolutegravir 50mg	≥ 13 years	Once daily #28 no refills	28 days	Dosing adjustments with renal dysfunction if CrCL <60 ml/min.  Dolutegravir should not be used in pregnant women If contraindications to raltegravir or dolutegravir exist, or for other reasons the preferred regimen cannot be given, then “alternative regimens” per CDC guidelines should be referenced and used.
		Twice daily #56 no refills		
		Once daily #28 no refills		

**TABLE 2 – ROUTINE REQUIRED MONITORING OF TREATMENT**

**Labs:**

- All efforts should be made to obtain a negative HIV test at baseline. However, the sooner PEP is initiated, the more effective it is.
- Ask the following screening question:
  - o Do you have existing kidney disease, or do you know if your kidney function is decreased for any reason?

In this event, pharmacist should make arrangements to refer patient for a Scr blood test urgently as nephrotoxicity can occur with acute/chronic kidney disease (CrCL <60 ml/min).

- Pharmacist is authorized to order the following labs for the patient OR can refer to another provider for ordering and accept lab work results.
- Pharmacist must make every reasonable effort to follow up with patient post-treatment regimen at 4-6 weeks and test for confirmation of HIV status and make known to patient that repeat HIV testing is recommended at 3 and 6 months as well.

Test	Frequency	CDC recommendations	Notes
<b>HIV</b>	Baseline + Post-exposure at week 4-6, and months 3 and 6	<b>Required</b>	If positive, refer.
<b>STI screenings (syphilis, gonorrhea, chlamydia)</b>	Baseline	Recommended	If positive – refer for care
<b>Serum creatinine</b>	Baseline + @4-6 weeks.	Recommended	
<b>ALT/AST</b>	Baseline + @4-6 weeks.	Recommended	
<b>Hepatitis B screening</b>	Baseline + 6 mo	Recommended	If positive – refer. If negative and clinically appropriate, vaccinate
<b>Hepatitis C screening</b>	Baseline + 6 mo	Recommended	If positive - refer
<b>Pregnancy</b>	Baseline + @4-6 weeks.	Recommended	Pregnancy is not a contraindication to NPEP

Counseling (at minimum):

- Proper use of medication dosage, schedule and potential common and serious side effects (and how to mitigate)
- The importance of medication adherence with relation to efficacy of nPEP
- Signs/symptoms of acute HIV infection and recommended actions
- The patient should be instructed on correct and consistent use of HIV exposure precautions including condoms and not sharing injection equipment
- For women of reproductive potential with genital exposure to semen, emergency contraception should be discussed
- The necessity of follow up care with a primary care provider for usual care

- The importance and requirement of follow up testing for HIV, renal function, hepatic function, hepatitis B and C, and sexually transmitted diseases
- If appropriate, general discussion of pre-exposure prophylaxis at future time.

#### Documentation:

- The pharmacist will notify the patient's primary care provider of a record of all medications prescribed. If a patient does not have a primary care provider, the pharmacist will provide the patient with a list of providers and clinics for which they may seek ongoing care.
- The pharmacist will also follow all documentation rules in 17.00

#### Referrals:

- If a patient tests positive for HIV infection, the pharmacist will refer/direct the patient to a primary care provider and provide a list of providers and clinics in that region for confirmatory testing and follow up care. A list of providers may be found at: <https://www.colorado.gov/pacific/cdphe/linkage-to-care>
- The patient should be referred immediately for guideline based follow-up HIV testing and care, and follow-up testing for STIs, Hepatitis C, and Hepatitis B.
- If a patient tests positive for an STI, the pharmacist will refer/direct the patient to a primary care provider and provide a list of providers and clinics in that region for confirmatory testing and follow up care. A list of providers may be found at: <https://www.colorado.gov/pacific/cdphe/linkage-to-care>
- If a patient tests positive for Hepatitis B or C, the pharmacist will refer/direct the patient to a primary care provider and provide a list of providers and clinics in that region for confirmatory testing and follow up care. A list of providers may be found at: <https://www.colorado.gov/pacific/cdphe/linkage-to-care>
- Signs of symptoms of acute drug toxicities or serious side effects
- Urgent evaluation referral for symptoms or signs of acute renal injury or acute HIV infection.
- Usual care for any other issues, stress importance of routine primary care and health maintenance.

<sup>3</sup> CDC. Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use or Other Nonoccupational Exposure to HIV – United States, 2016. Available at: <https://stacks.cdc.gov/view/cdc/38856>