**Template Guidelines for Oral Pre-Exposure Prophylaxis, PrEP Ring, and CAB PrEP**

*Updated on January 17, 2024*

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| The intent of this document is to provide adaptable guidelines to support the development and adoption of national guidelines that align with World Health Organization (WHO) pre-exposure prophylaxis (PrEP) recommendations and guidance, including those for tenofovir disoproxil fumarate (TDF)-based daily and event-driven oral PrEP, the monthly dapivirine vaginal ring (“PrEP ring” or “the ring”), and injectable cabotegravir (CAB PrEP). The document includes prompts for national-level consideration during the guideline adaptation process. Areas specifically requiring national updates are indicated in red font; sections for additional consideration by policymakers, shown in green boxes, are informed by regulatory bodies, available product information, and country-level insights. Once a decision has been made about the considerations in green boxes, text can be added, and the green boxes can be removed.  The content of this document was sourced largely from:   * [Australian Product Information for Apretude](https://www.tga.gov.au/sites/default/files/2022-12/auspar-apretude-221123-pi.pdf) (August 2022) * [Updated Differentiated and Simplified Pre-exposure Prophylaxis for HIV Prevention](https://www.who.int/publications/i/item/9789240053694) from WHO (July 2022) * [Guidelines on Long-Acting Injectable Cabotegravir for HIV Prevention](https://www.who.int/publications-detail-redirect/9789240054097) from WHO (July 2022) * [Consolidated Guidelines on HIV Viral Hepatitis and STI Prevention, Diagnosis, Treatment, and Care for Key Populations](https://www.who.int/publications/i/item/9789240052390) from WHO (July 2022) * [United States Food and Drug Administration Apretude Label](https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/215499s000lbl.pdf) (December 2021) * [Consolidated Guidelines on HIV Prevention, Testing, Treatment, Service Delivery and Monitoring: Recommendations for a Public Health Approach](https://www.who.int/publications/i/item/9789240031593)from WHO (July 2021) * [Summary of Product Characteristics for PrEP Ring](https://www.ema.europa.eu/documents/outside-eu-product-information/dapivirine-vaginal-ring-25-mg-product-information_en-0.pdf) from the European Medicines Agency (April 2021) * [Updated Recommendations on HIV Prevention, Infant Diagnosis, Antiretroviral Initiation and Monitoring Guidelines](https://www.who.int/publications/i/item/9789240022232) from WHO (March 2021)   This document was developed by MOSAIC (Maximizing Options to Advance Informed Choice for HIV Prevention) in close collaboration with the U.S. Agency for International Development (USAID) and The Global Fund to Fight AIDS, Tuberculosis and Malaria. The document is made possible by the generous support of the American people through the U.S. President’s Emergency Plan for AIDS Relief (PEPFAR) and USAID. The contents are the responsibility of the MOSAIC project and do not necessarily reflect the views of PEPFAR, USAID, or the U.S. Government. MOSAIC is a global cooperative agreement (Cooperative Agreement 7200AA21CA00011) led by FHI 360, with core partners Jhpiego, LVCT Health, Pangaea Zimbabwe AIDS Trust, Wits Reproductive Health and HIV Institute, and AVAC. |

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# List of Acronyms

|  |  |
| --- | --- |
| **3TC** | Lamivudine |
| **AFAB** | Assigned female at birth |
| **AHI** | Acute HIV infection |
| **AMAB** | Assigned male at birth |
| **ARV** | Antiretroviral |
| **CAB PrEP** | Injectable cabotegravir |
| **CKD-EPI** | Chronic Kidney Disease Epidemiology Collaboration |
| **ED-PrEP** | Event-driven pre-exposure prophylaxis |
| **eGFR** | Estimated glomerular filtration rate |
| **FTC** | Emtricitabine |
| **GBV** | Gender-based violence |
| **GFR** | Glomerular filtration rate |
| **HIVST** | HIV self-testing |
| **IPV** | Intimate partner violence |
| **ISR** | Injection site reactions |
| **LIVES** | Listen, Inquire, Validate, Enhance safety and Support |
| **MOSAIC** | Maximizing Options to Advance Informed Choice for HIV Prevention |
| **NNRTI** | Non-nucleoside reverse transcriptase inhibitor |
| **PEP** | Post-exposure prophylaxis |
| **PEPFAR** | U.S. President's Emergency Plan for AIDS Relief |
| **PrEP** | Pre-exposure prophylaxis |
| **PrEP Ring** | Dapivirine vaginal ring |
| **PWID** | People who inject drugs |
| **SOC** | Standard of care |
| **STI** | Sexually transmitted infections |
| **TB** | Tuberculosis |
| **TDF** | Tenofovir disoproxil fumarate |
| **USAID** | U.S. Agency for International Development |
| **VMMC** | Voluntary medical male circumcision |
| **WHO** | World Health Organization |

# Overview of Pre-exposure Prophylaxis

Pre-exposure prophylaxis (PrEP) is the preemptive use of antiretroviral (ARV) drugs by people who do not have HIV to reduce the probability of HIV acquisition. The level of effectiveness provided by PrEP is strongly correlated with effective use, meaning it is important for clients to use PrEP methods as prescribed during periods when they may be at increased likelihood of acquiring HIV. Current PrEP methods recommended by the World Health Organization (WHO) do not prevent pregnancy or sexually transmitted infections (STIs) other than HIV. WHO does not make any statements on minimum age, and PrEP can be used by adolescents, although additional support may be needed for adolescents to effectively use PrEP, and there is a minimum weight requirement for safety.

These guidelines focus on tenofovir disoproxil fumarate (TDF)-based daily or event-driven (ED) oral PrEP, the monthly dapivirine vaginal ring (hereafter referred to as the “PrEP ring” or “the ring”), and injectable cabotegravir (hereafter referred to as “CAB PrEP”) as the three PrEP methods currently recommended by WHO and approved for use in [country].

As more PrEP methods become available, informed choice is an important factor to consider in client-provider interactions and decision-making, especially because clients who can choose a preferred product may be more likely to use it effectively. Providing additional choices for PrEP and supporting clients to select their preferred methods offers the potential to increase uptake and effective use of PrEP. Beyond prevention of HIV acquisition, PrEP also has additional user-identified benefits related to emotional, social, and physical wellbeing; these value-based preferences also inform method selection and can be incorporated in shared-decision counseling making that centers a client’s desired experience while benefiting from PrEP. These guidelines include considerations for health care providers to support clients in making informed choices about their preferred PrEP methods. If possible, multiple PrEP products should be available to allow for informed choice.

Other PrEP products are being developed, tested, and reviewed. Guidance on additional approved PrEP products will be made available as appropriate. PrEP complemented by other HIV prevention strategies, such as condom and condom-compatible lubricant use; harm reduction and treatment for drug use; effective antiretroviral treatment for partners living with HIV, as needed; and provider engagement with a client to understand what support or referrals might be valuable to support effective use can further reduce the likelihood of HIV acquisition.[[1]](#footnote-2), [[2]](#footnote-3)

To prevent unwanted pregnancy *and* STIs other than HIV, it is important to use PrEP in combination with condoms and condom-compatible lubricant whenever possible. Effective contraception can prevent unintended pregnancy, but condoms are the only method that can prevent both pregnancy and most STIs with proper use.

## Overview of Oral PrEP

A systematic review and meta-analysis of TDF-based oral daily PrEP trials demonstrated that oral PrEP is effective in reducing the likelihood of HIV acquisition.[[3]](#footnote-4) The level of effectiveness did not differ by age, sex, regimen (TDF alone or TDF + emtricitabine [FTC]) or mode of potential sexual exposure (rectal, penile, or vaginal exposure) when PrEP was used as directed. There is limited evidence on oral PrEP effectiveness in parenteral exposure, though clients with potential parenteral exposures could still benefit from PrEP for sexual exposures.[[4]](#footnote-5)

Event-driven PrEP (ED-PrEP), also called on-demand PrEP or 2+1+1, is effective in reducing the likelihood of HIV acquisition during sex for people assigned male at birth (AMAB) who are not using estradiol-based exogenous hormones.[[5]](#footnote-6),[[6]](#footnote-7),[[7]](#footnote-8) More details on how ED-PrEP is used are provided below in *Additional Guidance for ED-PrEP Use.*

### Approved Drugs for Oral PrEP

In [country], either tenofovir TDF 300 mg/FTC 200 mg or TDF 300 mg/lamivudine (3TC) 300 mg can be used for oral PrEP. The current preferred drug for oral PrEP is [TDF/FTC or TDF/3TC].

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| **For consideration:** WHO recommends the use of oral PrEP containing TDF. Most national programs have adopted TDF/FTC and/or TDF/3TC for oral PrEP.[[8]](#footnote-9) Note that TDF monotherapy may not be suitable for all populations. Emtricitabine/tenofovir alafenamide (FTC/TAF) is not currently recommended for PrEP by WHO; the U.S. Food and Drug Administration has approved its use as a daily regimen to reduce the likelihood of sexual acquisition of HIV, excluding individuals who may be exposed to HIV via receptive vaginal sex. FTC/TAF has not been approved for prevention of parenteral acquisition. This document focuses only on the use of TDF/FTC and TDF/3TC for oral PrEP. Countries should consider including both TDF/FTC and TDF/3TC as approved medications for PrEP because having the option of using either set of approved drugs may be beneficial where first-line treatment for people living with HIV is transitioning to tenofovir, lamivudine, and dolutegravir, potentially freeing up TDF/3TC, or if supply chain challenges affect the availability of one of the recommended drugs. |

### Oral PrEP Effectiveness

When used as directed, daily oral PrEP can reduce the likelihood of HIV acquisition through sexual transmission by more than 90%.[[9]](#footnote-10),[[10]](#footnote-11),[[11]](#footnote-12) Among people AMAB who are not using estradiol-based exogenous hormones, ED-PrEP regimens are similarly effective at reducing the likelihood of HIV acquisition through sexual transmission.[[12]](#footnote-13),[[13]](#footnote-14)

### Potential Side Effects of Oral PrEP

Approximately 10 percent of people may experience side effects of oral PrEP use, which are mostly mild, including:

* Gastrointestinal symptoms (diarrhea and nausea, decreased appetite, abdominal cramping, and flatulence)
* Dizziness
* Headaches

Most of these side effects resolve within one month of continued use. Decreased kidney function, though rare, is another potential side effect.

Individuals who are counseled on potential side effects are more likely to continue oral PrEP and use it effectively. For information on less common side effects, review the product label.

### Oral PrEP and Other Drug Interactions

ARV drugs used for oral PrEP have no known interactions with contraceptive hormones and do not affect the levels of gender-affirming hormones used by transgender individuals. There is some indication that the use of estradiol-based exogenous hormones may reduce oral PrEP drug levels in people AMAB, which is why daily oral PrEP is recommended for these individuals, including trans women using estradiol-based exogenous hormones, but ED-PrEP is not. There are no known interactions between oral PrEP medications and alcohol or recreational drugs. However, if a client or potential client thinks that their use of alcohol or other substances is interfering or may interfere with them taking oral PrEP as directed, their PrEP provider should provide support and referrals and, where needed, offer additional prevention options, including the use of condoms and condom-compatible lubricant and linkage to harm reduction services when they are available.

For information on concurrent use of oral PrEP with other PrEP products, see the *Switching Between PrEP Methods and Simultaneous Use* section below.

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| **For consideration:** Taking multiple nephrotoxic agents (such as nonsteroidal anti-inflammatory drugs) with TDF has been shown to lead to nephrotoxicity and should be avoided when possible. |

### Contraindications for Oral PrEP Use

**Box 1. Signs of AHI**

* Fever
* Swollen lymph glands
* Skin rash
* Headache
* Sore throat
* Aches and pains
* Mouth sores

Oral PrEP should **NOT** be provided to people with:

* An HIV-positive test result using the national HIV testing algorithm
* Potential exposure to HIV in the past 72 hours (these clients should be offered post-exposure prophylaxis [PEP])
* Signs of acute HIV infection (AHI) (Box 1) *AND potential exposure to HIV within the past 14 days*
* Unwillingness or inability to commit to effectively using oral PrEP
* Allergy or hypersensitivity to an active substance or other substances listed in the product information sheet
* Known kidney function impairment, indicated by an estimated glomerular filtration rate (eGFR) of under 60 mL/min per 1.73m2 or a creatinine clearance of less than 60 mL/min

### Oral PrEP Use

Oral PrEP may be offered as a daily regimen to prevent HIV acquisition during all potential exposures for all populations. For people AMAB who are not using estradiol-based exogenous hormones, oral PrEP may be offered as an ED regimen to prevent HIV acquisition during sex. ED-PrEP may be appropriate for people AMAB who are not using estradiol-based exogenous hormones and who find it more convenient, have infrequent sex (for example, fewer than two times per week on average), and/or are able to plan for sex at least two hours in advance or can delay sex for at least two hours. People AMAB who are not using estradiol-based exogenous hormones should have an option to decide which regimen works for them and be supported to switch between daily and ED-PrEP to effectively prevent HIV.

For everyone else, including those using oral PrEP to prevent HIV from nonsexual exposures, only a daily regimen may be offered. ED-PrEP is not recommended for people AMAB who are using estradiol-based exogenous hormones, people AFAB, people AFAB taking gender affirming hormone therapy (GAHT), or PWID. Due to how the drug concentrates in the vagina, people AFAB or people AFAB taking GAHT, it would take at least seven days for the drug to reach effective levels for prevention. Details on starting and stopping oral PrEP for different populations are provided in Table 1. Clients starting oral PrEP should be counseled on using another HIV prevention strategy during the time it takes for the method to be fully effective. Note that the procedures for stopping oral PrEP are the same whether a client is stopping oral PrEP for a specific amount of time or intends to discontinue oral PrEP use indefinitely. Ideally, clients who are discontinuing oral PrEP use indefinitely will advise their provider(s) and receive support to use other HIV prevention strategies if still needed*.* For these clients in particular, regular HIV testing should be encouraged.

**Table 1. Starting, Using, and Stopping Oral PrEP Safely**

|  |  |  |  |  |
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| **Population (s)** | **Often includes**[[14]](#footnote-15) | **Starting Oral PrEP (daily or ED)** | **Using Oral PrEP** | **Stopping Oral PrEP** |
| People assigned female at birth who are using oral PrEP to prevent HIV acquisition during sex | cisgender women  transgender men  nonbinary people assigned female at birth | **Daily**: Take a single dose daily for seven days before potential exposure.  *ED-PrEP not recommended for this population* | Take one dose per day. | After a single dose is taken daily for seven days after the last potential exposure, PrEP can be stopped. |
| People assigned male at birth who are using estradiol-based exogenous hormones who are using oral PrEP to prevent HIV acquisition during sex | transgender women who are using estradiol-based exogenous hormones  nonbinary people assigned male at birth who are using estradiol-based exogenous hormones |  |  |  |
| People assigned male at birth who are not using estradiol-based exogenous hormones and are using oral PrEP to prevent HIV acquisition during sex | cisgender men  transgender women who are not using estradiol-based exogenous hormones  nonbinary people assigned male at birth who are not using estradiol-based exogenous hormones | **Daily:** Take a single dose daily for seven days before potential exposure.  **ED**: Take a double dose two to 24 hours before potential sexual exposure. Ideally, this loading dose should be taken closer to 24 hours before potential exposure. | Take one dose per day. | **Daily:** After a single dose is taken daily for two days after the last potential exposure, PrEP can be stopped.  **ED**: After a single dose is taken daily for two days after the last potential exposure, PrEP can be stopped. |
| People using oral PrEP to prevent HIV acquisition from nonsexual exposures | anyone who shares injection-related materials[[15]](#footnote-16) | **Daily**: Take a single dose daily for seven days before potential exposure.  *ED PrEP not recommended for this population* | Take one dose per day. | After a single dose is taken daily for seven days after the last potential exposure, PrEP can be stopped. |
|  |  |  |  |  |

#### Additional Guidance for ED-PrEP Use

Clients AMAB who are not using estradiol-based exogenous hormones may benefit from providers walking through some scenarios to support their effective use of ED-PrEP. See *Figures 1–6* below*.*

**Figure 1. Example of ED-PrEP use for sex one time or in one day**

Timeline

Description automatically generated

Figure 2. Example of ED-PrEP use for sex on multiple consecutive days

Timeline

Description automatically generated with medium confidence

Figure 3. Example of ED-PrEP use for sex on multiple non-consecutive days

Timeline

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Figure 4. Example of ED-PrEP use when sex does not occur

A picture containing timeline

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Clients AMAB who are not using estradiol-based exogenous hormones and using oral PrEP to prevent HIV acquisition during sex, may switch between ED-PrEP and daily oral PrEP as their HIV prevention needs evolve. Clients may decide to switch back and forth between ED-PrEP and daily oral PrEP due to changes in relationship status or sex partner(s), behavioral changes, moving to a new location, any situation affecting the frequency and predictability of sex, or when a client’s preferred regimen changes.

For clients who are taking ED-PrEP, transitioning to daily oral PrEP may be appropriate if sex becomes more frequent and/or less predictable. In addition, some clients may prefer daily oral PrEP for other reasons. There is no limit on the number of times a client can switch between ED-PrEP and daily oral PrEP. To transition from ED-PrEP to daily oral PrEP, a client should continue daily dosing indefinitely after the last exposure. Daily dosing would continue until sex becomes less frequent and more predictable again, or for as long as the client prefers the daily dosing option. See *Figure 5* below*.*

Figure 5. Example of transitioning from ED-PrEP to daily PrEP

Timeline

Description automatically generated

For clients AMAB who are not using estradiol-based exogenous hormones and using oral PrEP to prevent HIV acquisition during sex who are taking daily oral PrEP, transitioning to ED-PrEP may be appropriate if sex becomes less frequent and more predictable. To transition from daily oral PrEP to ED-PrEP, a client should stop daily dosing two days after the last potential exposure, and then start following the ED-PrEP regimen until sex becomes more frequent and/or less predictable. See *Figure 6* below*.*

Figure 6. Example of transitioning from daily PrEP to ED-PrEP

A picture containing diagram

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## Overview of the PrEP Ring

The PrEP ring is a long-acting HIV prevention method that has been studied for HIV prevention among people assigned female sex at birth (AFAB) and is recommended by WHO for use by cisgender women.[[16]](#footnote-17) Currently, the ring is recommended only for prevention of HIV acquisition through receptive vaginal sex. It is inserted into the vagina and should remain in place for 28 days. The ring is made of a flexible silicone material containing 25 mg of dapivirine, an ARV drug. Dapivirine belongs to a class of ARVs called non-nucleoside reverse transcriptase inhibitors (NNRTIs) that reduce the ability of HIV to replicate itself inside a healthy cell. The ring delivers the drug directly to the site of potential infection over the course of one month, with low absorption elsewhere in the body, lowering the likelihood of systemic side effects. Each month, clients can insert, remove, and replace the ring themselves or with the assistance of a health care provider if desired.

The number of pregnancies among participants actively using the ring during the clinical trials was small; however, the data collected to date shows the ring is safe during pregnancy and breastfeeding, with adverse pregnancy outcomes and complications proving uncommon and dapivirine concentrations detected at extremely low levels in infant plasma samples.[[17]](#footnote-18),[[18]](#footnote-19), [[19]](#footnote-20) In a small study of PrEP ring use among lactating people, ring use was associated with low concentrations of detectable dapivirine in breastmilk and plasma and was shown to have a favorable safety profile.[[20]](#footnote-21) Results from a clinical trial of ring use while breastfeeding demonstrated a favorable safety profile of the PrEP ring in both breastfeeding people and infants.[[21]](#footnote-22) For more information on ring use during pregnancy and breastfeeding, see *Management of Clients in Specific Situations* below*.*

### Formulation of the PrEP Ring

The PrEP ring is a flexible white silicone ring for vaginal insertion. The ring, which is available in only one size, contains approximately 25 mg of the NNRTI dapivirine.

### PrEP Ring Effectiveness

The ring was clinically shown to reduce the likelihood of HIV-1 acquisition through vaginal sex in two randomized controlled trials: by 35% in IPM-027/The Ring Study and 27% in MTN-020/ASPIRE. The subgroup analysis by age of The Ring Study and ASPIRE data did not show efficacy among women 18–21 years old, who were also shown to have low adherence to the ring during the trials. These trials reported no notable differences in reproductive health outcomes, including STIs and adverse events related to pregnancy, fetal outcomes, and/or infant outcomes, between the treatment and placebo arms.

Two subsequent open-label extension studies — DREAM and HOPE — found increased ring adherence compared to adherence in the clinical trials. In DREAM, 95% of returned rings showed some use compared to 83% in The Ring Study, while in HOPE, 90% of returned rings showed use compared to 77% in ASPIRE.[[22]](#footnote-23) Multiple efficacy analyses among participants who used the ring consistently suggest that the PrEP ring can reduce the likelihood of HIV acquisition during receptive vaginal intercourse by 50% or more with consistent use throughout the month.[[23]](#footnote-24),[[24]](#footnote-25) Further studies exploring the safety and acceptability of the ring among adolescents and young people AFAB ages 15–21 have demonstrated that the ring is acceptable to younger individuals, has a similar favorable safety profile among younger and older individuals, and can be used effectively by younger individuals with proper adherence support.[[25]](#footnote-26),[[26]](#footnote-27)

### Potential Side Effects of the PrEP Ring

Possible side effects of the ring are typically mild and include:

* Urinary tract infections (UTIs)
* Vaginal discharge
* Vulvar itching
* Pelvic and lower abdominal pain

Clients using the ring should be counseled on possible side effects and advised to contact their health care provider if they experience any urinary or reproductive tract changes, because these could be a sign of an STI or UTI needing treatment.

For information on less common side effects, review the product label.

### PrEP Ring and Other Drug Interactions

There are currently no data on concurrent use of vaginally administered antimicrobial products for vulvovaginal infections and the PrEP ring; therefore, concomitant use is not recommended.

Evaluations of co-administered use of miconazole and the ring have not been fully resolved, and clients should be advised to use additional preventative measure for HIV when co-treated with vaginal miconazole.

Co-administration of clotrimazole as a water-based vaginal cream with the ring was well-tolerated; however, given methodological issues that limit the reliability of the pharmacokinetic results of both clotrimazole and dapivirine, concurrent use should be undertaken with caution.

Because there are no data on concomitant use of the ring and metronidazole or clindamycin, and no current data on concomitant use of the ring and contraceptive rings or diaphragms, thus concurrent use is not recommended.

There are no known interactions between dapivirine and contraceptive hormones, hormones used for gender-affirming hormone therapy, alcohol, or recreational drugs. However, if a client or potential client thinks their use of alcohol or other substances is interfering or may interfere with effective use of the ring, the provider should engage the client to understand what support or referrals might be valuable to support effective use while also discussing additional prevention options, including other PrEP methods and the use of condoms and condom-compatible lubricant.

For information on concurrent use of the ring with other PrEP products, see the *Switching Between PrEP Methods and Simultaneous Use* section below.

### Contraindications for PrEP Ring Use

The ring should not be provided to people with:

* An HIV-positive test result according to the national HIV testing algorithm
* Potential exposure to HIV in the past 72 hours (these clients should be offered PEP)
* Unwillingness or inability to commit to effectively using the ring
* Allergy or hypersensitivity to active substance or other substances listed in the product information sheet

### PrEP Ring Use

The ring may be offered as an option for people AFAB who wish to prevent HIV acquisition through receptive vaginal sex and are unable or do not want to take a different PrEP method, or when different PrEP methods are not available. The ring must be inserted correctly into the vagina and worn for 28-days without removal. The ring must be in place for at least 24 hours before it is maximally effective. Clients starting the ring should be counseled on using another HIV prevention strategy during the time it takes for the method to be fully effective. If a client wishes to discontinue use of the ring, they can remove it. The ring can be reinserted after removal until the 28-day period has expired; however, levels of dapivirine in the vagina drop quickly after ring removal, and therefore removal is not recommended during the 28-day period. Because of the quick drop in levels of dapivirine in the vagina after ring removal, the need for other HIV prevention measures should be reinforced after removal if potential exposure to HIV continues. If removed and reinserted, the ring must be in place for at least 24 hours to reach maximum protection. It is not known how long the ring must remain in place after a potential exposure to be maximally effective. Ideally, clients who are discontinuing PrEP use should be encouraged to discuss discontinuation and be supported by providers to use other HIV prevention practices, if needed.

Due to the localized release of dapivirine and the resulting low possibility of drug resistance, there may be benefit to clients if they are offered a choice to start or continue to use the ring even if suspected of having AHI.

The ring does not interfere with sexual intercourse and should be worn during sex. It can be used with condoms (internal and external) and condom-compatible lubricant. Although it is unlikely, it is possible that a client’s partner(s) may feel the ring during sex. If this happens, the client may need to confirm ring placement, because it may mean that the ring should be pushed further into the vagina. The ring does not cause harm to any partner, but it does not prevent a client’s partner(s) from acquiring HIV.

The ring does not cover the cervix and does not interrupt the flow of menstrual fluids. There are no safety concerns related to the use of tampons, menstrual pads, or other menstrual products while using the ring. If using a tampon, the client should be careful not to accidentally remove the ring when removing the tampon.

Although it is unlikely, it is possible that the ring may fall out. If this happens in a clean location, the ring should be

rinsed in clean water and reinserted. If the ring falls out in a dirty location, the ring should be replaced with a new ring.

#### Inserting the PrEP Ring

Clients may need initial guidance and support to learn how to use the ring. Once they feel confident in doing so, they can continue to use the ring on their own. Some clients are comfortable using the ring on their own with minimal support from their first use. However, for clients who prefer support, a health care provider can help insert the ring or confirm placement. The ring is inserted by hand; there is no need to use a speculum or other tools to insert it. Clear visual instructions should be offered with the ring. Ring insertion steps for clients are listed in Box 2.

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| **Box 2. Ring insertion steps for clients**   1. Get into a position that is comfortable for inserting the ring, such as squatting, lifting one leg, or lying down. If a health care provider is assisting you, you should be in a reclining position. 2. With clean hands, squeeze the ring between the thumb and forefinger, pressing both sides of the ring together so that the ring forms a “figure 8” shape. 3. Use the other hand to open the folds of skin around the vagina. 4. Place the tip of the ring into the vaginal opening and use your fingers to push the folded ring gently up into the vagina. 5. Push the ring as far toward the lower back as possible. If the ring feels uncomfortable, it is probably not inserted far enough into the vagina. Use a finger to push it as far up into the vagina as is comfortable.   \**Ring insertion should be painless. If you have any bleeding or discomfort upon insertion, contact your health care provider.*  A picture containing clipart  Description automatically generatedShape, venn diagram, circle  Description automatically generatedShape, circle  Description automatically generatedA picture containing text, clipart  Description automatically generated  **1 2 3 4** |

#### Removing the PrEP Ring

Clients can remove the ring without the help of a health care provider. However, for clients who prefer support, a health care provider can help remove the ring. The ring is removed by hand; there is no need to use a speculum or other tools to remove it. If a client is being assisted by a health care provider, they should be in a reclining position during removal. Ring removal steps for clients are listed in Box 3.

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| **Box 3. Ring removal steps for clients**   1. Get into a position that is comfortable for removing the ring, such as squatting, lifting one leg, or lying down. 2. With clean hands, insert one finger into the vagina and hook it around the edge of the ring. 3. Gently pull the ring out of the vagina.   \**Ring removal should be painless. If you have any bleeding or discomfort upon removal, contact your health care provider*.  Shape, circle  Description automatically generatedShape, venn diagram, circle  Description automatically generatedA picture containing text, clipart  Description automatically generated  **1 2 3** |

## Overview of CAB PrEP

CAB PrEP is a long-acting PrEP method containing 600 mg of cabotegravir extended-release injectable suspension. It is an intramuscular injection injected into the gluteal muscle. CAB PrEP should be injected only into the gluteal muscle; the pharmacokinetics and efficacy of CAB PrEP when injected in other sites has not been studied. The first two injections are one month apart, followed by injections every two months. Cabotegravir belongs to a class of ARVs called integrase strand transfer inhibitors that reduce the ability of HIV to replicate itself inside a healthy cell. CAB PrEP delivers cabotegravir systemically, so the drug is absorbed throughout the body.

Evidence from two randomized controlled trials show CAB PrEP is highly effective at preventing sexual HIV acquisition and may be offered as an additional prevention choice as part of combination prevention approaches. It has not yet been studied for HIV prevention for parenteral exposure or for those who may be exposed during vertical transmission during pregnancy, childbirth, or breastfeeding. CAB PrEP may be suitable for clients seeking less frequent dosing or increased privacy around PrEP use.

### Formulation of CAB PrEP

CAB PrEP is an injection of cabotegravir extended-release injectable suspension (3 mL) at a dose of 600 mg.

### CAB PrEP Effectiveness

In clinical trials, CAB PrEP has been shown to be highly effective in cisgender and transgender women and cisgender men. In recent randomized controlled trials, CAB PrEP was shown to be more effective than oral PrEP, though it is likely due largely to better adherence to CAB PrEP. If a client is using CAB PrEP for HIV prevention, it is important they keep up with regular appointments for injections to make sure that there is enough cabotegravir in their body to continue to prevent HIV. When a client misses a scheduled injection or discontinues CAB PrEP, concentrations of the medication in the body slowly decline. During this pharmacokinetic “tail,” CAB PrEP becomes gradually less protective against HIV acquisition, and seroconversion may occur if the client continues to be exposed to HIV. For more information on the pharmacokinetic tail, refer to the below *Stopping CAB PrEP* section.

### Potential Side Effects of CAB PrEP

The most common side effects of CAB PrEP include:

* Headache
* Nausea
* Diarrhea
* Tiredness
* Injection site reactions (ISRs)

These side effects are usually mild or moderate. Mild or moderate ISRs are more common than other potential side effects, becoming less frequent over time as clients get used to the injection. ISRs can include redness, pain, and swelling at the injection site.

For information on less common side effects, review the product label.

### CAB PrEP and Other Drug Interactions

Some anticonvulsants (carbamazepine, oxcarbazepine, phenobarbital, and phenytoin), and some antimycobacterial medications (rifampin, sometimes named rifampicin, and rifapentine) may interact with CAB PrEP and reduce its efficacy by significantly decreasing concentrations of cabotegravir in blood plasma. These drugs should not be co-administered with CAB PrEP, and clients using them may need to select a different PrEP method or HIV prevention strategy. After a client completes rifampin or rifapentine, they can be considered for CAB PrEP after two weeks.

There are no known interactions between CAB PrEP and contraceptive hormones or other forms of contraception. Available evidence suggests that use of gender-affirming hormones by transgender women does not affect drug levels of cabotegravir.[[27]](#footnote-28)

There are no known interactions between CAB PrEP and recreational drugs or alcohol, but alcohol and drug use could affect the ability to attend necessary health appointments, potentially resulting in missed injections. If a client or potential client thinks that their use of alcohol or other substances is interfering or may interfere with effective use of CAB PrEP, the provider should engage the client to understand what support or referrals might be valuable to support effective use while also discussing additional prevention options, including other PrEP methods and the use of condoms and condom-compatible lubricant.

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| **For consideration:** Clients using either methadone or rifabutin may still be able to use CAB PrEP, but additional cautions may be warranted. Clients using methadone could require medication dose adjustments to maintain the effectiveness of the medication while they are using CAB PrEP, while clients using rifabutin may require dose adjustments of CAB PrEP, specifically more frequent injections. Clients using high-dose aspirin in the past week, such as non-steroidal anti-inflammatory drugs for pain or anticoagulants or other antiplatelets, may have a higher likelihood of bruising or bleeding at the injection site and should be made aware and counseled on mitigation strategies, if relevant.  If a client is using CAB PrEP and is diagnosed with tuberculosis (TB), they will need to temporarily discontinue CAB PrEP and receive treatment with a standard rifampin-based regimen. In the interim, the client may use another PrEP method or HIV prevention strategy. If the client completes TB therapy and wishes to continue with CAB PrEP, they should be assessed for CAB PrEP use and can restart CAB PrEP with initiation injection 1. CAB PrEP can be started two weeks after a client completes TB therapy.  Clients who receive TB preventative treatment with once-weekly rifapentine-isoniazid for 12 weeks (also known as 3HP) should temporarily discontinue CAB PrEP for the duration of their rifapentine use. Clients can restart CAB PrEP two weeks after completing 3HP. |

For information on concurrent use of CAB PrEP with other PrEP products, see the *Switching Between PrEP Methods and Simultaneous Use* section below.

### Contraindications for CAB PrEP Use

CAB PrEP should not be provided to people with:

* An HIV-positive test result according to the national HIV testing algorithm
* Potential exposure to HIV in the past 72 hours (these clients should be offered PEP)
* Signs of AHI (Box 1) *AND potential exposure within the past 14 days*
* Some co-administered anticonvulsants or antimycobacterials (see the *CAB PrEP and Other Drug Interactions* section above)
* Unwillingness or inability to commit to effectively using CAB PrEP
* Allergic or hypersensitivity reaction(s) with previous use of CAB or other integrase inhibitor medications

### CAB PrEP Use

CAB PrEP is a PrEP method given as a 600mg, 3ml injection into the gluteal muscle in the buttocks. The first two injections are one month apart, followed by injections every two months. The current evidence shows it takes about one week for drug concentrations to reach levels at which CAB PrEP is expected to be maximally effective after initiation injection 1, so clients should be counseled on using another HIV prevention strategy during the first week. The medication will stay in the body after a client stops using CAB PrEP because of its long half-life, but at levels that may not prevent HIV.

#### Starting CAB PrEP

CAB PrEP injections can be given by providers in nationally approved health care cadres. The injection requires a 23-gauge, 1.5-inch (3.8-cm) injection needle, though a client’s build should be considered to select an appropriate needle length. The provider can position the client on their side, in a prone position, or in another position comfortable for the client, and should clean the injection site on the gluteal muscle on the side or back of the buttocks. It is best to inject the medication as soon as possible once the injection site has been cleaned, though the medication can remain in the syringe for up to two hours. If that time limit is exceeded, discard the medicine, syringe, and needle; do not attempt to keep the medicine fresh by refrigerating it. After the injection, the provider can use dry gauze to apply gentle pressure to the puncture site and, if needed or requested by the client, apply an adhesive bandage.

After clients receive initiation injection 1 at initiation visit 1, providers should schedule initiation visit 2 for initiation injection 2 one month from the date of the first injection. After initiation injections 1 and 2, visits for follow-up injections should be scheduled every two months.

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| **For consideration:** The [United States Food and Drug Administration Apretude Label](https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/215499s000lbl.pdf) includes recommendations for injection visit scheduling. Whenscheduling initiation injections 1 and 2, providers can consider the date of initiation injection 1 as Day 0. Initiation injection 2 should be scheduled four weeks later, on approximate Day 28. There is a +/- 7-day window for receiving initiation injection 2. Once initiation injections 1 and 2 have been completed, follow-up visits should be scheduled beginning two months after initiation injection 2 and every two months after each follow-up injection. There is a +/- 7-day window for receiving follow-up injections.  Ideally, a client with ongoing exposures to HIV who is interested in CAB PrEP would have the following injection schedule (free of delays or discontinuations):   * Initiation injection 1 * Initiation injection 2: one month after initiation injection 1 +/- 7 days * Follow-up injections: two months after initiation injection 2 +/- 7 days, with continuing follow-up injections every two months, continuing for as long as the client wants to remain on CAB PrEP and has potential exposures to HIV |

#### Stopping CAB PrEP

If a client decides to stop using CAB PrEP, they may stop receiving injections. The amount of cabotegravir in the blood remains at effective levels for at least eight weeks after the final injection.[[28]](#footnote-29) The time after the last CAB PrEP injection when cabotegravir remains in the body but at levels that may not prevent HIV is known as the “tail period” see *Figure 7*).

**Figure 7. CAB PrEP “tail period”**

Chart

Description automatically generated

The “tail period” can last for up to a year, but this time frame varies for people based on sex assigned at birth.[[29]](#footnote-30) Data on HIV acquisition during the tail period are limited. For those who do acquire HIV during this time, delayed diagnosis of HIV may be possible and could result in HIV drug resistance, meaning that medicines used to treat HIV may be less effective or not work at all. As with all PrEP methods, if a client discontinues CAB PrEP, they should use another PrEP method or HIV prevention strategy during the tail period if exposure to HIV is possible.

If a client has a potential exposure to HIV during the tail period while not using an HIV prevention strategy, they should speak to a health care provider as soon as possible because PEP may be appropriate and ideally should be started as soon as possible within 72 hours of potential exposure.

#### Missing an Injection

Adherence to the injection schedule is important to effective use of CAB PrEP. A client who misses an injection should contact their health care provider immediately to get advice about how to continue using CAB PrEP or to talk about switching to a different HIV prevention strategy, which may include using another PrEP method.

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| **For consideration**: At the time of writing,WHO does not have guidance on missing injections and does not make recommendations about when a client taking PrEP should be considered discontinued or what procedures are required for restarting someone on PrEP once they have discontinued. If the client does not want to continue CAB PrEP, providers should support clients by counseling them on alternative PrEP methods or another HIV prevention strategy if the client is still potentially exposed to HIV while choosing to stop CAB PrEP use. The following are potential scenarios adapted from the [United States Food and Drug Administration Apretude Label](https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/215499s000lbl.pdf) for those clients who miss injection visits, based on the length of time between injections:  **Injection Dosing Recommendations after Missed Injections** | | |
| *Missed injection type* | *Time since last injection* | Recommended action for provider |
| **Initiation injection 2** | ≤ 2 months since initiation injection 1 | Proceed with initiation injection 2 and schedule the follow-up injection for 2 months later as a follow-up visit |
|  | > 2 months since initiation injection 1 | Assess the client for contraindications for CAB PrEP using the initiation procedure and, if contraindications are absent, re-administer initiation injection 1 that day and schedule initiation visit 2 in one month.  Follow-up visits should be scheduled every 2 months thereafter. |
| **Follow-up injection** | ≤ 3 months since last injection | Proceed with administering follow-up injection that day and schedule the subsequent follow-up injection for 2 months later as a follow-up visit. |
|  | > 3 months since last injection | Rescreen for potential restart and, if contraindications are absent, re-administer initiation injection 1 that day and schedule initiation injection 2 in 1 month.  Follow-up visits should be scheduled every 2 months thereafter. |

#### Restarting CAB PrEP

Clients who may have been on CAB PrEP at some point before stopping and wish to receive it again should contact their provider to discuss strategies for restarting CAB PrEP.

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| **For consideration:** For clients who have stopped CAB PrEP, the clinical management of restarting them may vary based on how much time has passed since a client’s last injection. Providers can refer to the injection dosing recommendations after missed injections table outlined in the green box above. |

## Switching Between PrEP Methods and Simultaneous Use

Clients may choose to switch between PrEP methods. Possible patterns of use of different PrEP methods are many; the ideal use pattern during a transition between methods is not currently known and will require careful support and assessment.

Safety data on using more than one PrEP method at a time is limited and does not exist for some PrEP methods. Although use of multiple methods is not likely to be less well-tolerated than use of each individually, more data are needed to confirm the safety and efficacy of simultaneous use.

Some clients may decide to use multiple PrEP methods at the same time. However, no evidence indicates that using them together will result in any advantage. Whatever the choice, using the chosen PrEP method in a way that is effectively prophylactic (as frequently as directed and for as long as is needed to cover periods of potential exposure) is important to optimize effectiveness of the method.

For instructions on switching between daily oral PrEP and ED-PrEP, see *Oral PrEP Use* above.

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| **For consideration:** The process for switching between PrEP methods will depend on the methods being used. When advising clients on switching between PrEP methods, providers should use their best clinical judgement, considering the time to effectiveness/waning effectiveness of each PrEP method after discontinuation, coverage of previous and future potential exposures to HIV, and client preferences. |

# PrEP Initiation Visit

For most clients, PrEP can be initiated the same day. However, in some scenarios, as outlined below, deferred PrEP initiation is recommended. Clients must meet four criteria to begin PrEP use. They must be:

* *HIV negative*
* *Not indicated for PEP*
* *Assessed for AHI[[30]](#footnote-31)*
* *Requesting PrEP or indicated for PrEP use*
* *Free from contraindications for use of their chosen PrEP method*

The four essential components of PrEP initiation visits are: 1) HIV testing and counseling, 2) assessments, 3) PrEP counseling, and 4) PrEP prescription. For clients choosing the PrEP ring or oral PrEP, there will be one initiation visit. For clients choosing CAB PrEP, there will be two initiation visits scheduled one month apart for initiation injection 1 and initiation injection 2, respectively.

## Component 1: HIV Testing and Counseling

HIV testing and counseling should be conducted per national guidelines. Same-day HIV testing is strongly suggested. If the test result is negative, a client can continue through the initiation visit and may be able to start PrEP. If their result is positive, the client must not be initiated on PrEP but should receive further testing per the national algorithm and, if the result is confirmed positive, the client should be immediately initiated on or referred for ART. If the test result is inconclusive, defer PrEP and follow the national algorithm/guidelines until a definitive HIV test result has been obtained. If available and in line with the national testing algorithm, HIV self-testing can complement existing HIV testing strategies for starting, restarting, or continuing oral PrEP and the ring.

As part of HIV testing and counseling, clients should be counseled on combination HIV prevention and provided with condoms and condom-compatible lubricant.

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| **For consideration:** In some settings, it may be difficult to offer a client PrEP on the same day when they test negative for HIV. Some programs accept the results of tests conducted within the last three to seven days if a client has had no potential exposure to HIV since their test. |

## Component 2: Assessments

The purpose of PrEP assessment is to make sure a client: 1) is prescribed PEP, instead of PrEP, if they have had potential exposure to HIV within the last 72 hours; 2) has been assessed for AHI and if AHI possible, use of PrEP deferred pending re-testing; 3) is indicated for PrEP use and/or requesting PrEP; and 4) is free of contraindications for use of their chosen PrEP method.[[31]](#footnote-32) Diagram 1 outlines the algorithm for ruling out HIV through HIV testing, and PEP and AHI assessment. Once HIV exposure or potential acquisition has been ruled out through these three steps, clinicians may assess for clinical contraindications to ensure the client is eligible for their chosen PrEP method.

**Assess for PEP Indication**

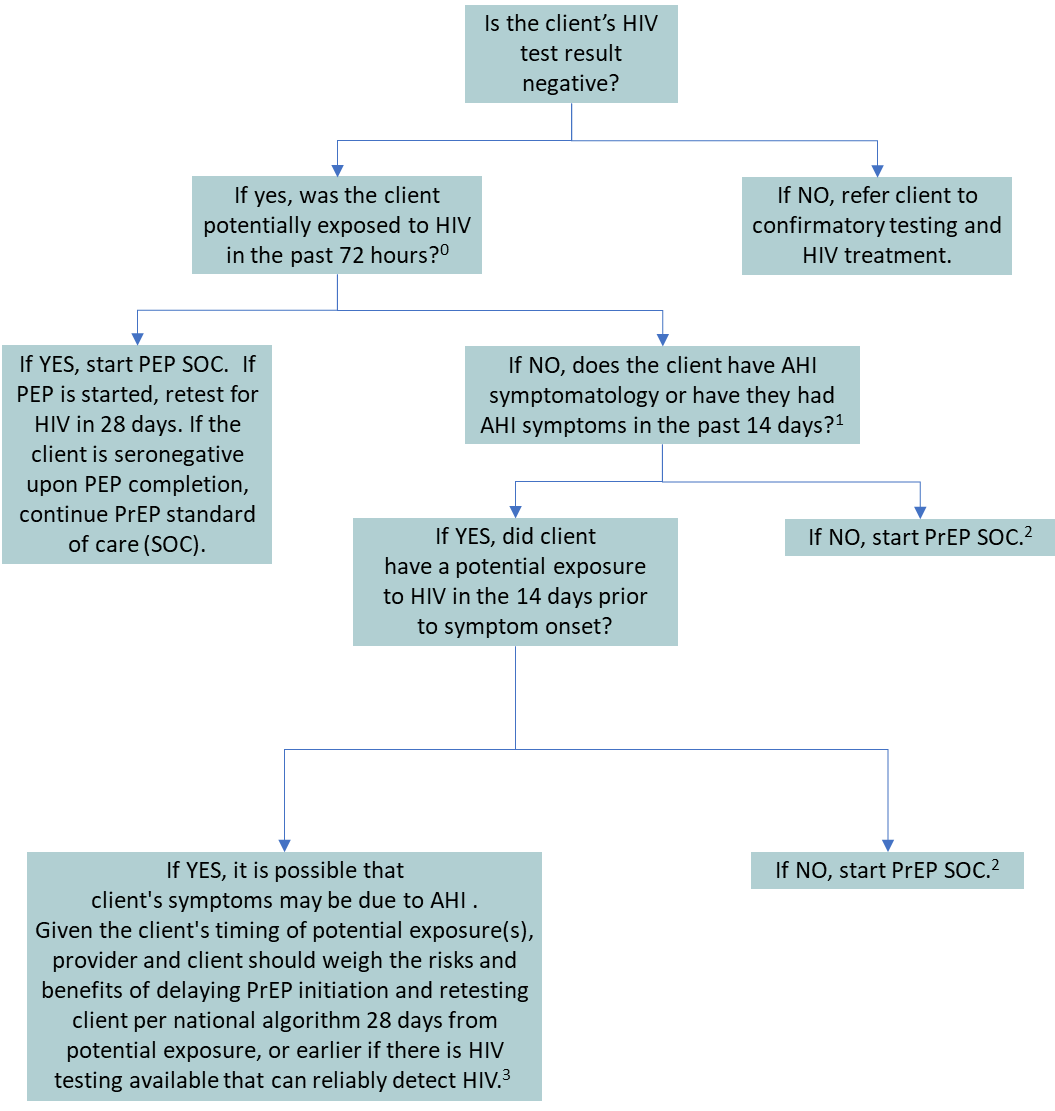
**Clients exposed to HIV within the past 72 hours:** If a client reports an exposure to HIV within the past 72 hours, screen for PEP indication instead of PrEP and provide PEP according to national guidelines. Educate clients on the differences among PEP, PrEP, and ART and offer HIV exposure reduction counseling. After 28 days of PEP, a client may be transitioned from PEP to PrEP without a gap after receiving an HIV-negative test result and if they meet other criteria for PrEP use.

**Assess for Acute HIV Infection**

**Clients suspected of having AHI:** If a client has or has had signs and symptoms of acute HIV infection (see *Box 1* above) AND possible exposure to HIV in the 14 days prior to symptom onset, it is possible that the client's symptoms may be due to AHI, especially if a prevention method was not being used or not being used effectively. Given the client's timing of potential exposure(s), provider and client should weigh the risks and benefits of delaying PrEP initiation and retesting client in 28 days per national algorithm, or earlier if there is HIV testing available that can reliably detect HIV.31 Clients should be provided with HIV exposure reduction counseling, as well as STI screening, diagnosis, and management, if available. If the client has an HIV-negative result after retesting and the client meets other criteria for PrEP use, the client can start PrEP.

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| **For consideration:** There are job aids currently available to support providers in assessing for PEP and AHI to rule out prior HIV acquisition in clients interested in starting or continuing PrEP, with separate job aids for oral PrEP, PrEP ring, and CAB PrEP. Found [here](https://www.prepwatch.org/resources/global-acute-hiv-infection-algorithm-job-aids-for-providers/), these resources help to formalize clinical assessments to complement HIV testing by identifying clients with PEP indication and suspected AHI, and offering clinical management suggestions for new and returning clients adherent and non-adherent to PrEP, categorized by PrEP method. |

**Diagram 1. PrEP Initiation – HIV Exposure and AHI Assessment**

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**0** An answer of “NO” to this question means no potential past exposure to HIV at all or potential HIV exposure that was 73+ hours ago.

1 Two-thirds of people will have symptoms of AHI within 2–4 weeks of HIV acquisition ([Letizia et al. 2022](https://journals.lww.com/md-journal/Fulltext/2022/02040/Clinical_signs_and_symptoms_associated_with_acute.14.aspx)). Signs/symptoms mimicking acute HIV infection (sore throat, fever, sweats, swollen glands, mouth ulcers, headache, rash, and muscle aches) are commonly due to illnesses other than HIV; providers need to use discretion in determining whether the symptomatology is consistent with HIV or may be explained by an alternative cause.

2 In order to make informed choice prior to starting PrEP, the client should be aware that available HIV testing may not have been able to detect HIV if the client acquired HIV fewer than 28 days ago, and that there is a possibility the HIV test may not have detected HIV if acquired beyond 28 days ago. The client should also be aware that while they do not have symptoms of AHI, they could be pre-symptomatic or be part of the one-third of individuals who do not develop symptoms of AHI within 2-4 weeks of acquiring HIV.

3 Possible AHI is not a contraindication for PrEP ring use. If AHI is suspected, strongly encourage the person to return in 4-6 weeks for retesting and not wait or 3 months.

**Assess Client’s Request for PrEP or if Client May Benefit from PrEP**

* **Client Request:** Clients who request PrEP should be counseled on and offered PrEP if HIV has been ruled out to the extent possible by HIV testing and assessments for PEP and AHI, and they are free from contraindications for the use of their chosen PrEP method. Clients should not have to qualify or explain their request in detail. *Requesting PrEP has been shown to be an indicator of client need for PrEP.*
* **Clients Who May Benefit from PrEP:** When a client is not asking for PrEP, the provider may need to initiate a conversation about what behaviors may indicate that a client may benefit from PrEP. Any tool used in PrEP initiation and continuation counseling should support clients to understand their likelihood of exposure to HIV; prompt discussion of available PrEP methods or other HIV prevention strategies; and support decision-making. These tools should not be used to ration PrEP or to determine a client’s eligibility and they are not required. Epidemiological measures such as population-level HIV incidence may guide programmatic targeting but should not be used as criteria for PrEP access. Clients who report any of the following characteristics could likely benefit from using PrEP:
  + Vaginal or anal sex without condoms with:
* more than one partner
* a partner with potential HIV exposures
  + - * Some clients’ potential exposures to HIV include being exposed through a partner who may have exposures to HIV through sexual or injection practices. Exploring the potential HIV exposures of a client’s sexual partners with the client may be particularly important for adolescent girls and young women, people who have sexual partners who are members of key populations, and pregnant and breastfeeding people.
      * a partner living with HIV who has not been on effective HIV treatment (on ART for less than six months or has inconsistent or unknown adherence)
  + Having an STI (based on lab test, syndromic STI treatment, or self-report)
  + Recent or current PEP use
  + Sharing of injection material and/or equipment

**Assess for contraindications for use of client’s chosen PrEP method**

Clients must be assessed for contraindications for the use of their chosen PrEP method. Since some clients will decide on a method during PrEP counseling, this portion of the assessment may occur before, during, or after counseling takes place. Contraindications for each method are found in the overviews of each method above.

## Component 3: PrEP Counseling

Education and counseling for clients considering PrEP, or clients already on PrEP, are important to ensure clients can make informed choices and effectively use PrEP.

**PrEP counseling should be based on the following right to health-based principles:**

* Be client-driven and person-centered, based on their needs, resources, and preferences
* Be based on a foundation of respect and include an open, honest relationship between provider and client
* Recognize that behavior change can take time
* Validate and normalize client concerns, seek to affirm and encourage client efforts, and not be prescriptive or judgmental
* Focus on identifying small wins and achievable next steps in reducing potential exposures and/or making effective use easier
* Include contingency planning when common barriers are encountered
* Promote choice among available options based on client preferences and acceptability

**Topics for Initial PrEP Counseling**

* Sexual behaviors
* Alcohol and drug use
* Plan for preventing HIV and other STIs
* Mental health
* Prevention needs and interest in and willingness to take PrEP
* Experience of gender-based violence (GBV), including intimate partner violence (IPV)
  + Provide appropriate GBV and IPV response, including first-line support and referral where necessary, and support clients to identify ways to effectively use and continue PrEP for as long as the client wishes to use it as part of their HIV prevention strategy. *(Clients experiencing GBV, including IPV, should not be prohibited from receiving PrEP if they can effectively use it.)*
* Contraceptive needs
* Key messages on PrEP, PEP, and specific PrEP methods, including starting, stopping, and effective use of chosen method (see *Table 4* in*Annex*)

## Component 4: PrEP Prescription

Clients who will use oral PrEP (daily or ED) or the PrEP ring could be prescribed a single bottle/ring and scheduled for a one-month follow-up visit. Based on client needs and preferences, clients could also be provided with multiple bottles/rings and scheduled for a one-month or three-month follow-up visit. Clients using oral PrEP or the ring who have some medication supply in reserve tend to show better effective use. All clients, especially those using ED-PrEP who may use fewer pills over a longer period of time, should be informed about where to find product expiration dates and instructed on proper disposal of expired product. Schedule the client’s next visit at least a week before the pill supply will run out based on daily use or at least a week before the client should change the last ring they have been given.

Clients who will use CAB PrEP will be given their initiation injection 1 at the first initiation visit and should have their second initiation visit scheduled one month later for initiation injection 2.

When possible, follow-up visits should be coordinated with visits for other services to reduce the number of times a client must return to receive services.

## Additional Components of PrEP Initiation Visit

The following components could be offered alongside PrEP services as part of comprehensive, person-centered care, depending on a client’s needs and preferences. This list is not exhaustive, and services needed will vary by individual and population. PrEP should still be provided even if these services are not available or if the client is unable to or does not wish to access these services.

**Table 2. Additional Components of PrEP Initiation Visit**

| **Component** | **Action** |
| --- | --- |
| Screening, testing, and treatment of other STIs | PrEP can be used if the client has STIs other than HIV and during treatment of STIs other than HIV. Manage STIs per STI standard treatment guidelines. If testing is not possible, symptomatically manage STIs per STI standard treatment guidelines.  PrEP should still be provided even if these services are not available or if the client is unable to or does not wish to access these services.  **Hepatitis B**  Testing clients using PrEP for hepatitis B at or within three months of PrEP initiation is strongly suggested where feasible. Daily or ED-PrEP and the PrEP ring can be safely offered to persons with acute hepatitis B, so awaiting hepatitis B test results should not delay initiation. If tested for hepatitis B, clients who are negative can be offered hepatitis B vaccination (per national hepatitis guidelines, if available). Clients with hepatitis B who are not interested in oral PrEP should be referred to relevant management/treatment services. Clients who stop using oral PrEP should also be referred to relevant management/treatment services because stopping oral PrEP has implications for the management of hepatitis B. Clients with chronic hepatitis B should not take ED-PrEP.  CAB PrEP should not be initiated in people with acute viral hepatitis and should be discontinued if hepatoxicity is confirmed. If a client is tested and the hepatitis B surface antigen (HBsAg) test is reactive (indicating hepatitis B infection), needs for HIV prevention and hepatitis B treatment should be evaluated on a case-by-case basis, and PrEP and hepatitis B treatment providers should (where possible) jointly manage these cases. CAB PrEP is not active against hepatitis B. For people eligible for hepatitis B treatment per WHO guidance, oral PrEP should be offered as the preferred PrEP option. Even where there is no indication for treatment for hepatitis B, oral PrEP should be strongly considered, as it will both suppress hepatitis B and prevent HIV.  Availability of or access to hepatitis B testing should not be a barrier to PrEP initiation or use. If hepatitis B testing is conducted, PrEP can be initiated before the results are available.  **Hepatitis C**  Testing for hepatitis C is strongly encouraged at or within the first three months of PrEP initiation and every 12 months thereafter where PrEP services are provided to populations with increased likelihood of hepatitis C acquisition. Daily or ED-PrEP and the PrEP ring can be safely offered to persons with hepatitis C, so awaiting hepatitis C test results should not delay initiation.  CAB PrEP should not be initiated in people with acute viral hepatitis and should be discontinued if hepatoxicity is confirmed. If a hepatitis C serology test is reactive and chronic infection has been confirmed, hepatitis C treatment should be offered per WHO guidelines, and PrEP and hepatitis C treatment providers should (where possible) jointly manage these cases. CAB PrEP is not active against hepatitis C. There are no known drug–drug interactions between CAB PrEP and treatment drugs for hepatitis C, but data are scarce. Alternative PrEP and HIV prevention options should be considered. |
| Kidney function assessment | Kidney function measurement is not suggested for use of the PrEP ring or CAB PrEP.  Measuring the kidney function of potential clients using oral PrEP at initiation and/or during follow-up visits is suggested for some populations. Table 3 outlines who kidney function measurement is suggested for and the frequency of ongoing monitoring. When kidney function is measured, initiation or continuation of oral PrEP should not be delayed; the results can be reviewed during a follow-up visit. *Box 4* below outlines how to calculate eGFR.  When measurement of kidney function is conducted for clients using oral PrEP, any individual with an estimated creatinine clearance of ≥60 mL/min or an eGFR of ≥60 mL/min per 1.73m2 can safely be prescribed oral PrEP.  If estimated creatinine clearance is <60 mL/min or the eGFR is <60 mL/min per 1.73m2,see *Management of Creatinine Elevation* below.  Availability of or access to kidney function measurement should not be a barrier to PrEP initiation or use. If kidney function is measured, oral PrEP can be initiated before the results are available. |
| Liver function testing | In clinical trials, hepatotoxicity (as indicated by raised liver function levels) has been reported in a small number of clients receiving CAB PrEP, although at similar levels to those receiving placebo injections. Liver function testing can be considered before and during CAB PrEP use. CAB PrEP should not be initiated in people with advanced liver disease or acute viral hepatitis (see above) and should be stopped if hepatotoxicity is confirmed.  CAB PrEP injections should not be delayed while waiting for the results of liver function tests, if conducted. |
| Pregnancy testing and provision of contraceptives | Assess fertility intentions and offer pregnancy testing and contraception or safer conception counseling. Regular pregnancy testing is recommended for clients who are using PrEP and have the potential to become pregnant.  PrEP should still be provided even if these services are not available or if the client is unable to or does not wish to access these services. These services should not be barriers to accessing PrEP.  If a client is pregnant, link them to antenatal care and pregnancy options counseling (see *Management of Clients in Specific Situations* below). |
| Provision of GBV services, including IPV services | Clients who are experiencing GBV, including IPV, should be provided appropriate services as needed and available.  PrEP should still be provided even if these services are not available or if the client is unable to or does not wish to access these services. |
| Assessment for mental health and substance abuse disorders and provision of supportive services or referrals as needed | Screen for mental health concerns, including depression and substance abuse disorders, which might increase potential HIV exposure or affect effective use of PrEP, and provide or link clients to follow-up services as needed. Clients with mental health or substance use concerns should not be prohibited from receiving PrEP if they can effectively use PrEP.  PrEP should still be provided even if these services are not available or if the client is unable to or does not wish to access these services. |
| Provision of or referral to voluntary medical male circumcision (VMMC) services | Clients who may benefit from VMMC can be provided with or referred to VMMC services in alignment with national guidelines.  PrEP should still be provided even if these services are not available or if the client is unable to or does not wish to access these services. |
| Screening for and treatment of noncommunicable diseases | Clients may have additional health needs that may come up during a visit with a health care provider or may be discovered through further assessment. Provide clients with relevant health care services or refer them to appropriate services as needed and available.  PrEP should still be provided even if these services are not available or if the client is unable to or does not wish to access these services. |

**Table 3. Suggested Procedures for Measuring Kidney Function of Clients Using Oral PrEP**

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| **Population (s)** | **Baseline Screening** | **Follow-up Screening** |
| Individuals 29 years and younger with no kidney-related comorbidities0 | Optional | If testing is not conducted or if baseline test is normal,1 follow-up is optional until client is 30 years of age or if kidney-related comorbidities develop.  If baseline test result suggests at least mild loss of kidney function,2 follow-up measurements every six to 12 months are suggested. |
| Individuals 30–49 years with no kidney-related comorbidities0 | Conduct once at initiation or during a follow-up visit one to three months after initiation. However, it can be considered optional if resources are limited and there is no history of kidney-related comorbidities, especially for individuals 30–39 years. | If baseline test is normal,1 further screening is optional until client is 50 years of age or if kidney-related comorbidities develop.  If baseline test result suggests at least mild loss of kidney function,2 follow-up measurements every six to 12 months are suggested. |
| Individuals 50 years and older  Individuals of any age with kidney-related comorbidities0  Individuals with previous measurement of kidney function suggesting at least mild loss of kidney fiunction2 | Conduct once at initiation or during a follow-up visit one to three months after initiation. | Conduct follow-up measurements every six to 12 months. |

0Kidney-related comorbidities include chronic kidney disease or risk factors such as diabetes or hypertension. People who are pregnant may be at an increased risk of kidney-related adverse events, and conditions such as preeclampsia may cause kidney impairment, so pregnant people can be considered for more frequent kidney function monitoring.

1eGFR ≥90 mL/min per 1.73 m2 or creatinine clearance of ≥90 mL/min

2eGFR <90 mL/min per 1.73 m2 or creatinine clearance of <90 mL/min

**Box 4. Measuring kidney function of clients using oral PrEP**

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| Glomerular filtration rate (GFR) is a measure of kidney function. A GFR of ≥90 mL/min per 1.73 m2 suggests normal kidney function. Urinary inulin clearance measurement is the gold standard for measuring GFR but is difficult to implement routinely. Alternative measures use serum creatinine to determine an estimated GFR (eGFR). National guidelines should be considered on preferred methods, and eGFR should be calculated using an equation that has been validated for the specific population. The units for eGFR are mL/min per 1.73m2. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, which is commonly used for eGFR determination, is considered a more accurate measure of GFR than Cockcroft-Gault estimated creatinine clearance.  The 2021 version of the CKD-EPI equation:  For people assigned female at birth0,1 with serum creatinine ≤0.7 mg/dL: eGFR = 142 × (Scr /0.7)-0.241 × 0.9938age × 1.012  For people assigned female at birth0,1 with serum creatinine >0.7 mg/dL: eGFR = 142 × (Scr /0.7)-1.2 × 0.9938age × 1.012  For people assigned male at birth0 with serum creatinine ≤0.7 mg/dL: eGFR = 142 × (Scr /0.9)-0.302 × 0.9938age  For people assigned male at birth0 with serum creatinine >0.7 mg/dL: eGFR = 142 × (Scr /0.9)-1.2 × 0.9938age  Where Scr is serum creatinine given in mg/dL and age is given in years  0Exposure to gender-affirming hormones may influence eGFR estimates. Gender identity, rather than sex assigned at birth, may be more appropriate for individuals who have been using gender-affirming hormone therapy for over six months. However, given the limited research on estimating eGFR in transgender and nonbinary populations, the ideal equation for estimating eGFR in individuals who have been receiving gender-affirming hormones should be considered on a case-by-case basis.  1Equations to estimate eGFR may be inaccurate during pregnancy and may underestimate eGFR at lower values. National guidelines should be considered for preferred methods on estimating kidney function during pregnancy. |
| **For consideration:** Urinalysis is not included in WHO guidance, but some countries are using it as a proxy if creatinine testing is not available or results are delayed. If urinalysis is not normal, oral PrEP initiation is delayed until creatinine results are available. This section could be updated based on national preferences. Note that albuminuria is better than proteinuria for detection of early disease/impairment. Proteinuria indicates an elevated presence of protein in the urine (normal excretion should be < 150 mg/dL), while albuminuria is defined as an “abnormal loss of albumin in the urine.” Albumin is a type of plasma protein normally found in the urine in small quantities. Albuminuria is a common (though not universal) finding in individuals with chronic kidney disease; is the earliest indicator of glomerular diseases, such as diabetic glomerulosclerosis; and is typically present even before a decrease in the GFR or a rise in the serum creatinine. Albuminuria lasting more than three months, without or with a reduction in eGFR, is considered a marker of kidney damage. |

# PrEP Follow-Up Visits

It is recommended that once on PrEP, clients using oral PrEP or the PrEP ring return after one month for assessment and confirmation of HIV-negative test status, assessment for early side effects, and discussion of any difficulties with effective use and any other client concerns. After the first follow-up visit, clients using oral PrEP or the PrEP ring may return for follow-up visits according to their needs and preferences; for example, every three months. For clients using CAB PrEP, follow-up visits will be every two months after initiation injection 2. Some clients using the ring may prefer to return used rings to the health care provider/service provision point. If clients choose to return used rings, those rings should be disposed of along with other medical waste, such as used gloves, or in accordance with local requirements. Younger clients using PrEP and clients with other health, mental, emotional, and social needs may benefit from more frequent contact with PrEP providers.

PrEP follow-up visits have four essential components: 1) HIV testing and counseling, 2) assessments, 3) PrEP counseling, and 4) PrEP prescription refills, as described below.

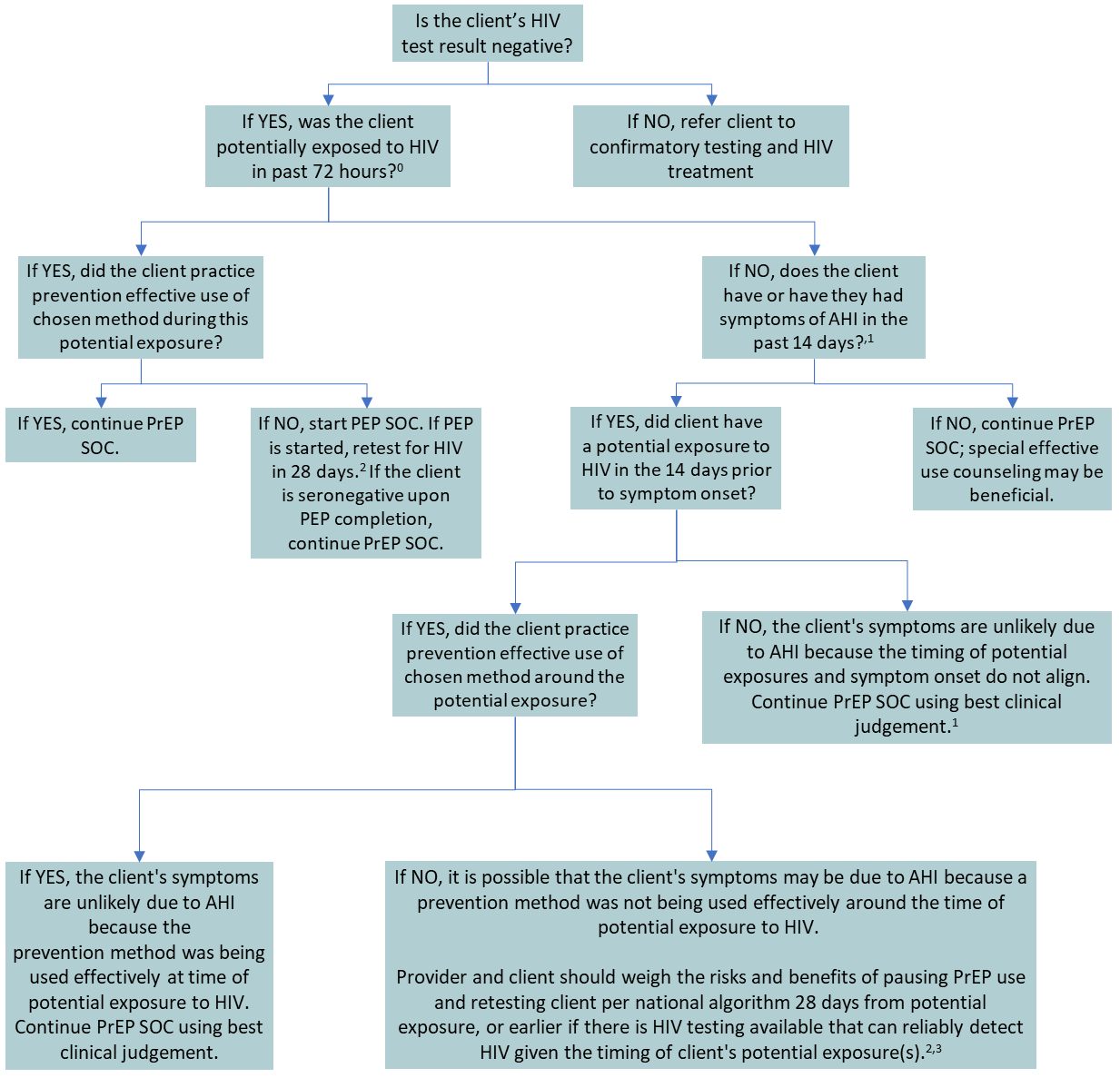
## Component 1: HIV Testing and Counseling

HIV testing and counseling should be conducted per national guidelines one month after starting PrEP (suggested) and every three months thereafter for clients using oral PrEP and the ring, and before each injection for clients using CAB PrEP, to inform decisions on whether to continue or discontinue PrEP. HIV tests are limited in identifying AHI in the “window” period from HIV acquisition to detection of antibodies.

## Component 2: Assessments

At each follow-up visit, clients should be assessed for effective PrEP use and provided with support to identify and address challenges with effective PrEP use. It is essential that this be done in an open-ended, nonjudgmental manner. A neutral assessmentof PrEP use allows for a constructive discussion that can support the client in finding solutions to effective use challenges. If effective use is poor, the client should be assessed for PEP indication and symptoms of AHI. *Diagram 2* outlines the algorithm for these assessments.

**Diagram 2. PrEP Follow-Up – HIV Exposure, AHI, and Prevention Effective Use Assessment**

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0 An answer of “NO” to the question “Potentially exposed to HIV in past 72 hours?” means no potential past exposure to HIV at all or potential HIV exposure that was 73+ hours ago.

1 Two-thirds of people will have symptoms of AHI within 2–4 weeks of HIV acquisition ([Letizia et al. 2022](https://journals.lww.com/md-journal/Fulltext/2022/02040/Clinical_signs_and_symptoms_associated_with_acute.14.aspx)). Signs/symptoms mimicking acute HIV infection (sore throat, fever, sweats, swollen glands, mouth ulcers, headache, rash, and muscle aches) are commonly due to illnesses other than HIV; providers need to use discretion in determining whether the symptomatology is consistent with HIV or may be explained by an alternative cause.

2If HIV testing that can reliably detect HIV given these clients’ potential exposures and time frames is available, PrEP may be started earlier than 28 days if results are nonreactive.

3 Suspected AHI is not a contraindication for PrEP ring use. If AHI is suspected, strongly encourage the person to return in 4-6 weeks for re-testing and not wait for 3 months.

## Component 3: PrEP Counseling

In addition to re-enforcing any of the key messages and counseling topics discussed at initiation, as needed, (see *Table 4* in *Annex*), providers should discuss:

* Any side effects or adverse drug reactions the client has experienced (and manage them as needed — *see Management of Side Effects and Adverse Drug Reactions* below)
* If there is ongoing exposure to HIV and whether the client feels continued PrEP use is necessary

## Component 4: PrEP Prescription Refill

Clients who are using oral PrEP or the PrEP ring could be prescribed multiple bottles/rings, enough so they don’t need to return for a refill until their next follow-up appointment. Some clients, however, may not prefer multi-month dispensing due to challenges with storage, so providers should have conversations with their clients and come to agreement based on client needs and preferences. Clients who have some medication supply in reserve tend to show better effective use. In some situations, and based on client needs and preferences, it may be appropriate to separate follow-up visits from PrEP refills.

For clients who may use ED-PrEP, a full refill may not be needed at each follow-up visit. At each visit, ask these clients how many full bottles of oral PrEP they have and provide enough bottles so that they can use oral PrEP daily should they need to. Generally, this would mean prescribing them three minus the number of full bottles the client has.

For clients who are using oral PrEP or the ring, schedule the client’s next visit at least a week before the pill supply will run out based on daily use, at least a week before the client should change the last ring they have been given, at least every three months. For clients using CAB PrEP, schedule the follow-up visit two months after initiation injection 2 and every two months thereafter.

When possible, follow-up visits should be coordinated with visits for other services to reduce the number of times a client must return to receive services.

## Potential Components of PrEP Follow-Up Visits

Potential components of PrEP follow-up visits are the same as the potential components for initiation visits.

If estimated creatinine clearance is <60 mL/min or the eGFR is <60 mL/min per 1.73m2, see *Management of Creatinine Elevation* below.

# Unscheduled PrEP Visits

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| **For consideration:** Procedures for unscheduled visits might include:   * Determining if the reason for the visit is PrEP-related or not, e.g., adverse drug reactions * Assessing and managing the reason for the unscheduled visit according to national guidelines, e.g., acute or chronic illness, exposure to HIV while not using PrEP effectively, worsening existing condition(s) * Providing HIV exposure reduction and PrEP effective use counseling * Agreeing on a follow-up schedule |

# Discontinuing PrEP Use

The duration of PrEP use may vary, and individuals are likely to start and stop PrEP depending on their individual assessments of potential HIV exposures at different periods in their lives, including changes in relationships and behaviors. Ideally, a client will inform their service provider when they want to discontinue PrEP. Often, however, clients may not return to their providers at all or the provider is informed after a client has already discontinued PrEP. It is therefore important that clients are informed during initiation and continuation visits about safely stopping PrEP (or stopping and restarting as appropriate).

During counseling, providers should discuss with clients when it may be appropriate to discontinue PrEP. PrEP use may be discontinued for any of the following reasons:

* Client request
* Positive HIV test (clients who seroconvert while on PrEP should be linked to care and initiated on ART in line with national guidelines)
* Safety concerns, such as estimated creatinine clearance of <60 mL/min or an eGFR of <60 mL/min per 1.73m2 (if known) for clients using oral PrEP (appropriate clients should also be counseled on using the PrEP ring, if applicable) or confirmed hepatotoxicity for clients using CAB PrEP.
* No longer likely to be exposed to HIV
* Persistent side effects that are not manageable
* Decision to switch to another HIV prevention strategy
* Starting use of contraindicated medications

Instructions on how to discontinue PrEP are included in information about each method’s use above and in the counseling messages.

For clients with chronic hepatitis B who stop TDF-based oral PrEP, regular monitoring to detect relapse and management of hepatitis B are important. Clients taking TDF for treatment of hepatitis B who wish to stop oral PrEP can be switched to a TDF-only regimen.

# Restarting PrEP Use

Individuals restarting PrEP will need to be tested again for HIV and free of any contraindications for their chosen PrEP method.

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| **For consideration:** In national guidelines, some countries have chosen to specify when a client should be considered discontinued based on the number of days after a client stops PrEP use or the number of days after a missed appointment. Typically, this has been followed by procedures to restart someone on PrEP. If a country decides to include a discontinuation definition, restarting procedures that include more than the essential components may become barriers to PrEP use by delaying or preventing someone from restarting PrEP and may increase program costs. |

# Management of Clients in Specific Situations

This section outlines the management of clients in specific situations.

## Management of Creatinine Elevation Among Clients Using Oral PrEP

Very few clients experience creatinine elevation. Most creatinine elevations are self-limiting, can be addressed without stopping oral PrEP, and are caused by dehydration, exercise, diet, diabetes mellitus, hypertension, liver failure, or hepatitis C virus. Some may reflect a false-positive test result. Rule out and manage other causes of elevated creatinine.

If the estimated creatinine clearance is <60 mL/min or the eGFR is <60 mL/min per 1.73m2, the kidney function test should be repeated on a separate day before stopping oral PrEP. Oral PrEP should be stopped if the repeat test results also show the estimated creatinine clearance is <60 mL/min or the eGFR is <60 mL/min per 1.73m2. These clients should be counseled on other HIV prevention strategies, including other PrEP methods. Kidney function usually returns to normal levels after stopping oral PrEP. Oral PrEP can be restarted if an estimated creatinine clearance of ≥60 mL/min or eGFR of ≥60 mL/min per 1.73m2 is confirmed one to three months after stopping oral PrEP. If kidney function does not return to normal levels after stopping PrEP, other causes of kidney insufficiency should be evaluated.

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| **For consideration:** National guidelines may want to consider stopping oral PrEP use if a client’s creatinine clearance on the initial test is < 50 mL/min, but this is not per WHO guidance and is an area where national guidelines have varied. Example text from other national guidelines is as follows:  If the calculated creatinine clearance is:   * < 50 mL/min: Stop oral PrEP and refer to [clinical staff cadre] immediately. * 50-60 mL/min: Repeat serum creatinine within two weeks. If the repeat sample creatinine clearance is <60 mL/min, stop oral PrEP and consult with [clinical staff cadre] for further investigation and management. |

## Management of HIV Seroconversion

If a client seroconverts while on PrEP or after starting PrEP (even if not taking PrEP or not taking PrEP consistently):

* Discontinue PrEP use immediately.
* Confirm using national testing algorithm.
* Immediately link to care and initiate on ART (per national ART guidelines).
* Document seroconversion and possible reason for seroconversion (non-effective use, stopped taking PrEP, or PrEP failure, i.e., breakthrough HIV while adherent to PrEP) and, if available and indicated, link to HIV drug resistance testing.

## Management of Side Effects and Adverse Drug Reactions

Side effects should be managed symptomatically, and most will resolve within the first month of use. Counseling to support management of side effects should be provided. Any side effects should be recorded in client records and [relevant forms] regardless of severity. Major toxicities (including renal toxicity and metabolic complications) associated with TDF and FTC are rare in oral PrEP exposure to date. No major toxicities or severe adverse reactions have been shown to be related to ring use. Severe adverse reactions, both injection site and non-injection site related, are rare in CAB PrEP exposure to date. Consult [clinical staff cadre] if these occur. Complete the national [adverse drug reaction form] and report per standard operating procedures.

In some cases, side effects may cause a client to discontinue PrEP use. If PrEP is discontinued, record the outcome in the PrEP register. Side effects and potential adverse drug reactions for each method are found in the overviews of each method above.

## Pregnancy and Breastfeeding

Given the increased likelihood of HIV acquisition during pregnancy and the postnatal period, as well as reassuring safety data, PrEP use is a reasonable option for people who are pregnant or breastfeeding. There is no safety-related rationale for disallowing or discontinuing oral PrEP use during pregnancy and breastfeeding.

Data are limited (fewer than 300 pregnancy outcomes) on the use of the ring by people who are pregnant, but results from a safety trial of ring use during pregnancy show that adverse pregnancy outcomes and complications were uncommon among clients using the ring and generally similar to the rates observed in the surrounding study community.[[32]](#footnote-33) Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity that are relevant to use of the ring. Providers and clients should weigh client preferences and ability to effectively use HIV prevention methods when considering whether the ring or another HIV prevention method, such as oral PrEP, should be used during pregnancy. Additionally, PrEP ring use is not recommended for 6 weeks postpartum.

Dapivirine has been shown to be excreted at very low levels in human milk in one clinical study conducted among 16 mothers who received HIV-1 negative test results and were lactating but not breastfeeding. Because milk concentrations remained low (<1420 pg/ml), infant exposure to dapivirine is anticipated to be low (below 1µg/day). Results from a recent trial of ring use during breastfeeding showed a favorable safety profile with low drug transfer to breastmilk.[[33]](#footnote-34) At this time, the potential impact of ring use during breastfeeding is not known. When making decisions about HIV prevention methods, providers and clients should consider the known benefits of breastfeeding for mothers and infants and the risks associated with human milk substitutes. A shared decision-making process should guide selection of HIV prevention options.

One clinical trial to further assess the safety of ring use during pregnancy is ongoing.

During pregnancy, the ring should be removed if a client experiences active labor at any gestation, vaginal bleeding, spontaneous or therapeutic abortion, suspected or confirmed rupture of amniotic membranes (water breaking), cervical cerclage, or suspected or confirmed intrauterine infection.

Data are limited on the use of CAB PrEP during pregnancy and breastfeeding. Dolutegravir, a medication in the same drug class as cabotegravir, was found safe to use during pregnancy, and the very limited data available from a small number of women who became pregnant in clinical trials suggest CAB PrEP may be safe during pregnancy and breastfeeding. There are no data on whether cabotegravir is present in human milk, impacts human milk production, or affects breastfeeding infants among clients using CAB PrEP.

Due to the potential for adverse reactions and residual concentrations of cabotegravir in systemic circulation for 12 months or longer after CAB PrEP injections are discontinued, clients who are or may become pregnant or are breastfeeding, especially during the tail period, should be counseled on the risks and benefits of using CAB PrEP. Research is ongoing.

# Who Can Deliver PrEP and Where?

PrEP implementation can be integrated in any setting with appropriately trained individuals who have been authorized to provide components of PrEP initiation and/or follow-up visits according to national guidelines. It is important that places where PrEP is provided also have systems and tools in place for completing all the necessary steps of PrEP initiation and follow-up and the monitoring, documentation, and reporting of PrEP use.

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| **For consideration:** Because the roles and responsibilities of different cadres of health care workers can change over time, it may be beneficial to not specify which cadres are involved in specific aspects of PrEP service delivery. This allows for task-sharing among nonclinical (or less specialized) cadres to occur and supports further movement of PrEP from health facilities into the community. Alternatively, in some cases it could be useful to specify certain providing groups, such as peer providers, where the type of provider is critical to client acceptability of PrEP. Likewise, it may be beneficial not to include an exhaustive list of possible PrEP service delivery locations in guidelines to avoid limiting programmatic expansion and differentiated service delivery. Some service delivery locations may include: one-stop shops; drop-in centers (including in community and facility settings); HIV clinics (for people without HIV who have a partner or partners who do not have suppressed viral load or when viral suppression is unknown); antenatal care and maternal, newborn, and child health clinics; family planning, reproductive health, and STI clinics; mobile health clinics; community settings meeting the criteria for initial client assessment and evaluation (e.g., integrated prevention centers and youth-friendly outlets); and primary care settings, as well as virtual or blended in-person and virtual models. |

# Annex

**Table 4. Key Messages for Counseling**

| **Topic** | **Key Messages** |
| --- | --- |
| What is PrEP? | Pre-exposure prophylaxis, or PrEP, is the use of antiretroviral drugs by people without HIV before a potential exposure to prevent HIV. It is one of several HIV prevention strategies and, where possible, should be used in combination with condoms and condom-compatible lubricants and other HIV prevention strategies. Currently there are three methods for PrEP: pills that are taken by mouth (oral PrEP), a ring that is inserted into the vagina (PrEP ring), and an injection given in the buttocks muscle (CAB PrEP). |
| Effectiveness of PrEP | When used as prescribed, oral PrEP is more than 90% effective at preventing HIV acquisition, the PrEP ring is about 50% effective (likely more with consistent use), and CAB PrEP is highly effective in cisgender and transgender women and cisgender men. In recent randomized controlled trials, CAB PrEP was shown to be more effective than oral PrEP, though it is likely due largely to better adherence to CAB PrEP.  When choosing a PrEP method, it is important to consider which method(s) will work best for you to prevent HIV during the types of exposures you anticipate, among other factors.  **For people assigned female at birth interested in daily oral PrEP, the PrEP ring, or CAB PrEP:**  Daily oral PrEP reduces your chances of getting HIV during all types of exposures to HIV; CAB PrEP works for sexual exposures and, as a systemic product, may also cover injection-related exposures. The PrEP ring works only for sexual exposures during receptive vaginal sex.  **For people assigned male at birth interested in oral PrEP (daily or ED-PrEP) or CAB PrEP:**  Daily oral PrEP reduces your chances of getting HIV during all types of exposures to HIV; event-drive PrEP, known as ED-PrEP, works only for sexual exposures and you can only use it if you aren’t using any estradiol-based hormones. CAB PrEP works for sexual exposures and , as a systemic product, may also cover injection-related exposures. |
| PrEP is not  for life. | You should take PrEP or use another HIV prevention strategy for as long as you feel you may be exposed to HIV. Some people need to take PrEP only during certain times in their lives, while others have an ongoing need to use PrEP. If you decide to start the PrEP ring or oral PrEP, it is suggested that you come back in a month for a follow-up visit, and then return every three months after that. If you choose CAB PrEP and decide to continue with it, you will need to come back for your second initiation injection one month after the first initiation injection and every two months thereafter for follow-up injections. |
| Starting and stopping PrEP | For PrEP to be most effective, you must use PrEP as prescribed. When choosing a PrEP method, it is important to consider which method(s) you can use effectively. Now, I will tell you about how long you should use PrEP before and after potential HIV exposures, which is different for different methods. If you choose to start PrEP, it is particularly important to try to avoid potential exposures to HIV until adequate drug levels are achieved by using condoms with condom-compatible lubricant and using sterile and non-shared injection-related materials.  **For people assigned female at birth interested in daily oral PrEP, the PrEP ring, or CAB PrEP:**  Your choice between daily oral PrEP, CAB PrEP, or the PrEP ring depends on your potential exposures to HIV, including the types of sex you have, as well as your preferences.  **Oral PrEP** must be taken daily and should be used for at least seven consecutive days before it is considered effective. It must be continued for seven days after the last potential exposure. Taken this way, oral PrEP is effective at preventing HIV during all types of exposures to HIV. Oral PrEP can be taken with or without food.  **The PrEP ring** is also an option for you. You can insert the PrEP ring into the vagina yourself or with help from a provider if you’d like. The ring should remain in place for one month without removal and should be replaced with a new ring at the end of the month. The ring must be in place for at least 24 hours before it is considered maximally effective. The ring prevents HIV acquisition only during receptive vaginal sex. The ring can be removed by hand, so you can remove it without help. However, if you would prefer support, you can receive help removing it and there is no need for a speculum or other tools.  **CAB PrEP** is another option. CAB PrEP is injected into the buttocks. The first two injections are one month apart, followed by injections every two months thereafter. For sexual exposures, the current evidence shows it takes about one week after initiation injection 1 for drug concentrations to reach levels anticipated for CAB PrEP to be maximally effective, so you should use another HIV prevention strategy during that time. The medication will stay in the body at levels effective for preventing HIV acquisition for at least eight weeks after your last injection, but then levels decline and may not prevent HIV acquisition. At these reduced levels, if you get HIV, you may develop drug resistance, meaning that medicines used to treat HIV may be less effective or not work at all. This period where drug resistance is possible is called the “tail period.” To prevent HIV drug resistance during the tail period, it is important for you to use an effective HIV prevention strategy if you might be exposed to HIV.  When stopping any PrEP method, it is important to use another PrEP method or HIV prevention strategy if your need for HIV prevention continues.  **For people assigned male at birth interested in oral PrEP (daily or ED-PrEP) or CAB PrEP:**  Your choice between daily oral PrEP, ED-PrEP, or CAB PrEP depends upon your potential exposures to HIV, including the frequency and predictability with which you have sex, as well as your preferences. ED-PrEP may be more appropriate if you find it more effective and convenient, have infrequent sex (for example, less than two times per week on average), and are able to plan for sex at least two hours in advance or delay sex for at least two hours. You may wish to transition between daily and ED-PrEP use according to your circumstances. Oral PrEP can be taken with or without food.  **To start daily oral PrEP,** take a loading dose of two pills at PrEP initiation and delay sex for at least two hours, ideally closer to 24 hours, at which time drug levels will be maximally effective to prevent HIV acquisition from sexual exposures. Continue taking one pill of oral PrEP at the same time daily. For injection-related exposures, you will need to take one pill daily for seven days prior to exposure for drug levels to be maximally effective. To discontinue, continue one pill of oral PrEP daily until two days after the last potential sexual exposure or seven days after the last potential injection-related exposure, whichever is longer.  **To start ED-PrEP,** take a loading dose of two pills two to 24 hours before having sex, ideally closer to 24 hours, at which time drug levels will be maximally effective to prevent HIV acquisition from sexual exposures. Continue taking one pill daily at the same time you took the loading dose until two days after the last potential sexual exposure. This process should be repeated for each period of potential sexual exposure to HIV.  **CAB PrEP** is another option. CAB PrEP is injected into the buttocks. The first two injections are one month apart followed by injections every two months thereafter. For sexual exposures, the current evidence shows it takes about one week for CAB PrEP to reach full efficacy after initiation injection 1, so you should use another HIV prevention strategy during that time. The medication will stay in the body for at least eight weeks after you stop using CAB PrEP, but then levels decline and may not prevent HIV acquisition. At these reduced levels, if you get HIV, you may develop drug resistance, meaning that medicines used to treat HIV may be less effective or not work at all. This period where drug resistance is possible is called the “tail period.” To prevent HIV drug resistance during the tail period, it is important for you to use an effective HIV prevention strategy if you might be exposed to HIV.  When stopping any PrEP method, it is important to use another PrEP method or HIV prevention strategy if your need for HIV prevention continues. |
| PrEP and alcohol or other recreational drugs | Taking PrEP while you are using alcohol or other recreational drugs will not hurt you. However, alcohol or other recreational drugs may make it challenging to use PrEP correctly, such as by causing you to miss an appointment, a dose of oral PrEP, or switching of a ring, so make a plan to continue using PrEP effectively if you use alcohol or other substances. We can talk about planning together if that would be helpful. |
| PrEP and other medications | The drugs in some PrEP methods may interact with other medications you may take. Are you taking any medications?  **PROVIDER NOTE:** Depending on the PrEP method the client is interested in or using, refer to the relevant “[PrEP method] and Other Drug Interactions” section above. |
| PrEP, pregnancy,  and breastfeeding | PrEP does not prevent pregnancy. To avoid unintended pregnancy, use a contraceptive method.  The likelihood of acquiring HIV is higher during pregnancy and the postnatal period. Taking oral PrEP while you are pregnant or breastfeeding will not hurt you or your baby. Because HIV can be transmitted during pregnancy and breastfeeding, taking oral PrEP during this time prevents both you and your baby from acquiring HIV. You can use oral PrEP throughout pregnancy and breastfeeding.  There is some information about use of the ring or CAB PrEP during pregnancy or when breastfeeding, but the available data suggest both are likely safe. If you are pregnant or breastfeeding, or intend to be, we should discuss this. If you are pregnant and using the ring, you should remove the ring if you begin experiencing active labor or vaginal bleeding or if your water breaks.  CAB PrEP can stay in your system for 12 months or longer after you stop injections. If you think you might have the potential or want to become pregnant after stopping CAB PrEP, we should discuss the risks and benefits of CAB PrEP use.  **PROVIDER NOTE:** If a client is pregnant, link them to antenatal care or pregnancy options counseling (see *Management of Clients in Specific Situations* above for more information on PrEP for clients who are pregnant or breastfeeding and refer to national guidance). |
| No STI prevention other than HIV | PrEP reduces the likelihood of HIV acquisition but does not prevent any other sexually transmitted infections (STIs). To prevent other STIs, use a condom and if needed, condom-compatible lubricant, correctly whenever you have sex. It is important to regularly test for STIs, especially if you are not able to use condoms consistently.[[34]](#footnote-35) If you experience discharge from the penis or the vagina that has a bad odor, causes irritation, or is a different color/amount than usual; bleeding that is not your period; or bumps, warts, swelling, redness, rash, or severe itching on or near your genitals, mouth, or anus, these could be signs that you may have an STI and should see a health care provider as soon as possible and abstain from sexual contact if you can. |
| Side effects | **Oral PrEP:** Few people using oral PrEP experience side effects. Those who do will typically experience only mild side effects, including gastrointestinal symptoms (diarrhea and nausea, decreased appetite, abdominal cramping, and flatulence), dizziness, and headaches. Most of those side effects disappear within one month. However, I can help you manage them.  **CAB PrEP:** Some people who use CAB PrEP may experience side effects. Side effects while using CAB PrEP are usually mild and can include headache, nausea, diarrhea, and tiredness. Mild or moderate injection site reactions are also possible, becoming less frequent over time. These reactions can include redness, pain, and swelling at the injection site. If having a visible injection site reaction is of concern for you, please let me know and we can discuss ways to approach this for you. Some people may also experience depressive disorders while using CAB PrEP, although these are uncommon. If you experience changes in how you’re feeling emotionally, let me know so we can discuss how to get you the support you need.  **PrEP Ring:** Some people who use the PrEP ring may experience side effects. Typically, these are mild and include urinary tract infections (UTIs), vaginal discharge, vulvar itching, and/or pelvic and lower abdominal pain.  Contact me if you experience any urinary or reproductive tract changes, as these could be a sign of an STI or UTI needing treatment.  Some people taking PrEP report positive effects on physical, emotional, or mental wellbeing. These include increased feeling of control over one’s health and community belonging, and reduced anxiety as fear of HIV acquisition has decreased with PrEP use. |
| Switching between HIV prevention options | It is okay to start one PrEP method now and decide later that you want to use another PrEP method or another HIV prevention strategy. Many people switch between methods as their needs change. I am here to help you make the best decision for you.  Some other strategies to prevent HIV include:   * Using condoms and condom-compatible lubricant consistently * Accessing post-exposure prophylaxis (PEP) as early as possible, ideally within 72 hours of potential exposure to HIV * Having other types of sex that come with no or nearly no likelihood of HIV acquisition (such as mutual masturbation or oral sex) * Receiving screening, diagnosis, and treatment for other STIs (left untreated, other STIs can increase the likelihood of HIV acquisition when exposed to HIV) * Receiving voluntary medical male circumcision * Having fewer sexual partners * Accessing drug harm reduction and treatment services * Ensuring that a partner living with HIV has been on effective ART for at least six months, has an undetectable viral load, and remains adherent to ART |
| Follow-up visits | What is required for follow-up visits does vary by method. If you decide to use oral PrEP or the PrEP ring, you will typically have another visit in a month, and then every three months after that. If you choose CAB PrEP, you will have another visit in one month and one every two months thereafter. It is important that you attend follow-up visits for the following reasons:   * To get support on effective use and managing side effects and to address other concerns you may have * To verify your HIV status and, if positive, be referred for effective treatment. Between now and your next visit, if you experience sore throat, fever, sweats, swollen glands, mouth ulcers, rash, or muscle aches, please contact me or come back here for a follow-up visit. * To reduce your likelihood of drug resistance if you have acquired HIV   Do you have any upcoming travel, or do you anticipate any other challenges with returning for regular visits that we can discuss and maybe I can help you plan for?   |  | | --- | | **For consideration**: Many settings are implementing strategies to reduce the number of times clients using PrEP need to return for follow-up visits while ensuring they have access to ongoing care, including HIV testing. These strategies may include the deployment of community health workers, mobile clinics, pharmacy models, the use of HIV self-testing, and many others. This section may need to be modified based on how differentiated service delivery for clients using PrEP is structured in your country. | |
| **PROVIDER NOTE**: It is likely that the client will have enough information now to make an informed choice about whether they want to use a PrEP method or not and, if so, which one. You can ask the client which method they prefer, if any, and what outstanding questions they may have, and then continue with the key messages. | |
| Discontinuing PrEP use | As we already discussed, PrEP use is rarely for life. How long you use PrEP may vary, and you may start and stop PrEP depending on potential HIV exposures during different periods of your life, including changes in your relationships or behaviors. If you want to stop PrEP use indefinitely, it would be helpful if you let me know, and we can discuss necessary next steps relevant to your chosen method. If you decide to restart PrEP later, you can always come back, and then we can discuss the next steps.  **PROVIDER NOTE:** Be sure to inform clients about any post-exposure use of PrEP that is needed for their chosen method to effectively stop PrEP use. Encourage ongoing links to appropriate HIV prevention and contraceptive services and strategies as needed. Clients with hepatitis B who are using oral PrEP should be referred to relevant management/treatment services, because stopping oral PrEP may have implications for the management of hepatitis B. |
| Partner disclosure | People have different reasons for sharing or not sharing their PrEP use with their partner(s). Generally, individuals who can disclose their PrEP use with their partners can use it more effectively. If you’d like, we can discuss your thoughts on sharing or not sharing your PrEP use together. If you choose not to tell your partner, we can also discuss your plan if your partner happens to learn about your PrEP use.  **PROVIDER NOTE:** Assess client’s experience of gender-based violence (GBV), including intimate partner violence (IPV). If the client discloses that they have experienced or are at risk of GBV, including IPV, provide first-line support and make referrals as appropriate. Discuss how violence and fear of violence affects their potential HIV exposures and prevention behaviors and discuss ways they can stay safe and protect themselves in the context of their relationship(s). Although the ring or CAB PrEP may be options for clients concerned about IPV due to their discreet natures, clients who wish to keep their ring use private from their sexual partner(s) should be counseled on the possibility that a partner may feel the ring during sex and be assisted with a plan to implement should this occur. Similarly, clients who wish to keep CAB PrEP use private should be counseled on the possibility of visible injection site reactions and be assisted with a plan to implement should this occur.  Supportive LIVES (Listen, Inquire, Validate, Enhance safety, and Support) tools for routine enquiry can be found [here](https://www.prepwatch.org/resources/sop-job-aid-ipv-prep-services/). While the job aid specifies oral PrEP, it is applicable for clients using any PrEP method. |
| **FOR CLIENTS WHO CHOOSE ORAL PrEP** | |
| Supporting effective use | During instances or periods of potential exposure to HIV, some people find it easy to remember to take their oral PrEP when they integrate it into a daily routine and take it the same time each day. For example, you could take oral PrEP (or consider taking oral PrEP if using ED-PrEP) when you brush your teeth (either in the morning or evening) or while watching a favorite TV show or listening to a favorite radio program. It is helpful to pair taking oral PrEP with a routine that makes you feel good. Other potential strategies include:   * Taking oral PrEP with food or at night to help with any nausea * Using pill boxes for traveling around with extra pills to be used within 7 days preferably * Joining or starting an in-person or virtual support group with friends or to connect with others who can support effective oral PrEP use.   *What challenges do you anticipate with taking oral PrEP as prescribed that maybe I can work with you to find solutions for? (Providers should explore and emphasize effective use and pill-taking reminders specific to everyone. This may be an appropriate time to explore gender and intimate partner violence.)* |
| Oral PrEP storage | Store oral PrEP in its original packaging (if possible) in a cool, dry place, away from children and direct sunlight and secured from any pets or animals. Oral PrEP does not need to be refrigerated. You can check the package for the expiration date. |
| **FOR CLIENTS WHO CHOOSE DAILY ORAL PrEP** | |
| Missed daily oral  PrEP dose | If you forget to take a pill or miss a dose, take it as soon as you remember. For example, if you usually take oral PrEP in the morning but realize at 10 p.m. or the next day that you forgot, it is okay to take your pill then and resume your usual schedule the following morning. If you forget more than once a week, come back here or quickly contact someone here and we can discuss what to do. |
| **FOR CLIENTS WHO MAY USE ED-PrEP** | |
| Delayed ED-PrEP loading dose | If it is less than two hours before you plan to have sex, take the loading dose, and try to delay sex until two hours after the loading dose. However, if you do NOT take the loading dose at least two hours before sex and cannot delay sex you could:   * Use a condom and condom-compatible lubricant. * Have other types of sex that come with no or nearly no likelihood of HIV acquisition (such as mutual masturbation or oral sex).   If you have sex before two hours have passed and do not use a condom, you may be a candidate for a 28-day course of PEP, depending upon other factors (per the national guidelines). |
| Missed ED-PrEP dose(s) | If you miss an ED-PrEP dose (loading or post-sex), you may be a candidate for a 28-day course of PEP per the national guidelines.  **PROVIDER NOTE:** Because the timing and type of the sexual event will vary for each client in relation to the timing of the missed dose(s), such cases will require individual adjudication and best clinical judgment. |
| Switching between ED-PrEP and daily PrEP | Because the frequency and predictability of sex may vary over time, the best PrEP dosing option for you may also vary over time.  To transition from ED-PrEP to daily oral PrEP: You should continue taking PrEP every day after your last exposure. You should continue this daily dosing until sex becomes less frequent or more predictable again, or for as long as you prefer the daily dosing option.  To transition from daily oral PrEP to ED-PrEP: You should stop daily dosing two days after the last potential exposure, and then start following the ED-PrEP regimen until sex becomes more frequent or less predictable. |
| Dosing scenarios | It is very important for you to try to take the follow-up doses around the same time of day when you took the loading dose. For ED-PrEP to be effective, take PrEP according to the dosing schedule prescribed. Let’s walk through some common scenarios together.  **PROVIDER NOTE:** Walk through basic regimen with client (2+1+1). Provide client with information, education, and counseling materials showing different scenarios for ED-PrEP use (see *Oral PrEP Use* above) |
| **FOR CLIENTS WHO CHOOSE THE RING** | |
| Supporting effective use | The ring is designed to be in place for a full month without being removed. However, if you decide to remove the ring, it is important to rinse it with clean water only and insert it again as soon as possible. The ring can be reinserted after removal until the 28-day period has expired; however, the level of dapivirine in the vagina drops quickly after ring removal, and therefore removal is not recommended during the window of use. Also, because dapivirine levels drop quickly after ring removal, the need to use other HIV prevention measures until the ring is reinserted should be reinforced. If a PrEP ring is removed for a longer period than just a removal and reinsertion as soon as possible, it should be cleaned prior to reinsertion. Once reinserted, the ring must be in place for at least 24 hours for maximum protection. Since it needs to be changed monthly, it could be helpful to set a reminder on your phone if you have one or to record it somewhere else where you look frequently to help you remember when it is time to replace your ring with a new one.  **PROVIDER NOTE:** Walk through insertion and removal instructions with the client (see *PrEP Ring Use* above)  *What challenges do you anticipate with using the ring as prescribed that maybe I can work with you to find solutions for? Do you feel confident you can insert and remove the ring yourself, or do you think you will need help from me or another provider? (Providers should explore and emphasize effective use and ring replacement reminders specific to everyone. This may be an appropriate time to explore gender-based and intimate partner violence.)* |
| Cleaning the ring | The ring does not need to be removed and cleaned for any reason. However, if desired, it is acceptable to remove the ring, rinse it in clean water only, and then reinsert it immediately. |
| Ring reinsertion | Although it is unlikely, it is possible that the ring may fall out. If this happens in a clean location, the ring should be rinsed in clean water and reinserted. If the ring falls out in a dirty location, the ring should be replaced with a new ring. |
| Ring use during sex | The ring does not interfere with sexual intercourse and should be worn during sex. It can be used with condoms (internal and external) and condom-compatible lubricant. Although it is unlikely, it is possible that your partner may feel the ring during sex. If this happens, you may need to confirm ring placement, as it may mean that the ring should be pushed further into the vagina. The ring does not cause harm to your partner, but it does not prevent your partner from acquiring HIV. |
| The ring and menses | The ring should be worn for one month, including during menses, to be most effective. The ring does not cover the cervix and does not interrupt the flow of menstrual fluids. There are no safety concerns related to the use of tampons, menstrual pads, or other menstrual products while using the ring.  If you are using a tampon, be careful not to accidentally remove the ring when removing the tampon. Although it is unlikely, it is possible that the ring may fall out. If this happens in a clean location, the ring should be rinsed in clean water and reinserted. If the ring falls out in a dirty location, the ring should be replaced with a new ring.  **PROVIDER NOTE:** Some clients may choose to time insertion and removal of the ring with their menstrual cycle. For clients who chose to do so, they should be reminded that levels of dapivirine drop quickly after ring removal and that if not reinserted or replaced immediately, a PrEP ring must be in place for at least 24 hours for maximum protection. If they choose to remove the ring for the duration of menstruation and anticipate sexual exposures during that time, they should be counseled on other effective HIV prevention strategies until they can reinsert and restart ring use. |
| Sharing the ring | The ring should not be shared with others. If other people you know are interested in using the ring, they can come here. |
| The ring and douching | It is possible that flushing the vagina with water to clean it (or any form of douching) may dilute the concentration of dapivirine in the vagina. Douching is not recommended at any time, including while using the ring, because it may have a negative impact on the health of the vagina. |
| Ring storage | Store rings in their original packaging in a cool, dry place, away from children and direct sunlight and secured from any pets or animals. The ring does not need to be refrigerated and can be safely stored at or around 25°C or 77°F for up to five years from when it was made. You can check the package for the expiration date. |
| Ring disposal | Used rings can be placed inside the original wrapper provided with the ring or wrapped in tissue or toilet paper and disposed of in a trash bin out of the reach of children. If you prefer, you can return your used ring to your health care provider/service provision point. |
| **FOR CLIENTS WHO CHOOSE CAB PrEP** | |
| Missed CAB PrEP injection(s) | If you miss an injection visit, it is important to contact your health care provider immediately and schedule an appointment for the missed injection as soon as possible. If keeping to the injection schedule is not working for you, we can discuss changing to a different PrEP method or HIV prevention strategy. |
| Switching from CAB PrEP to other PrEP methods | It is okay to stop CAB PrEP and switch to another PrEP method. Depending on the method you would like to switch to, we can discuss the best way to switch safely and effectively.  If you think you might want to become pregnant and are still potentially exposed to HIV, we can talk about switching from CAB PrEP to a method that has been shown to be safe during pregnancy. |
| Stopping CAB PrEP and the “tail period” | When you stop getting CAB PrEP injections, the drug cabotegravir can remain in your body for about a year, but not at high enough levels to prevent HIV. At these levels, if you acquire HIV, you may develop drug resistance, meaning that medicines used to treat HIV may be less effective or not work at all. This period when HIV drug resistance is possible is called the “tail period.” If you decide to stop your CAB PrEP injections, we should talk about transitioning you to another PrEP method or another HIV prevention strategy during the tail period for as long as exposure to HIV is possible.  We do not yet have enough information about pregnancy and breastfeeding during the tail period; therefore, if you are thinking of becoming pregnant or don’t want to use contraception during the tail period, we should discuss what options will be best for you. |

1. Injection drug use is mentioned in this guidance; however, first-line prevention strategies for people who inject drugs (PWID) are needle exchange and/or drug use harm reduction and treatment. Daily oral PrEP has some preventative effects for this population and should be offered as part of a larger prevention package. Importantly, PWID may also have sexual exposures for which needle exchange and/or drug use harm reduction and treatment do not provide necessary prevention strategies. [↑](#footnote-ref-2)
2. WHO. Consolidated guidelines on HIV, viral hepatitis and STI prevention, diagnosis, treatment and care for key populations [Internet]. Geneva: WHO; 2022 [cited 2022 Nov 15]. Available from: <https://www.who.int/publications/i/item/9789240052390>. [↑](#footnote-ref-3)
3. Fonner VA, Dalglish SL, Kennedy CE, Baggaley R, O’Reilly KR, Koechlin FM, et al. Effectiveness and safety of oral HIV preexposure prophylaxis for all populations. AIDS. 2016 July 31;30:1973–83. [↑](#footnote-ref-4)
4. Parenteral exposure to HIV means exposure via subcutaneous, intramuscular, or intravenous contact with the blood or other body fluid of someone living with HIV. This can include injection-related exposures. [↑](#footnote-ref-5)
5. People assigned male at birth may include cisgender men, transgender women, and some nonbinary people. Cisgender denotes a person whose sense of personal identity and gender corresponds with their sex assigned at birth. [↑](#footnote-ref-6)
6. Estradiol is an estrogen hormone and is sometimes used as part of gender-affirming hormone therapy by some transgender or nonbinary people. [↑](#footnote-ref-7)
7. Exogenous hormones originate outside the body, meaning an individual is ingesting or injecting the hormone. [↑](#footnote-ref-8)
8. WHO. Appropriate medicines: options for pre-exposure prophylaxis [Internet]. Geneva: WHO; 2018 [cited 2022 Nov 15]. Available from: <https://www.who.int/publications/i/item/WHO-CDS-HIV-18.22>. [↑](#footnote-ref-9)
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13. Molina JM, Capitant C, Spire B, Pialoux G, Cotte L, Charreau I, et al. On-demand pre-exposure prophylaxis in men at high risk for HIV-1 infection. N Engl J Med. 2015 Dec 3;373(23):2237–46. [↑](#footnote-ref-14)
14. *This list is provided to support interpretation of this guidance and is not inclusive of all gender identities or terms that may be used by people with diverse gender identities to describe themselves and/or their communities. Starting and stopping oral PrEP should be based on the factors in the first column.* [↑](#footnote-ref-15)
15. *Injection drug use is mentioned in this guidance; however, first-line prevention strategies for people who inject drugs are needle exchange and/or drug use harm reduction and treatment. Daily oral PrEP has some preventative effects for this population and should be offered as part of a larger prevention package.* [↑](#footnote-ref-16)
16. People assigned female at birth may include cisgender women, transgender men, and some nonbinary people. [↑](#footnote-ref-17)
17. Bunge K, Balkus JE, Fairlie L, Mayo AJ, Nakabiito C, Mgodi N, et al. DELIVER: A safety study of a dapivirine vaginal ring and oral PrEP for the prevention of HIV during pregnancy. J Acquir Immune Defic Syndr. Forthcoming 2023. doi: 10.1097/QAI.0000000000003312 [↑](#footnote-ref-18)
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29. Landovitz RJ, Li S, Grinsztejn B, Dawood H, Liu AY, Magnus M, et al. Safety, tolerability, and pharmacokinetics of long acting injectable cabotegravir in low-risk HIV uninfected individuals: HPTN 077, a phase 2a randomized controlled trial. PLoS Med. 2018 Nov 8;15(11):e10026900. [↑](#footnote-ref-30)
30. While AHI should be assessed for prospective PrEP clients regardless of method, those suspected of AHI may still be able to use the ring. If AHI is suspected, strongly encourage the person to return in 4-6 weeks for re-testing and not wait for 3 months. [↑](#footnote-ref-31)
31. Clients may use the PrEP ring while awaiting HIV re-testing, if ring is an appropriate alternative HIV prevention method given a client’s needs and preferences. [↑](#footnote-ref-32)
32. Bunge KE, et al. 17. [↑](#footnote-ref-33)
33. Owor M, et al. 20. [↑](#footnote-ref-34)
34. WHO. Implementation tool for pre-exposure prophylaxis of HIV infection – Integrating STI services. [Internet]. Geneva: WHO; 2022 [cited 2022 Nov 15]. Available from <https://www.who.int/publications/i/item/9789240057425>. [↑](#footnote-ref-35)