Baseline Evaluation and Starting HIV PrEP

This is a PDF version of the following document:
Module 1: HIV PrEP Fundamentals
Lesson 4: Baseline Evaluation and Starting HIV PrEP

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Background

There are four medications approved by the United States Food and Drug Administration (FDA) for use as HIV preexposure prophylaxis (PrEP): oral tenofovir DF-emtricitabine (TDF-FTC), oral tenofovir alafenamide-emtricitabine (TAF-FTC), long-acting injectable cabotegravir (CAB-LA), and lenacapavir subcutaneous injections (LEN-SQ). During the baseline evaluation, all persons considered for starting HIV PrEP with any one of these medications should undergo assessment for the following:[1]

- **Need for Nonoccupational HIV Postexposure Prophylaxis (PEP)**: Any significant exposures to HIV in the past 72 hours that suggest a need to immediately start nonoccupational postexposure prophylaxis (PEP) should supersede the plan for starting HIV PrEP. Following completion of nonoccupational PEP, the individual can immediately transition to starting HIV PrEP if indicated. For details on the indications and management of nonoccupational HIV PEP see the 2025 Center for Disease Control and Prevention (CDC) recommendations for management of nonoccupational exposure to HIV.[2] In addition, an updated approach to management of nonoccupational exposure to HIV is addressed in detail in the *National HIV Curriculum* lesson on Nonoccupational Postexposure Prophylaxis.
- **Baseline Laboratory Studies**: Prior to starting HIV PrEP, baseline laboratory studies, as outlined in detail in the next section, should be ordered to rule out preexisting HIV infection, to obtain baseline safety laboratory studies, and to evaluate for other important infectious diseases that are transmitted through sexual activity or injection drug use.
- **Possible Acute HIV Infection**: Any clinical manifestations that suggest acute (primary) HIV infection should prompt a thorough laboratory evaluation for acute HIV infection and should delay the start of HIV PrEP while awaiting the laboratory results. For details on the diagnosis and treatment of acute HIV, see the *National HIV Curriculum* lesson on Acute and Recent HIV Infection. The figure below summarizes the most common signs and symptoms associated with acute HIV (Figure 1).[1,3]

Baseline Laboratory Evaluation When Starting HIV PrEP

For the baseline laboratory evaluation, it is essential to perform HIV testing to ensure that a person starting HIV PrEP has not already acquired HIV. The four regimens that are used for HIV PrEP (TDF-FTC, TAF-FTC, CAB-LA, or LEN-SQ) are inadequate if used alone for the treatment of HIV, and use of HIV PrEP medications alone in a person with established HIV infection may result in the development of HIV drug resistance. When ordering baseline laboratory studies, it is ideal to know which HIV PrEP medication the patient is starting because the recommended laboratory studies differ slightly depending on the medication used. The following table summarizes recommendations for baseline laboratory tests outlined in the 2021 CDC HIV PrEP Guidelines and the 2025 CDC LEN-SQ HIV PrEP Guidelines, including recommendations for the specific type of HIV test to order (Figure 2).[1,4] Following the table, additional detail for each of these tests is provided.[1,4]

- **HIV Antigen-Antibody Immunoassay**: A negative blood-based HIV antigen-antibody test must be confirmed prior to starting any HIV PrEP medication. This test should reflect current HIV status and therefore should be obtained in the 7-day period prior to starting HIV PrEP. The blood-based HIV antigen-antibody test must be a test approved or cleared by the FDA for the diagnosis of acute or primary HIV-1 infection. There are two options for obtaining the FDA-approved blood-based HIV antigen-antibody test: (1) draw a blood sample and obtain a laboratory blood-based HIV-antigen antibody test, or (2) perform a rapid, point-of-care blood HIV antigen-antibody test. Ideally, a laboratory blood-based test is used, but, since this test often requires longer than 24 hours to obtain a result, it may not allow for initiation of HIV PrEP on the same day of the visit. If a rapid point-of-care blood-based test is used to document the initial negative HIV test, a laboratory blood-based HIV antigen-antibody test should also be obtained. In this situation, the HIV PrEP can be started while the laboratory blood-based HIV antigen-antibody test result is pending. For persons who take an oral cabotegravir lead-in prior to starting CAB-LA, the blood-based HIV antigen-antibody test should be done within 7 days prior to starting the oral lead-in and then repeated within 7 days prior to the first injection of CAB-LA. Oral fluid point-of-care HIV testing should not be used for HIV testing prior to starting HIV PrEP medications.
- **HIV-1 RNA**: An HIV-1 RNA test is recommended as part of the routine initial evaluation for all individuals initiating CAB-LA or LEN-SQ. The blood sample for HIV-1 RNA test should be drawn within 7 days prior to starting HIV PrEP with CAB-LA or LEN-SQ. For persons who take an oral cabotegravir lead-in prior to starting CAB-LA, the HIV-1 RNA should be done within 7 days prior to starting the oral lead-in and then repeated within 7 days before receiving the first injection of CAB-LA. The first dose of LEN-SQ can be administered if the HIV-1 RNA test has been drawn, the results are pending, and a blood-based HIV antigen-antibody test is negative. If a baseline HIV RNA is not done, and the person starts LEN-SQ, a blood-based HIV antigen-antibody test should be repeated 4 weeks from the initial injection. For individuals starting oral HIV PrEP with TDF-FTC or TAF-FTC, a baseline qualitative or quantitative HIV-1 RNA polymerase chain reaction (PCR) assay is not routinely recommended, but it is indicated if any of the following circumstances pertain to the person planning to start HIV PrEP:
    - Has taken oral HIV PrEP or HIV PEP within the past 3 months, *or*
    - Received CAB-LA for HIV PrEP within the past 12 months, *or*
    - Had high-risk HIV exposure in the prior 4 weeks, *or*
    - Had symptoms in the prior 4 weeks that are consistent with acute HIV infection.
- **Estimated Creatinine Clearance (eCrCl)**: A serum creatinine is recommended to assess renal function prior to starting oral HIV PrEP. Most laboratory reports routinely provide an estimated creatinine clearance (eCrCl), which is used as a proxy for renal function. This test is important to order at baseline due to restrictions on the use of TDF-FTC and TAF-FTC for individuals with renal insufficiency.
- **Syphilis Serology**: Testing for syphilis usually requires a blood draw to obtain a serum sample that can be used for either the reverse screening method (treponemal-specific antibody screening testing followed by a nontreponemal assay) or the traditional method (screening with a nontreponemal assay).[5,6] Rapid point-of-care treponemal (antibody) syphilis fingerstick tests are now available, but they are only useful for individuals with no prior history of syphilis.[7] For the nontreponemal tests,

two options can be used: rapid plasma reagin (RPR) or venereal disease research laboratory (VDRL). Persons with a known prior history of syphilis should have a nontreponemal assay (RPR or VDRL) as their screening test, since they will likely have a positive treponemal-specific antibody test for life.

- **Gonorrhea**: The preferred test for gonorrhea is a nucleic acid test (NAAT). Most laboratories now perform the gonorrhea NAAT as a tandem sample test with chlamydia. Testing should involve obtaining samples from all sites of sexual activity, such as throat, urethra, vagina, and rectum. Swabs can be self-collected by patients or collected by a clinician. Urine samples can be used instead of swabs for testing urethral and cervical/vaginal infection.
- **Chlamydia**: The preferred type of test for chlamydia is a NAAT. Most laboratories now perform the chlamydia NAAT as a tandem sample test with gonorrhea. Testing should consist of obtaining samples from all sites involved with sexual activity, such as throat, urethra, vagina, and rectum. Swabs can be self-collected by patients or by a clinician. Urine samples can be used instead of swabs for testing urethral and cervical/vaginal infection.
- **Hepatitis B Serology**: The recommended screening for hepatitis B virus (HBV) consists of a triple screen panel that includes hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (anti-HBs), and hepatitis B core antibody (anti-HBc).[8] The oral HIV PrEP options, TDF-FTC and TAF-FTC, are active against HBV, so baseline hepatitis B serologic testing for individuals starting these HIV PrEP regimens is important, since starting and then stopping these medications can lead to an HBV flare in persons with underlying chronic HBV infection. In addition, in March 2023, the CDC recommended one-time HBV screening for all adults in the United States, with periodic, repeat testing recommended for susceptible persons with ongoing risk of acquiring HBV.[8] Individuals who are HBV-seronegative should receive HBV vaccination. The injectable HIV PrEP medications, cabotegravir and lenacapavir, do not have activity against HBV.
- **Hepatitis C Serology**: The recommended serologic testing for hepatitis C virus (HCV) infection is an anti-HCV antibody test, with reflex HCV PCR testing for all positive antibody results.[9] In 2020, the CDC recommended one-time testing for HCV for all adults in the United States.[9] Repeat annual testing should also be performed for persons who have ongoing risk of acquiring HCV, including people who inject drugs (PWID) and men who have sex with men (MSM).[9,10] If a person is seronegative and at risk, counseling can be performed to reduce the risk of acquiring HCV. Persons who test positive for HCV RNA by PCR (indicating active infection) should be evaluated or referred for HCV treatment.[10]
- **Lipid Panel**: The recommended lipid panel to order should include total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides. Several studies have shown that taking TAF-FTC may lead to minor unfavorable changes in serum lipid parameters, but these changes are not seen with TDF-FTC, CAB-LA, or LEN-SQ. Accordingly, a baseline serum lipid panel is recommended only for individuals who initiate TAF-FTC for HIV PrEP.
- **Pregnancy Testing**: For all women with childbearing potential, a baseline pregnancy test is recommended prior to starting HIV PrEP, primarily for counseling purposes. The oral HIV PrEP regimens, TDF-FTC and TAF-FTC, have both been shown to be safe and effective for the treatment of HIV during pregnancy. The Department of Health and Human Services (HHS) Perinatal Guidelines recommend the use of TDF-FTC for HIV PrEP during pregnancy and breastfeeding.[11] At this time, there are still limited data CAB-LA as HIV PrEP in pregnancy. The CDC recommends that LEN-SQ for HIV PrEP may be used in pregnant women or continued in women who become pregnant while receiving injections, considering the woman's risk for HIV acquisition without HIV PrEP, after provider-client shared decision-making.[4]

[Q] Baseline Lipid Panel

Baseline Testing when Starting TDF-FTC

The following interactive exercise is based on recommendations in the 2021 CDC HIV PrEP Guidelines for baseline laboratory studies to order when considering starting a person on TDF-FTC for HIV PrEP (Figure 3).

Baseline Testing when Starting TAF-FTC

The following interactive exercise is based on recommendations in the 2021 CDC HIV PrEP Guidelines for baseline laboratory studies to order when considering starting a person on TAF-FTC for HIV PrEP (Figure 4).

Baseline Testing when Starting CAB-LA

The following interactive exercise is based on recommendations in the 2021 CDC HIV PrEP Guidelines for baseline laboratory studies to order when considering starting a person on CAB-LA for HIV PrEP (Figure 5).

Baseline Testing when Starting LEN-SQ

The following interactive exercise is based on recommendations in the 2025 CDC LEN-SQ HIV PrEP Guidelines for baseline laboratory studies to order when considering starting a person on CAB-LA for HIV PrEP (Figure 6).

[Q] Hepatitis B Serologic Studies when Starting Tenofovir alafenamide-Emtricitabine

[Q] HIV Testing when Starting Cabotegravir

Starting HIV PrEP

Prescribing Oral HIV PrEP

Persons initiating daily oral HIV PrEP (TDF-FTC or TAF-FTC), are typically prescribed a 90-day supply of medication without refills.[1] Prescribing 90 days of medication, as opposed to 30 days, minimizes opportunities for treatment interruption and aligns with CDC recommendations for repeat HIV and STI testing every 3 months.[1] Typically, refills of oral HIV PrEP are provided after repeat testing has been ordered, and the HIV PrEP medication is continued only if testing confirms the individual continues to have negative HIV test results. Less often, TDF-FTC is prescribed as on-demand (2-1-1) HIV PrEP for men who have sex with men and have infrequent sex, can anticipate sex, have normal renal function, and do not have hepatitis B virus (HBV).[1] For persons planning to take on-demand (2-1-1) oral TDF-FTC HIV PrEP, a maximum 30-day supply, without refills, is typically given.[1]

Administering CAB-LA

All doses of CAB-LA require an intramuscular injection that should be administered by a health care professional. Typically, this is done in a clinic setting. The preferable site for the injections is the ventrogluteal region; the alternative site is the dorsogluteal region. CAB-LA is administered as a single 600 mg (3 mL) intramuscular injection on day 0, followed by an injection 1 month (or 4 weeks) later, and then every 2 months (or 8 weeks) thereafter.[1] Note that the prescribing information for CAB-LA recommends follow-up intervals based on months and not weeks (scheduling by the month selects a follow-up target data based on the same calendar date). In contrast, the 2021 CDC HIV PrEP Guidelines recommend using weeks as the designated interval for follow-up (e.g., 4 weeks instead of 1 month or 8 weeks instead of 2 months).[1] To assess for tolerability, an optional lead-in with oral cabotegravir 30 mg daily may be administered, typically for 1 month. If the oral lead-in is given, the first injection of CAB-LA should preferably be administered on the last day of the oral lead-in phase and always within 3 days of completing the oral cabotegravir lead-in. The standard CAB-LA injection kit contains a 1 ½-inch needle for the intramuscular injection. In some individuals, especially those who have a higher body mass index (e.g., greater than 30 kg/m^2), a 2-inch needle may be needed to deliver the cabotegravir into the muscle. For clinics using CAB-LA, it is advisable to stock 2-inch needles in the clinic since they may be difficult to obtain.

Administering LEN-SQ

Lenacapavir requires initiation phase dosing that includes oral doses administered on days 1 and 2 and subcutaneous lenacapavir administered on day 1.[4] The oral lenacapavir dose for each day is 600 mg orally (2 x 300 mg tablets). The LEN-SQ is administered on day 1 in the clinic and the dose is 927 mg (3 mL) (2 x 1.5 mL injections, each containing 463.5 mg of lenacapavir).[4] The day-2 oral dose can be provided to the patient on day 1 so that the patient can self-administer the day-2 oral dose at home, without a visit to the clinic; if this approach is used, a phone call or video appointment is recommended on day 2 to ensure that the oral doses are taken and to assess for any adverse reactions to the day-1 injections. A visit to the clinic on day 2 should be considered optional. After the initiation phase dosing, LEN-SQ is administered every 6 months (26 weeks).[4] All doses of LEN-SQ require a subcutaneous injection that should be administered by a health care professional. The abdomen is the preferred site for the LEN-SQ injection and the anterior thigh is considered an alternative site. If the injection is given on the abdomen, it should be at least 2 inches from the umbilicus. Regardless of where the two injections are given, they should be given at least 4 inches apart.[4]

Paying for HIV PrEP

Most health insurance plans, including Medicare and Medicaid, will cover the cost of HIV PrEP, but there may be variability in the types of HIV PrEP covered (e.g., the more expensive option of TAF-FTC, CAB-LA, and LEN-SQ may not be covered under each plan). Note that for persons who are candidates to receive TDF-FTC, there are now multiple TDF-FTC generic preparations that are FDA-approved, and these generic formulations are

dramatically less expensive than brand-name HIV PrEP options.

- State PrEP Assistance Programs: The National Alliance of State and Territorial AIDS Directors (NASTAD) provides a directory and contact information for states that have HIV PrEP medication assistance programs. This site also includes a table with information from some states on co-pay assistance, medication assistance, coverage for clinic visits and laboratory tests, and access based on patient income level.
- NASTAD PrEP Billing and Coding Guide: On October 12, 2023, NASTAD released an HIV PrEP and HIV postexposure prophylaxis (PEP) billing and coding guide. This billing and coding guide provides highly valuable information for health care providers, pharmacists, and clinic administrative staff who are working in clinics that provide HIV prevention services.
- Gilead Advancing Access: This program includes a co-pay coupon program and a patient support program. This program is specific for Gilead-manufactured HIV PrEP medications: TDF-FTC, TAF-FTC, or LEN-SQ,
- ViiVConnect: This program provides information to help health care professionals, pharmacists, patient representatives, and patients explore ways to access prescribed ViiV Healthcare medications; for HIV PrEP, this is specific to long-acting injectable cabotegravir.

Managing Side Effects Associated with HIV PrEP

In general, all HIV PrEP medications (oral and injectable) are relatively well tolerated and rarely require discontinuation due to an adverse effect. The following summarizes the management of adverse effects with the medications FDA-approved for HIV PrEP.

- **Tenofovir-DF-emtricitabine (TDF-FTC)**: Oral TDF-FTC is usually well tolerated, except for start-up symptoms (headache, nausea, and abdominal discomfort) that develop in about 15% of people after starting TDF-FTC.[12] If start-up symptoms occur, they typically peak within several weeks after starting TDF-FTC and typically resolve within 2 months.[12] The start-up symptoms can be easily managed with over-the-counter medications, but sometimes require prescription antiemetics to use on an as-needed basis. Use of daily TDF-FTC for HIV PrEP has been associated with minor decreases in estimated creatinine clearance, but these changes reverse rapidly upon discontinuation of TDF-FTC.[13,14,15] Similarly, use of daily TDF-FTC has been associated with a decrease in bone mineral density during HIV PrEP, but these changes were typically small and reversed after stopping the medication.[16,17] For persons taking tenofovir DF-based HIV PrEP, monitoring for renal adverse events is recommended every 6 to 12 months, but monitoring for bone mineral density changes is not recommended.[16,17,18]
- **Tenofovir alafenamide-emtricitabine (TAF-FTC)**: Oral TAF-FTC is generally well tolerated, except for start-up symptoms (headache, nausea, and abdominal discomfort) that develop in fewer than 10%. As with TDF-FTC, these symptoms usually resolve within several months, and the headaches can be managed with over-the-counter acetaminophen. In the main clinical trial involving TAF-FTC for HIV PrEP, there was a small weight gain (mean 1.1 kg) after 48 weeks of taking TAF-FTC.[19] Although TAF-FTC can adversely impact lipids, these changes are usually slight and not clinically significant.[19]
- **Long-Acting Injectable Cabotegravir (CAB-LA)**: Injection site reactions—most often pain and tenderness—are common in people receiving CAB-LA.[20,21] Over time, the percentage of persons who reported injection site reactions declined significantly (Figure 7). Most injection site reactions are mild or moderate and can be managed with over-the-counter pain medications and warm compresses or heating pads.[1]
- **Lenacapavir Subcutaneous Injection**: The major adverse effects associated with LEN-SQ are injection site reactions, including immediate-onset and delayed reactions.[22,23] The immediate-onset reactions have an onset within 48 hours (often within several hours) and typically resolve within 10 days. These reactions typically manifest as pain, tenderness, erythema, warmth, swelling, bruising, or itching of the injection site area. The delayed or prolonged reactions typically have an onset after 1–2 days, and the reactions often persist for months. These delayed reactions typically present as subcutaneous nodules, with associated pain, induration, and skin pigment changes.

Adherence with HIV PrEP

Correlation of HIV PrEP Adherence and Efficacy

The efficacy of daily oral HIV PrEP directly correlates with adherence. Among MSM, an adherence analysis of participants in the iPrEX trial showed the efficacy of TDF-FTC in preventing HIV was 99% when taken daily and 96% when taken 4 or more times per week; the efficacy declined to 76% with 2 doses per week (Figure 8).[1, 24] For women, laboratory data suggested 6 to 7 doses per week of TDF-FTC were needed to achieve protective concentrations in vaginal tissue.[1,25] More recent studies and reviews have concluded that women who have adherence of at least four doses per week of TDF-FTC have sufficient protection against HIV acquisition, and this adherence threshold (at least 4 doses per week) in women is similar to that observed in MSM.[26,27,28,29]

Counseling to Support HIV PrEP Adherence

If a person forgets to take their daily oral dose of HIV PrEP, and they realize it before the next dose is due, the CDC guidance recommends taking this missed dose as soon as the person is aware they missed the dose; if, however, it is nearly time for the next dose of oral HIV PrEP, then the missed dose should be skipped, as opposed to taking a double dose.[1] Unfortunately, the 2021 CDC HIV PrEP Guidelines do not precisely define what “nearly time for the next dose” means; in our opinion, we would recommend taking the missed dose if at least 6 hours remain before the next dose of oral HIV PrEP is due.[Q] Adherence and Oral PrEP Efficacy Because of the important role adherence plays in conferring protection against HIV, providers should counsel patients on the benefits of taking oral HIV PrEP daily and discuss how to best fit oral HIV PrEP into one’s daily routine.[1] Health care providers should similarly counsel patients on anticipated side effects, identify and address any anticipated barriers to adherence, and reinforce success while normalizing occasional missed doses.[1]

Table 1. HIV PrEP Adherence

Key Components of Oral Medication Adherence Counseling	**Establish Trust and Bidirectional Communication**
	Provide simple explanations and education
	• Medication dosage and schedule
	• Management of common side effects
	• Relationship of adherence to the efficacy of PrEP
	• Signs and symptoms of acute HIV infection and recom
	Support adherence
	• Tailor daily dose to patient’s daily routine
	• Identify reminders and devices to minimize forgetting
	• Identify and address barriers to adherence
	• Reinforce benefit relative to uncommon harms
	Monitor medication adherence in a non-judgmenta
	• Normalize occasional missed doses, while ensuring pat optimal protection
	• Reinforce success
	• Identify factors interfering with adherence and plan wi
	• Assess side effects and plan how to manage them

Source:

- Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States—2021 Update: a clinical practice guideline. December 2021:1-108. [CDC]

Same-Day HIV PrEP

Same-day HIV PrEP refers to the prescription of HIV PrEP and initiation of HIV PrEP on the same day as the initial clinic visit. This strategy of rapid HIV PrEP initiation aims to decrease barriers to HIV PrEP uptake and reduce the number of people who drop out of the HIV PrEP care cascade before they fill their first HIV PrEP prescription.[30,31] Same-day initiation of HIV PrEP also aims to minimize an individual's time at risk for HIV by expediting the achievement of protective tenofovir levels in serum and tissues.[30,31] At this time, same-day HIV PrEP usually pertains only to oral HIV PrEP, since logistical insurance issues often prohibit starting same-day HIV PrEP with CAB-LA or LEN-SQ. Programs with strong infrastructure for providing HIV PrEP may have the capacity to achieve same-day HIV PrEP starts with CAB-LA or LEN-SQ. Any setting that has access to point-of-care (POC) HIV testing, the ability to order laboratory-based HIV and renal function testing, and the capacity to provide prescriptions and appropriate follow-up care can implement same-day HIV PrEP.[1] For details related to Same-Day HIV PrEP, see the lesson on Same-Day (Rapid) Start for HIV PrEP in the HIV PrEP In-Depth Topics Module.

Time for Protection after Starting HIV PrEP Medications

Unfortunately, no study has directly assessed the time from HIV PrEP initiation to clinical protection against HIV infection, but extrapolations have been made from pharmacokinetic and modeling studies.

Time to Protection with Oral HIV PrEP

Most of the data and recommendations regarding time to protection for oral HIV PrEP have focused on time to protection after administering medications that contain TDF or TAF. With both of these medications, the intracellular levels of tenofovir diphosphate, which is the phosphorylated metabolite, is the measurement reported in pharmacologic studies. For both TDF and TAF, tenofovir diphosphate is the active form of the drug and a proxy for protection against infection with HIV.[32,33] Note the metabolism of TDF and TAF are distinct, with TAF having greater selectivity for generating higher levels of tenofovir in lymphoid tissues relative to plasma levels of tenofovir (Figure 9).[32,33]

- **Tenofovir DF (TDF)**: Studies have shown that with the use of oral TDF, higher concentrations of tenofovir diphosphate—the active form of TDF—are achieved in rectal mucosa than in cervicovaginal mucosa and that it takes longer to achieve steady-state concentrations in the female genital tract than in the rectum.[34,35] Pharmacologic data that show the approximate time to achieve maximal intracellular levels of tenofovir diphosphate with daily dosing of TDF-FTC depends on the tissue: 7 days for peripheral blood mononuclear cells, 7 days for rectal tissue, and 20 days for cervicovaginal tissue (Figure 10).[1,25,34]
- **Tenofovir alafenamide (TAF)**: For persons taking daily TAF-FTC, less is known about the tissue levels of the active drug tenofovir diphosphate than is known with TDF-FTC. In a pharmacokinetic study in women that compared tissue tenofovir diphosphate concentrations with TDF-FTC or TAF-FTC, the vaginal tissue tenofovir diphosphate concentrations were approximately 6-fold higher in women taking TAF-FTC than with TDF-FTC.[36] In this same study, the rectal tissue tenofovir diphosphate levels were lower with TAF-FTC than with TDF-FTC, though still above the protective levels.[36]
- **Emtricitabine (FTC) and Lamivudine (3TC)**: Pharmacologic data suggest that emtricitabine and lamivudine have a high ratio of female genital tract tissues to blood plasma levels at a steady state.[37] Additional studies have also shown that emtricitabine levels are relatively lower than tenofovir levels in rectal tissues but higher than tenofovir in vaginal and cervical tissues.[34]
- **Recommendations**: Although the time to steady-state or maximal intracellular concentration does not necessarily equate with time to protection, extrapolations for time to achieve tissue protective levels have been made for daily TDF dosing. The 2021 CDC HIV PrEP Guidelines do not provide an exact time for how long to wait until protected by oral HIV PrEP, but pharmacokinetic data suggest that persons initiating daily oral TDF-FTC for HIV PrEP should wait approximately 7 days before having condomless rectal sex and wait approximately 20 days before having condomless vaginal sex.[1] For daily oral TAF-FTC, data are insufficient to make estimates for time to protection after initiating this medication.

[Q] Active Tenofovir Metabolite

[Q] Time to Protection with Tenofovir DF-Emtricitabine

Initial Double-Dose of Oral HIV PrEP

The 2021 CDC HIV PrEP Guidelines do not address initiating HIV oral PrEP with a double dose of medication on day 1 versus standard (single-dose) medication on day 1 (Figure 11).[1] In the iPERGAY study, on-demand (2-1-1) use of TDF-FTC was protective against HIV infection among men having condomless anal sex with men.[38] Some experts have extrapolated from the iPERGAY trial to recommend that MSM who are prescribed daily oral HIV PrEP can use a double dose (2 pills) of TDF-FTC on day 1, followed by daily dosing thereafter. This approach (double dose on day 1) is thought to generate protective tissue concentrations more rapidly

than with standard (single dose on day 1) initiation, without needing to wait 7 days before having condomless sex. Indeed, the International Antiviral Society-USA (IAS-USA) guidance recommends that for men, oral dosing should be initiated with a double dose of TDF-FTC for the first day, followed by a standard single dose of TDF-FTC taken daily; this approach is expected to provide protection against HIV acquisition within 24 hours of the initial dosing.[39] It is important to note the on-demand (2-1-1) dosing approach used with TDF-FTC in MSM (in the iPERGAY trial) has not been studied in women.[38] Further, on-demand HIV PrEP has not been studied with TAF-FTC.

Time to Protection with Cabotegravir

The 2021 CDC PrEP guidelines state that no data are available from clinical trials in men or women that provide an estimated time from initiation of cabotegravir to protection.[1] In a multicompartment pharmacologic study that involved measuring cabotegravir levels in plasma, genital fluids, and tissue following CAB-LA administration, investigators found mean plasma levels of cabotegravir exceeded the in vitro protein-adjusted 90% maximal inhibitory concentration by day 3, peaked at day 8, and maintained above this level through week 12.[41] In addition, fluid and tissue levels were significantly lower than plasma levels, but were proportionate and strongly correlated with plasma concentrations. The highest levels in fluids and tissue were in rectal fluid and the next highest in cervical tissue.[41] Pharmacokinetic and modeling studies suggest that for oral cabotegravir, maximal plasma concentrations should be reached by 4 hours after ingesting a 30 mg dose; for CAB-LA, 95% of individuals will achieve target tissue concentrations by 7 days following an initial injection.[42,43,44] Based on these pharmacokinetic data, some experts have suggested that cabotegravir provides protection against HIV acquisition within 24 hours after the first dose, even with direct-to-inject methods. Despite this, formal guidance is not yet available on how to counsel patients for time to protection after starting cabotegravir.[1]

Time to Protection with Lenacapavir

Based on unpublished, available pharmacokinetic data for persons starting lenacapavir with initiation phase dosing suggest that protective levels of lenacapavir are achieved approximately 2–4 hours after the day-2 oral lenacapavir dose.[4] If a person does not receive the initiation phase oral lenacapavir doses, it is estimated that lenacapavir will not reach protective levels until around day 21 to day 28 after the injection.[4]

HIV PrEP Tools for Clinicians: Laboratory Tests

The *National HIV PrEP Curriculum* team has created **HIV PrEP Tools for Clinicians** based on 2021 CDC HIV PrEP Guidelines and 2025 CDC LEN-SQ HIV PrEP Guidelines.[1,4] These tools include a component on **Laboratory Tests for HIV PrEP** that provides specific recommendations for Baseline Labs (when starting HIV PrEP) and Monitoring Labs. These tools also provide guidance for assessing HIV PrEP indications and choosing medications for HIV PrEP. These tools also provide a guide for determining appropriate medication options for HIV PrEP and a guide for monitoring of laboratory tests. It is important to note these HIV PrEP tools are intended to help guide and educate clinicians, but all final decisions regarding indications for HIV PrEP, medication choices, and laboratory test monitoring should be based on the clinician's judgment (Figure 12). Access these tools by clicking TOOLS on the top navigation bar. Once on the Tools page, you can use any of the tools directly on the website and by installing them on your mobile device.

Summary Points

- All persons considered for starting HIV PrEP should have a complete initial assessment, including the need for HIV nonoccupational PEP, baseline laboratory tests, and screening for possible acute HIV infection.
- Initial laboratory evaluation in persons starting on HIV PrEP must include HIV testing that is performed within 7 days of the planned HIV PrEP start (HIV antigen-antibody immunoassay for persons starting oral HIV PrEP and HIV antigen-antibody immunoassay plus HIV-1 RNA for those starting CAB-LA or LEN-SQ).
- Baseline laboratory studies differ slightly based on the HIV PrEP regimen prescribed, but all should include baseline testing for HBV, HCV, and STIs.
- Persons initiating daily oral HIV PrEP (TDF-FTC or TAF-FTC) are typically prescribed a 90-day supply of medication. For persons planning to take on-demand (2-1-1) oral HIV PrEP with TDF-FTC, a 30-day supply is typically given.
- CAB-LA is administered as a single 600 mg (3 mL) injection, with the first 2 injections given 1 month apart, and then all subsequent injections 2 months apart. To assess for tolerability, an optional oral lead-in with cabotegravir 30 mg PO daily may be administered, typically for 1 month.
- LEN-SQ is administered as an every 6-month dose (927 mg) consisting of two injections each containing 463.5 mg. When starting lenacapavir, initiation phase dosing must be used, and it consists of oral lenacapavir 600 mg on days 1 and 2 and LEN-SQ (927 mg) on day 1.
- All HIV PrEP medications (oral and injectable) are usually well tolerated. The most common side effects with oral HIV PrEP are start-up symptoms (headache, nausea, and abdominal discomfort), which, if they occur, are most prominent during the first month of taking oral HIV PrEP and often resolve within 3 months. Injection site reactions are the most common adverse events with CAB-LA and LEN-SQ.
- The efficacy of HIV PrEP directly correlates with adherence. Adherence counseling should address the benefits of taking HIV PrEP, how to fit taking HIV PrEP into a daily routine, potential barriers to adherence, and anticipated side effects.
- Same-day HIV PrEP refers to the prescription and initiation of oral HIV PrEP on the same day as the initial clinic visit. Settings with access to point-of-care HIV testing, the ability to order laboratory-based HIV and renal function testing, and the capacity to provide prescriptions and appropriate follow-up care can implement same-day HIV PrEP.
- Pharmacokinetic data on time to protection suggests that persons initiating oral TDF-FTC for HIV PrEP should wait approximately 7 days before having condomless rectal sex and wait approximately 20 days before having condomless vaginal sex. Data are less well established for TAF-FTC . It is likely that CAB-LA provides protection within 7 days of the first injection. Data with lenacapavir suggest that protective levels of lenacapavir are achieved approximately 2–4 hours after the day-2 oral initiation phase lenacapavir dose.

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Figures

Figure 1 Clinical Signs and Symptoms of Acute (Primary) HIV Infection

*Adenopathy = cervical adenopathy

Source: Daar ES, Pilcher CD, Hecht FM. Curr Opin HIV AIDS. 2008;3:10-5.

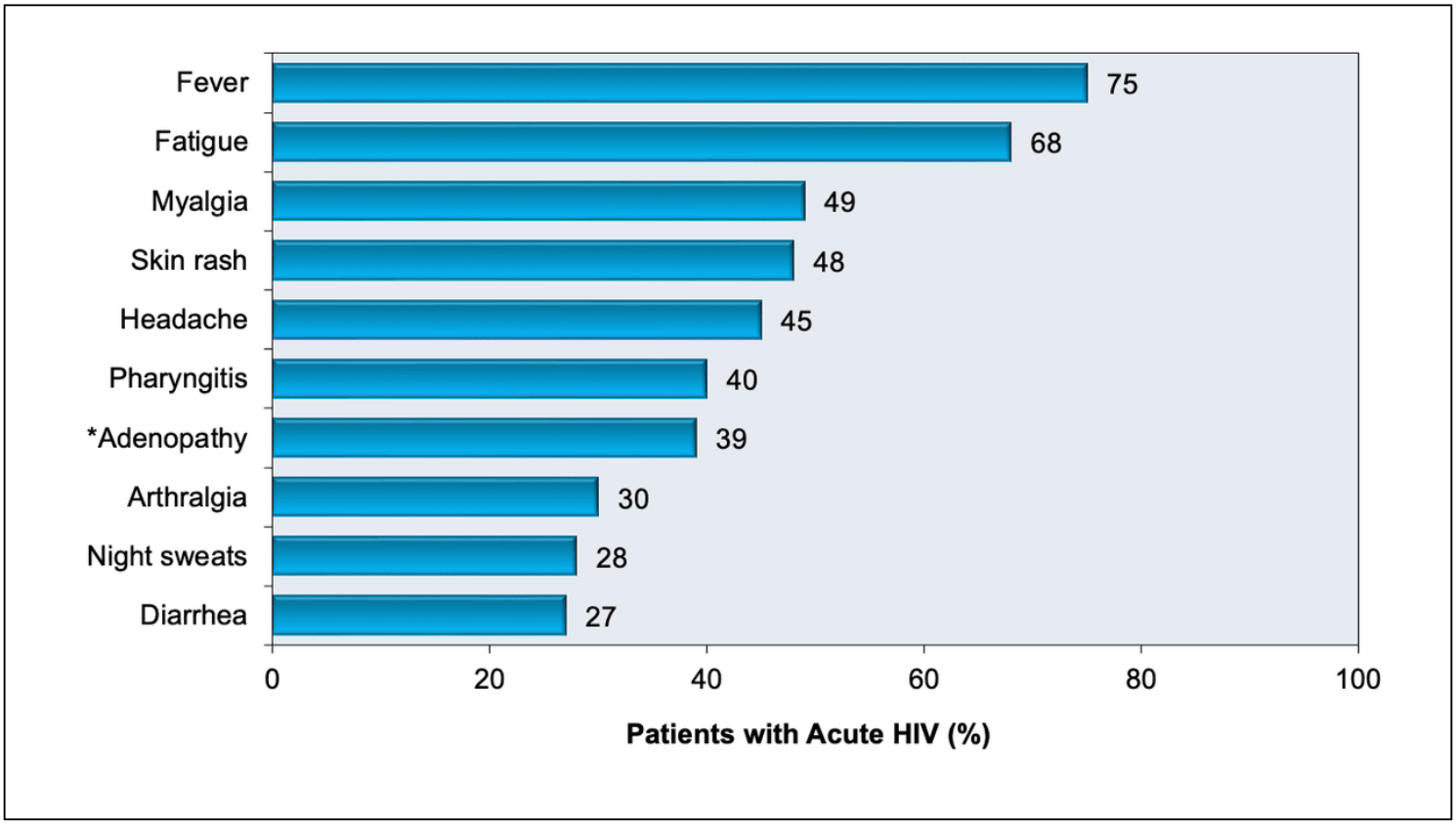


Figure 2 CDC Recommendations for Initial Laboratory Evaluation in Persons starting HIV PrEP

Source: Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States—2021 Update: a clinical practice guideline. December 2021:1-108.

Table based on 2021 CDC Clinical Practice Guidelines for HIV PrEP and Clinical Recommendation for the Use of Injectable Lenacapavir as HIV Preexposure Prophylaxis — United States, 2025

Initial Laboratory Evaluation in Persons Starting HIV PrEP

Test	TDF-FTC	TAF-FTC	CAB-LA	LEN-SQ
HIV Antigen/ Antibody	ALL*	ALL*	ALL*	ALL*
HIV-1 RNA	If indicated†	If indicated†	ALL‡	ALL‡
Renal Function (eCrCl)	ALL	ALL		
Syphilis Serology	ALL	ALL	ALL	ALL
Gonorrhea	ALL	ALL	ALL	ALL
Chlamydia	ALL	ALL	ALL	ALL
Hepatitis B Serology	ALL§	ALL§	ALL§	ALL§
Hepatitis C Serology	ALL§	ALL§	ALL§	ALL§
Lipid Panel		ALL		
Pregnancy Test	ALL¶	ALL¶	ALL¶	ALL¶

ABBREVIATIONS:

TDF-FTC = tenofovir DF-emtricitabine
TAF-FTC = tenofovir alafenamide-emtricitabine
CAB-LA = long-acting injectable cabotegravir
LEN-SQ = lenacapavir subcutaneous injections

LEGEND:

* The HIV antigen-antibody test must be a blood-based assay approved or cleared by the FDA for the diagnosis of acute or primary HIV-1 infection. The test must be on a sample obtained in the 7-day period prior to starting HIV PrEP. Two testing options are acceptable: (1) a laboratory blood-based HIV-antigen antibody test, or (2) a rapid, point-of-care blood HIV antigen-antibody test. If the rapid test is used to document the initial negative HIV test, a laboratory blood-based HIV antigen-antibody test should also be obtained as a supplemental test, but HIV PrEP can be started while the laboratory blood-based HIV antigen antibody test result is pending. Oral fluid point-of-care HIV testing should not be used for HIV testing prior to starting HIV PrEP medications.

† Not routinely recommended, but order if any apply: (1) received oral HIV PrEP or HIV PEP medications in past 3 months; (2) received cabotegravir injection in the past 12 months; (3) had high-risk exposure to HIV in prior 4 weeks; or, (4) has symptoms that suggest acute HIV.

‡ A blood sample for an HIV-1 RNA test should be drawn within 7 days prior to starting cabotegravir or lenacapavir; HIV PrEP can be initiated if the HIV-1 RNA test result is pending and the blood-based HIV antigen-antibody test is negative.

§ One-time screening recommended for all adults in the United States. Give hepatitis B immunization if nonimmune.

¶ For women with childbearing potential; pregnancy testing advised for counseling purposes.

Figure 3 Baseline Lab when Starting Tenofovir-DF-Emtricitabine (TDF-FTC)

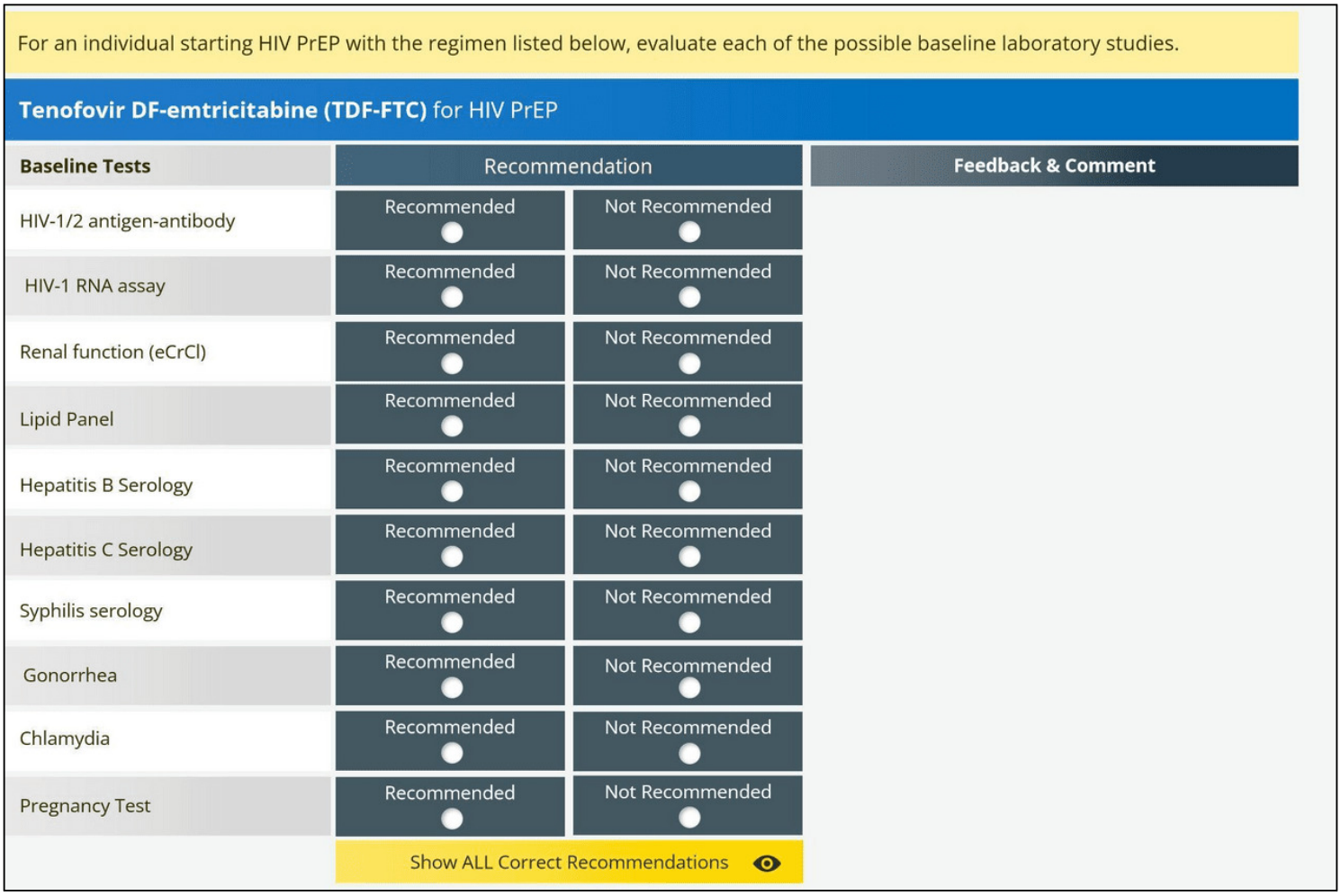


Figure 4 Baseline Lab when Starting Tenofovir alafenamide-Emtricitabine (TAF-FTC)

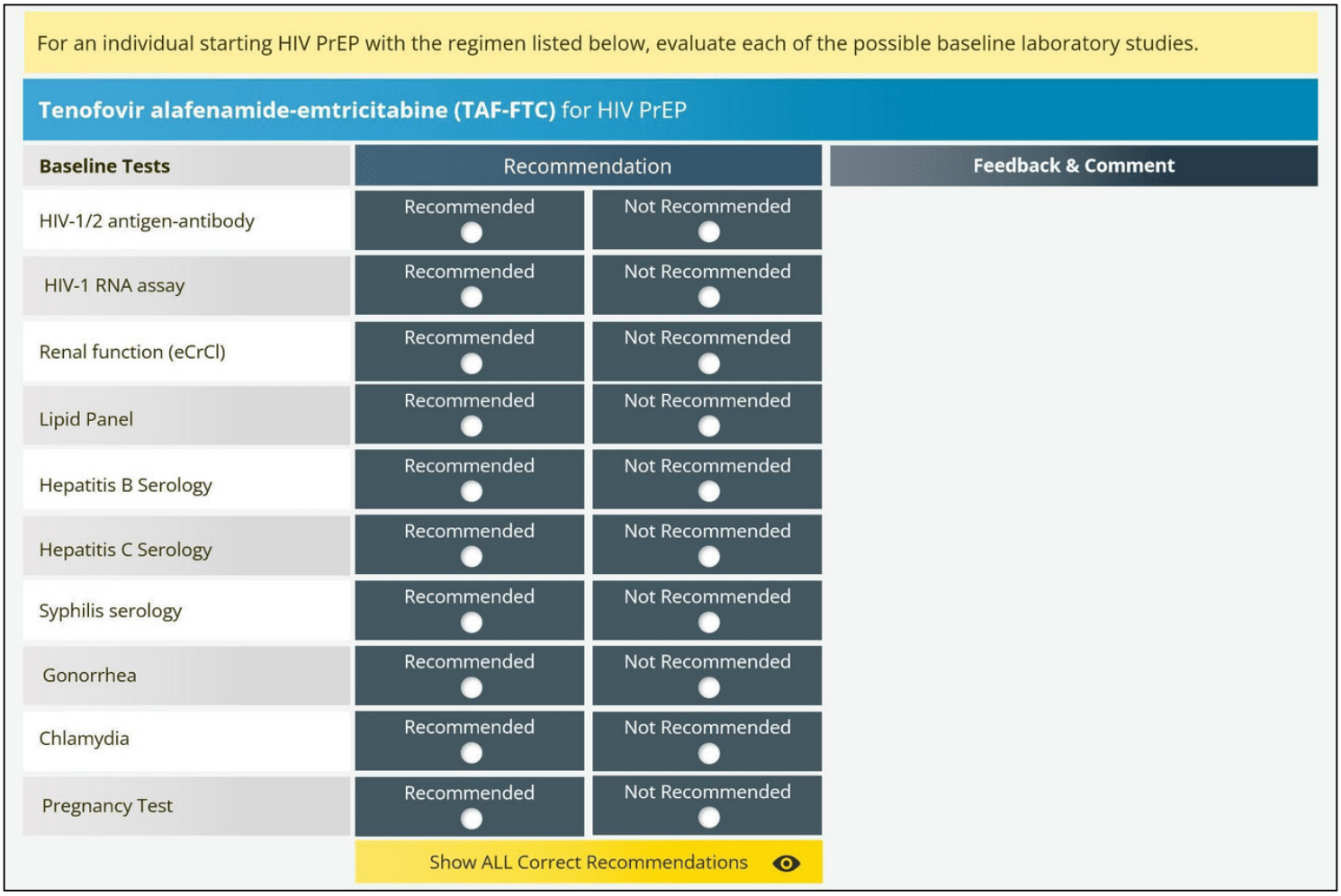


Figure 5 Baseline Lab when Starting Long-Acting Injectable Cabotegravir (CAB-LA)

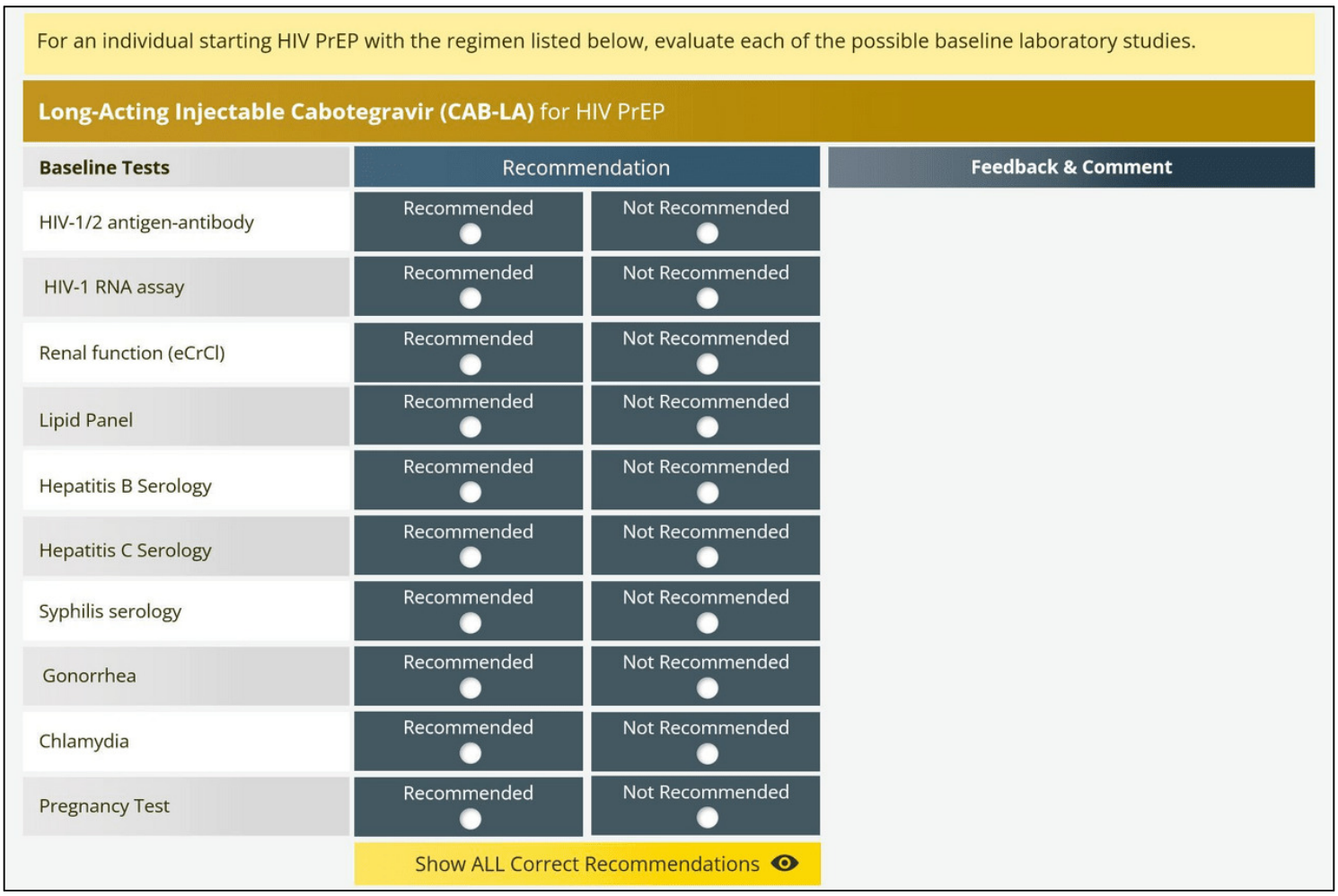


Figure 6 Baseline Lab when Starting Lenacapavir

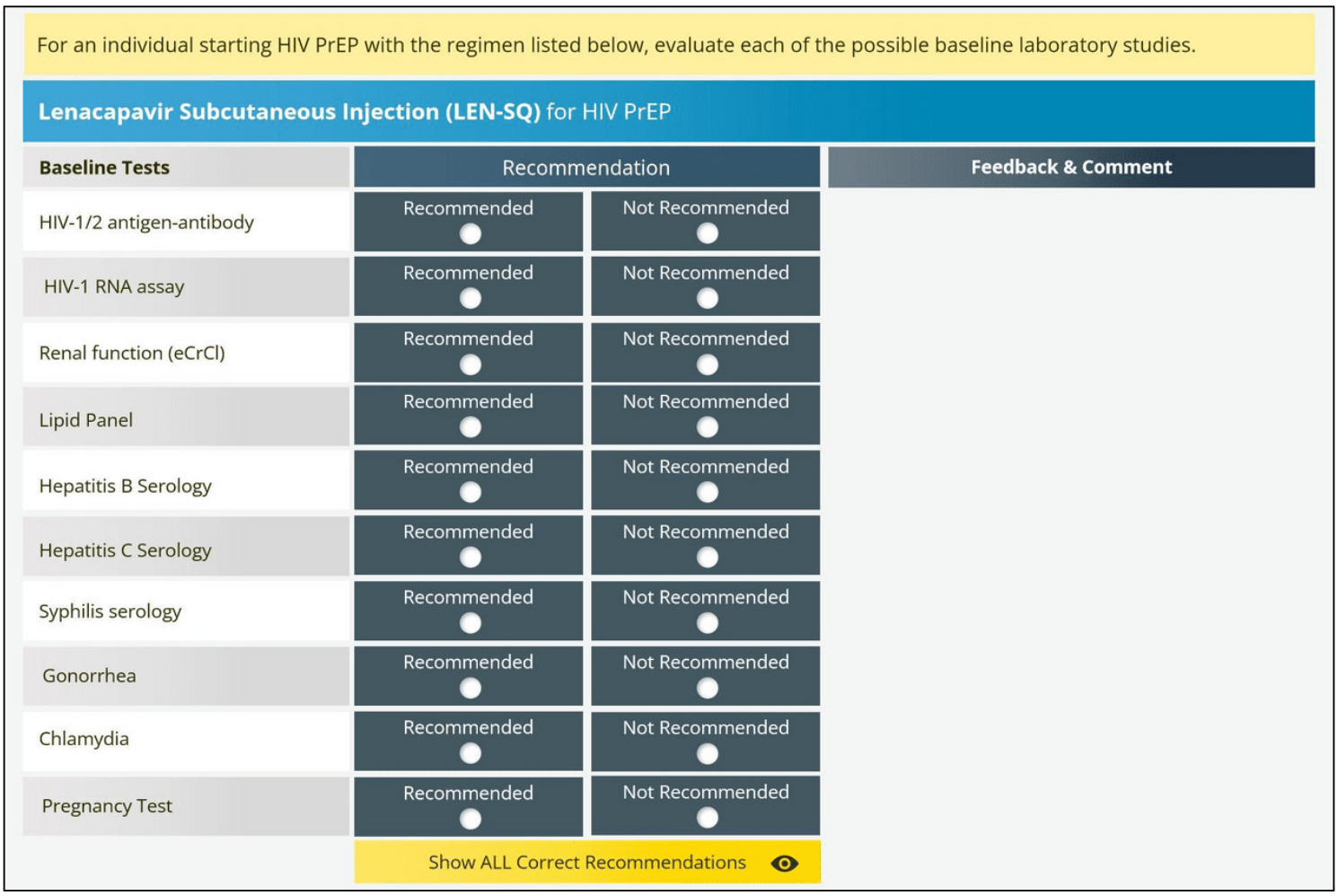


Figure 7 Cabotegravir Injection Site Reactions Over Time

Source: Landovitz RJ, Donnell D, Clement ME, et al. N Engl J Med. 2021;385:595-608.

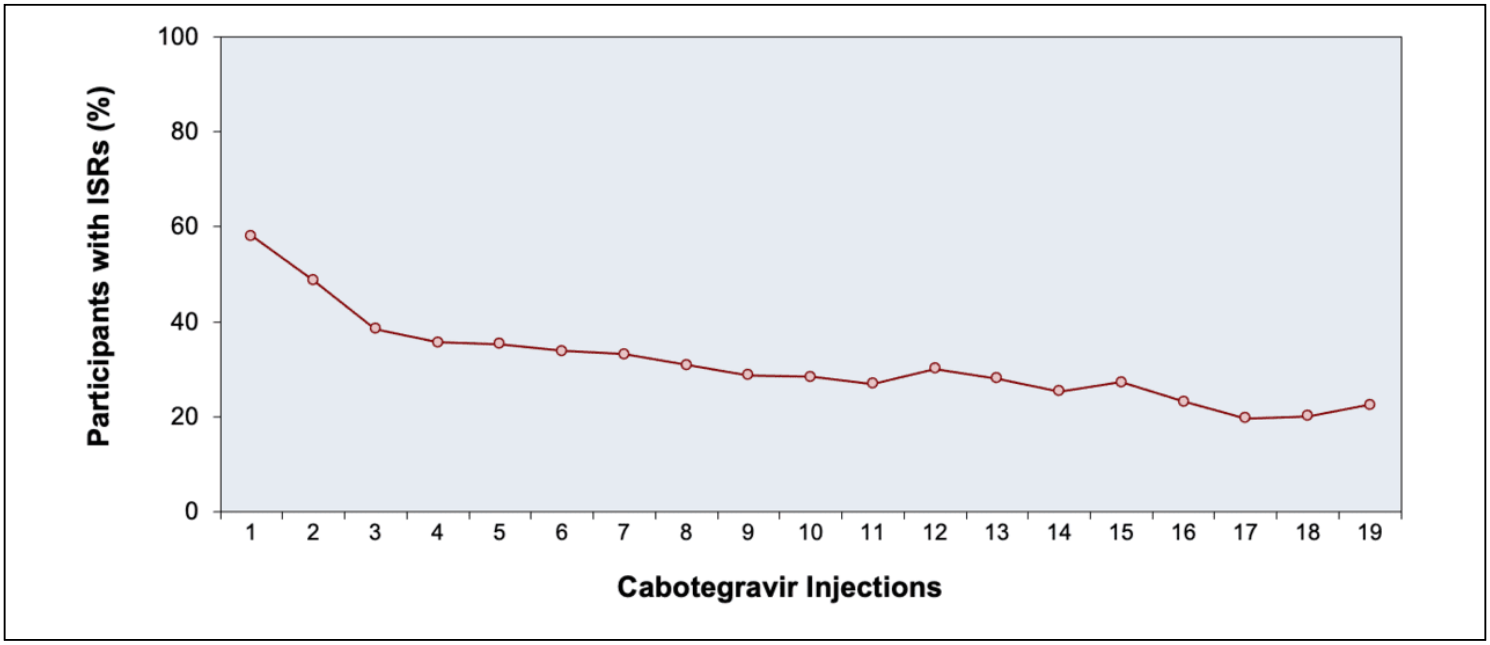


Figure 8 Adherence and HIV PrEP Efficacy in MSM with Daily TDF-FTC

Source: Grant RM, Anderson PL, McMahan V, et al. Lancet Infect Dis. 2014;14:820-9.

Adherence and HIV PrEP Efficacy in MSM with Daily Tenofovir DF-Emtricitabine	
Weekly Medication Adherence Estimated by Drug Concentration	**HIV Incidence per 100 Person-Years**
None	4.7
<2 pills/week	2.3
2-3 pills/week	0.6
≥4 pills/week	0.0

Figure 9 Metabolism of Tenofovir DF and Tenofovir alafenamide

The prodrug tenofovir disproxil fumarate (tenofovr DF, TDF) is primiarly hydrolyzed by gut and plasma esterase enzymes to generate tenofovir, which is thus present in high levels in the plasma. Tenofovir alafenamide, which is also a prodrug, undergoes relatively little hydrolysis in the gut and plasma, but instead is very heavily metabolized to tenofovir within lymphoid cells by the enzyme cathepsin.

Illustration: David H. Spach, MD

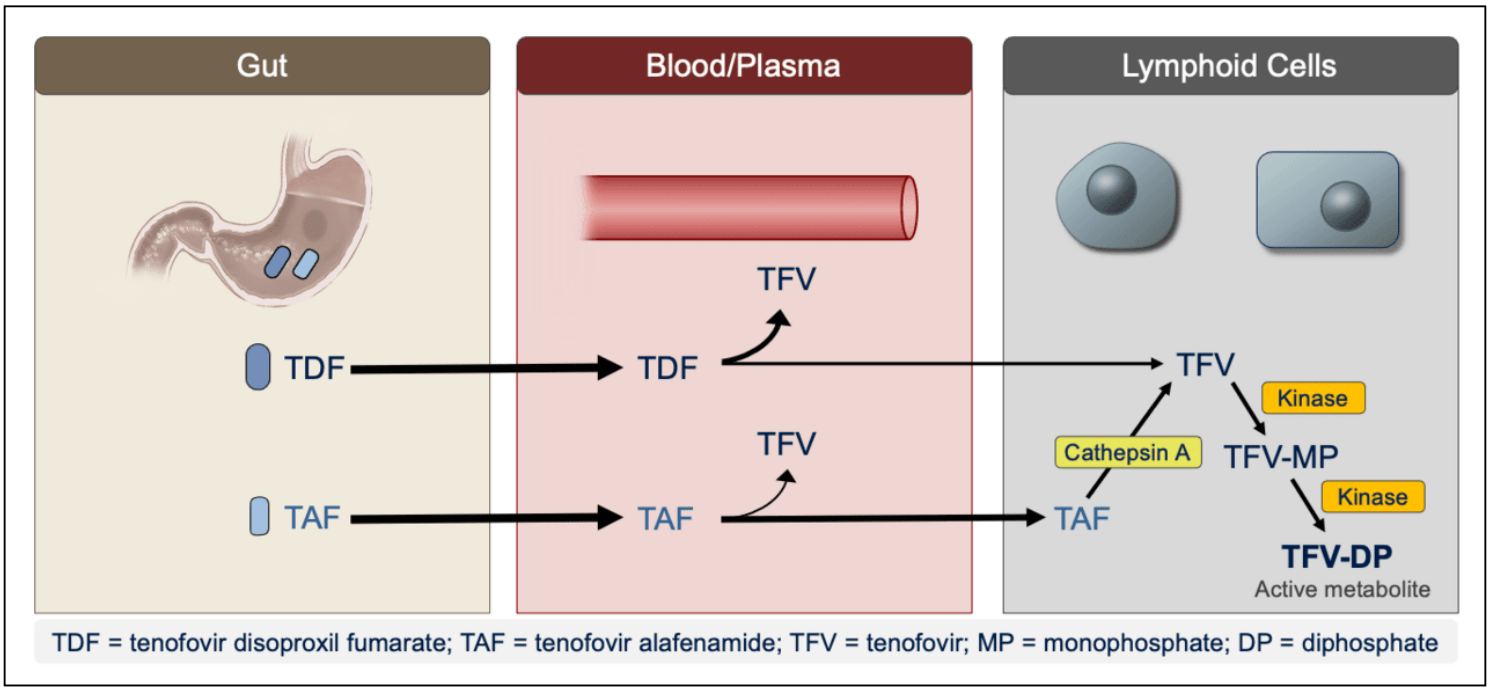


Figure 10 Time to Maximal Intracellular Tenofovir-Diphosphate Concentration with Daily Oral Dosing

PBMC = peripheral blood mononuclear cells; Tenofovir DP = tenofovir diphosphate (the active metabolite of tenofovir DF and tenofovir alafenamide)

Source:Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States—2021 Update: a clinical practice guideline. December 2021:1-108. Illustration: Cognition Studio, Inc. and David H. Spach, MD

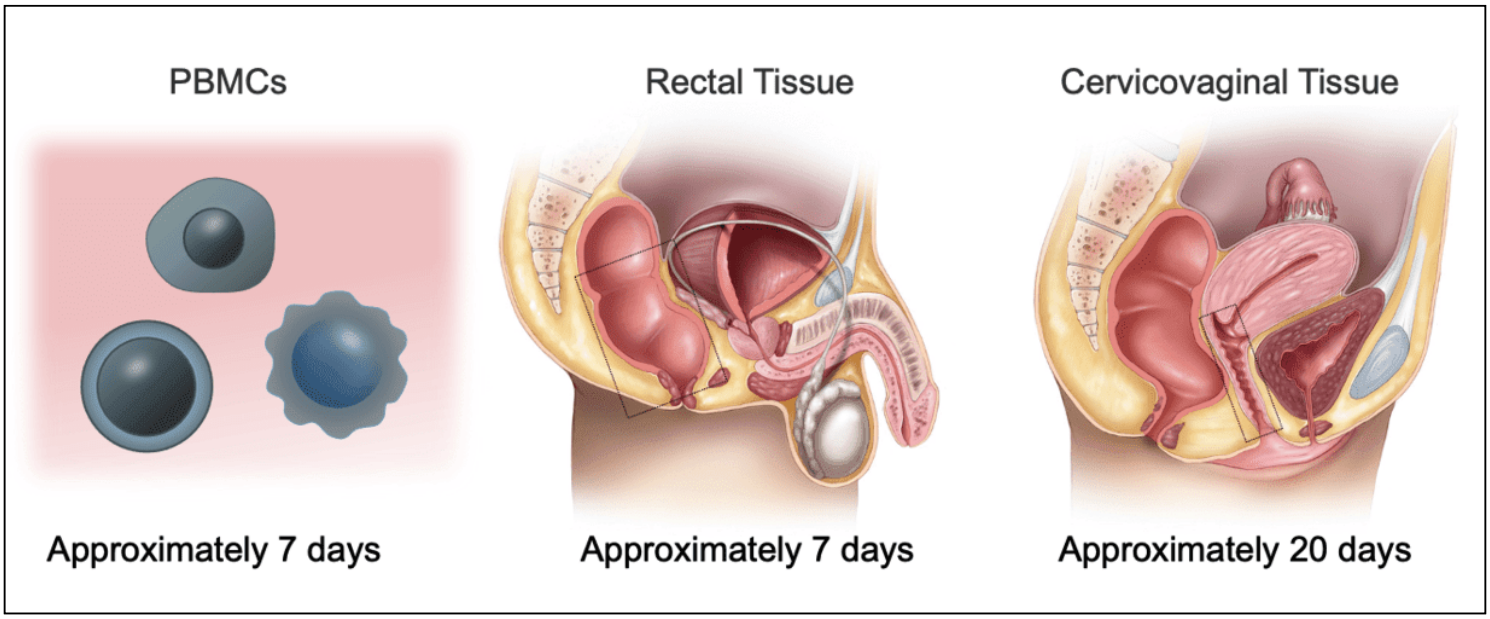


Figure 11 Standard and Double-Dose HIV PrEP Initiation

Abbreviation: TDF-FTC = tenofovir DF-emtricitabine

Illustration: David H. Spach, MD

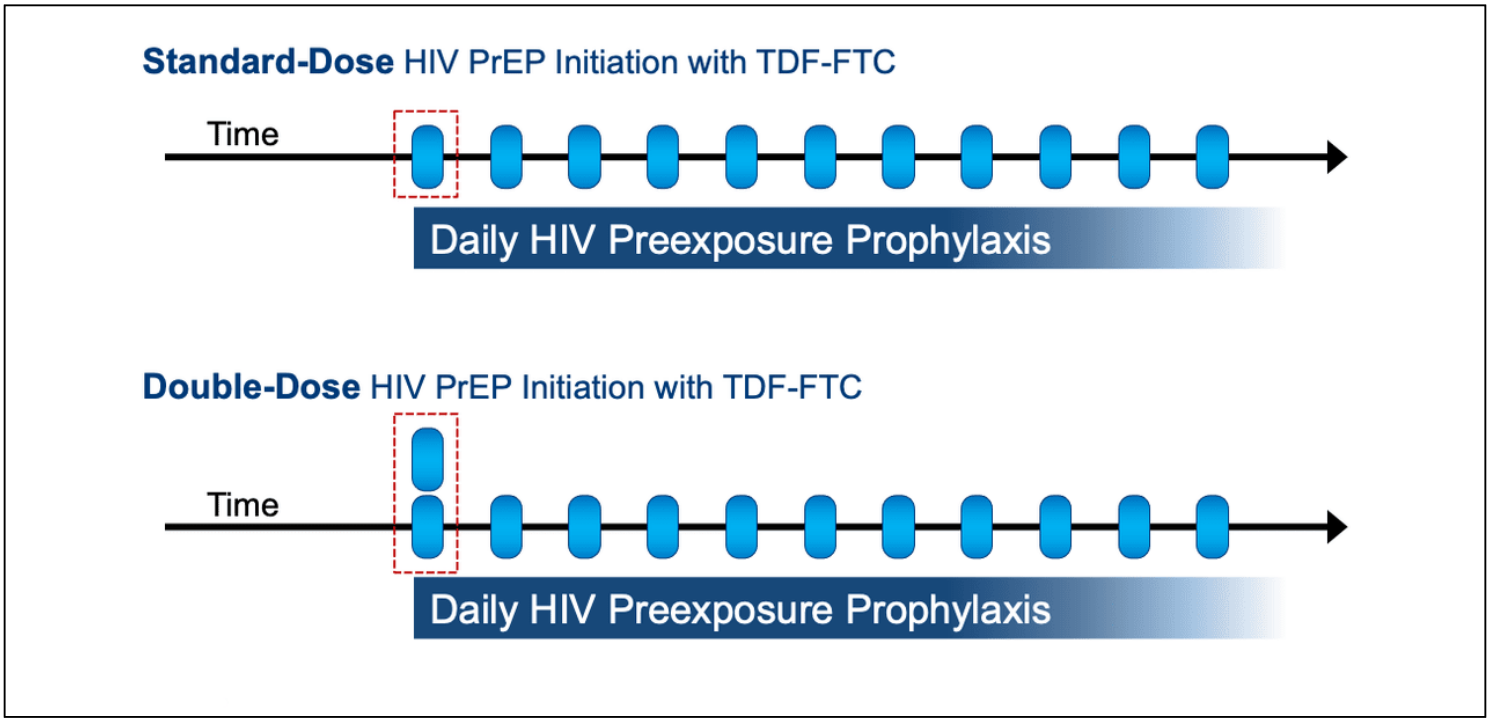


Figure 12 HIV PrEP Tools for Clinicians

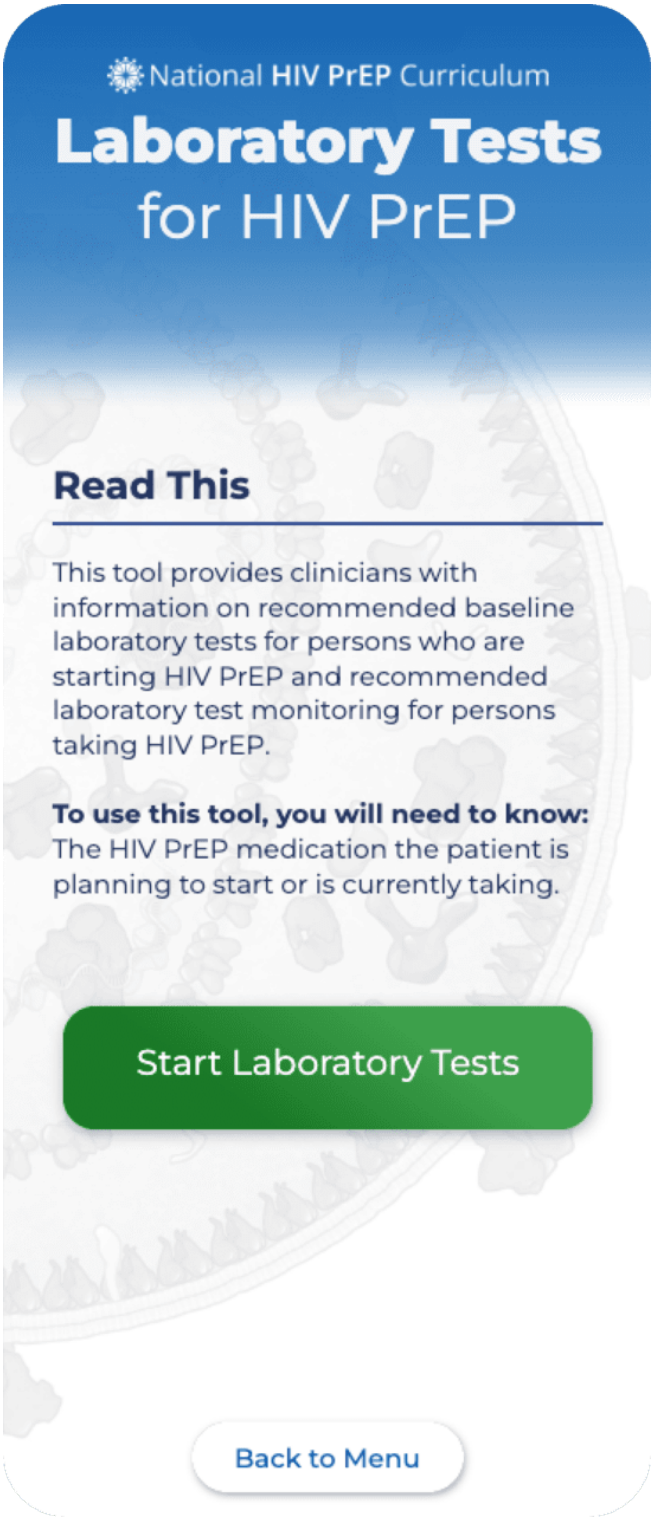


Table 1. HIV PrEP Adherence

Key Components of Oral Medication Adherence Counseling	**Establish Trust and Bidirectional Communication**
	Provide simple explanations and education
	• Medication dosage and schedule
	• Management of common side effects
	• Relationship of adherence to the efficacy of PrEP
	• Signs and symptoms of acute HIV infection and recom
	Support adherence
	• Tailor daily dose to patient's daily routine
	• Identify reminders and devices to minimize forgetting
	• Identify and address barriers to adherence
	• Reinforce benefit relative to uncommon harms
	Monitor medication adherence in a non-judgmenta
	• Normalize occasional missed doses, while ensuring pat optimal protection
	• Reinforce success
	• Identify factors interfering with adherence and plan wi
	• Assess side effects and plan how to manage them

Source:

- Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States—2021 Update: a clinical practice guideline. December 2021:1-108. [CDC]