

# Pre-Exposure Prophylaxis (PrEP) to Prevent HIV During Periconception, Antepartum, and Postpartum Periods

Updated: January 31, 2024

Reviewed: January 31, 2024

Panel's Recommendations
<ul style="list-style-type: none"><li>• Health care providers should discuss PrEP with all sexually active people without HIV, including individuals who are trying to conceive, pregnant, postpartum, or breastfeeding, to prevent HIV acquisition (AII); counseling should include the benefits of PrEP to prevent HIV acquisition and perinatal transmission (AI) and potential adverse effects of PrEP during periconception, pregnancy, postpartum, and breastfeeding periods (AII). Health care providers should offer PrEP to those who desire PrEP or have specific indications for PrEP (AII).</li><li>• The preferred PrEP option for HIV prevention in people who have receptive vaginal sex during pregnancy and breastfeeding is tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) (AII). TDF/FTC is currently the only U.S. Food and Drug Administration (FDA)-approved PrEP option with known safety and efficacy data during pregnancy and breastfeeding. People who become pregnant while using TDF/FTC as PrEP can continue PrEP throughout pregnancy and breastfeeding. Risk for HIV acquisition should be reassessed, and people should be counseled regarding the benefits and risks of PrEP use in pregnancy and during breastfeeding (AII).</li><li>• Providers should counsel patients about the importance of daily adherence to oral TDF/FTC PrEP to prevent HIV acquisition (AI). Patients should be counseled to use additional HIV prevention strategies (e.g., condoms) for the first 20 days after initiating TDF/FTC PrEP (BII). For patients with a planned PrEP discontinuation, people should continue use for 7 to 28 days after their last potential vaginal exposure (BII). Given the lack of data, episodic or non-daily PrEP is not recommended for protection against vaginal exposure to HIV (AIII).</li><li>• Providers should offer routine PrEP follow-up, including testing for HIV every 3 months and counseling on signs and symptoms of acute retroviral syndrome (AI) (see <a href="#">Center for Disease Control and Prevention's PrEP for the Prevention of HIV in the United States 2021 Update</a> and <a href="#">Pregnancy and Postpartum HIV Testing and Identification of Perinatal and Postnatal HIV Exposure</a>). Consider more frequent testing when clinically indicated (e.g., adherence challenges, nonstandard visit schedule).</li><li>• Long-acting injectable cabotegravir (CAB-LA) is FDA-approved for people with vaginal exposure to HIV; however, for people with PrEP indications in pregnancy, CAB-LA dosing, efficacy, and safety remain unknown. If a person receiving cabotegravir (CAB) PrEP becomes pregnant, the limited available safety data and long half-life of CAB should be discussed with the patient with shared decision-making around ongoing PrEP use and options (AIII). Consider expert consultation.</li></ul>
<p><b>Rating of Recommendations:</b> A = Strong; B = Moderate; C = Optional</p> <p><b>Rating of Evidence:</b> I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion</p>

HIV **pre-exposure prophylaxis** (PrEP) is the use of specific antiretroviral (ARV) drugs to prevent HIV acquisition. Susceptibility to HIV acquisition is greater during the periconception period, throughout pregnancy, and through 6 months postpartum. Acute or recent HIV infection during pregnancy or breastfeeding is associated with an increased risk of perinatal HIV transmission (see [Early \[Acute and Recent\] HIV Infection](#)).<sup>1,2</sup> The Panel on Treatment of HIV Infection During Pregnancy and Prevention of Perinatal Transmission (the Panel) recommends that people without HIV who are planning to have a child or who are pregnant, postpartum, or breastfeeding should be

routinely counseled about PrEP for HIV prevention and offered PrEP or referred for PrEP services when indicated to prevent HIV acquisition and potential perinatal HIV transmission.<sup>3</sup> In cases when the individual has a partner with HIV and that partner is on antiretroviral therapy (ART) with sustained viral suppression, HIV is not transmitted through condomless sexual intercourse (see [Reproductive Options When One or Both Partners Have HIV](#)).

The use of combination tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) as daily oral PrEP to reduce HIV acquisition was approved by the U.S. Food and Drug Administration (FDA) in 2012 and the use of cabotegravir (CAB) as long-acting injectable PrEP was approved in 2021. When taken as prescribed, TDF/FTC provides greater than 90% protection against HIV acquisition. The HIV Prevention Trials Network (HPTN) 084 study found CAB to be 89% more effective than TDF/FTC.<sup>4</sup> Of the FDA-approved PrEP agents for people with receptive vaginal exposure, TDF/FTC is currently the only option with demonstrated safety in pregnancy and during breastfeeding. Tenofovir alafenamide (TAF)/FTC has not yet been studied for efficacy in people with vaginal exposure; therefore, TAF/FTC is not recommended for this population, including during pregnancy and postpartum.<sup>5,6</sup> The guidance in this section focuses on the use of TDF/FTC as PrEP during periconception, antepartum, and postpartum periods (through 6 months postpartum and/or throughout breastfeeding). Information about other PrEP agents is included below in “What Is Known About Other PrEP Agents During Periconception, Antepartum, and Postpartum Periods?”

Most research on PrEP cited in this section was conducted with participants who self-identified as women (presumed to be predominantly cisgender women). However, individuals who do not identify as women (i.e., transgender men, genderqueer or nonbinary individuals) can become pregnant, give birth, and breast/chestfeed. PrEP should be offered and promoted for all individuals with an indication for PrEP using a gender-affirming approach to care (see [Perinatal HIV Prevention for Transgender and Gender-Diverse People Assigned Female at Birth](#) and [Transgender People with HIV in the Adult and Adolescent Antiretroviral Guidelines](#)). Patients should be asked about their gender identity, including the pronouns they use, how they want to be referred to as a parent (e.g., birth parent, mother, father, another name), and terms they prefer to use (e.g., breastfeeding, chestfeeding).

## Clinical Management of PrEP Use During Periconception, Antepartum, and Postpartum Periods

### *Initiating PrEP*

The Centers for Disease Control and Prevention (CDC) provides guidelines (see [PrEP for the Prevention of HIV in the United States 2021 Update](#)) for discussing PrEP with all adults and adolescents who have sex or inject drugs.<sup>3</sup> The Panel recommends that PrEP be discussed with all people without HIV who are planning for pregnancy and/or sexually active and those who are pregnant or postpartum. To address underutilization of PrEP and disparities in PrEP use among women,<sup>7</sup> it is important for clinicians and clinical programs to consider strategies such as provider education, standard protocols, clinic champions, and resource tools to optimize implementation and reduce barriers to accessing PrEP.<sup>8-11</sup> PrEP can be prescribed to those who request it and is also specifically indicated for individuals who—

- Have a history of bacterial sexually transmitted infection (STI), including gonorrhea, syphilis, or chlamydia<sup>12,13</sup>;

- Have infrequent condom use with one or more partners of unknown HIV status, especially within a sexual network **with high HIV prevalence**;
- Are taking non-occupational post-exposure prophylaxis (nPEP) and anticipate ongoing indications for prevention, or have used multiple courses of nPEP<sup>14</sup>;
- Engage in transactional sex;
- Have substance use disorder and/or substance use associated with sex;
- Have a partner with HIV with **unknown or inconsistent** virologic suppression;
- Have a history of experiencing intimate partner violence<sup>15</sup>; *or*
- Have a partner with any of the factors listed above.

Providers should counsel people with HIV whose partners may have indications for PrEP about benefits and indications for PrEP. When prescribing PrEP, clinicians should:

- Counsel individuals about potential risks and benefits of PrEP and all available strategies for reducing HIV acquisition risks during periconception, antepartum, and postpartum periods (see [Reproductive Options When One or Both Partners Have HIV](#)). People who become pregnant while using TDF/FTC PrEP can continue PrEP throughout their pregnancy.
- Explain that condomless sex with a partner who has sustained viral suppression is associated with no risk of HIV sexual transmission.<sup>16-19</sup>
- **Explain that** although it is unknown how long PrEP needs to be taken in order to be protected from vaginal HIV exposure, daily oral TDF/FTC **must be taken for at least 20 days before drug levels are high in cervicovaginal tissues. Therefore, the Panel recommends 20 days of PrEP before** considering an individual fully protected **from HIV acquisition via vaginal exposure**. See Time to Protection below for more details.
- Counsel about the importance of adherence and suggest adherence supports, such as use of a pillbox (see Adherence Support below).
- Counsel that episodic, “**2-1-1,**” “on-demand,” and/or non-daily PrEP has not been **evaluated** for vaginal exposure.
- Counsel individuals who are taking PrEP about the symptoms associated with acute HIV infection and instruct them to contact their provider immediately for HIV testing and further evaluation if symptoms occur (see [Early \[Acute and Recent\] HIV Infection](#)). Individuals experiencing symptoms of acute HIV infection should be advised to use a condom during sex, stop attempts at conception, and stop breastfeeding.
- **Explain that** PrEP does not protect against other STIs. Condom use is important for reducing STI acquisition.
- Regularly assess and discuss ongoing needs for PrEP.
- Inquire about partner status and offer partner HIV testing.
- **Be aware that** additional prescribing details, including for same day PrEP start and PrEP follow-up via telehealth, are offered in the CDC Guidelines for PrEP (see [PrEP for the Prevention of HIV in the United States 2021 Update](#)).<sup>3</sup>

- For people who become pregnant while receiving PrEP, clinicians are encouraged strongly to register them with the [Antiretroviral Pregnancy Registry](#). The purpose of the Antiretroviral Pregnancy Registry is to detect any major teratogenic effect involving any of the registry drugs to which pregnant people are exposed, including ARV drugs used for PrEP.

An individual's indications for PrEP may change across periconception, antepartum, and postpartum periods. Therefore, discussions regarding the need for PrEP should be ongoing.

## ***Laboratory Testing***

Recommended laboratory testing for individuals receiving PrEP includes—

- HIV diagnostic testing with an antigen/antibody combination immunoassay at baseline. For people exposed to antiretrovirals as PrEP, delays can be seen in antigen/antibody detection during acute infection.<sup>20</sup> Therefore, the CDC recommends antigen/antibody combination immunoassay as well as HIV-RNA testing every 3 months, or more frequently if indicated based on clinical symptoms, for people taking tenofovir-containing PrEP regimens.
- HIV testing (i.e., antigen/antibody combination immunoassay, as well as HIV-RNA testing) for individuals taking PrEP during pregnancy should include HIV testing at entry into antenatal care, with re-testing in the second and third trimester. More frequent testing may be appropriate when clinically indicated (e.g., known adherence challenges) (see [Pregnancy and Postpartum HIV Testing and Identification of Perinatal and Postnatal HIV Exposure](#)).
- In the case of documented new HIV infection, discontinuation of PrEP and immediate referral to an HIV specialist for [initiation of ART are recommended](#). If the patient is pregnant, they should receive appropriate care to prevent perinatal transmission. See [Early \(Acute and Recent\) HIV Infection and Pregnant People with HIV Who Have Previously Received Antiretroviral Medications but Are Not Currently on Antiretroviral Medications](#).
- Renal function testing at baseline and then every 12 months for people <50 years of age and/or with estimated creatinine clearance (CrCl) over 90 mL/min. Otherwise, renal function should be monitored every 6 months. TDF/FTC as PrEP should not be initiated in patients with a confirmed calculated CrCl <60 mL/min. Clinicians should discontinue daily TDF/FTC as PrEP if a patient develops a confirmed calculated CrCl <50 mL/min.
- Testing for hepatitis B virus (HBV) infection for patients initiating PrEP, but PrEP initiation need not be delayed while awaiting results. Individuals with no prior HBV infection who lack HBV immunity should be vaccinated if they have not received HBV vaccination, or consider reimmunization if they have been vaccinated but still lack immunity. Individuals with chronic HBV should be counseled regarding the risk for possible hepatitis flares when tenofovir-based PrEP is stopped.<sup>21</sup>
- Pregnancy testing at baseline and then as indicated.
- Testing for STIs (gonorrhea, chlamydia, syphilis) at baseline. Testing every 6 months is recommended for gonorrhea and syphilis for women. Annual testing for chlamydia is also recommended. [More frequent testing can be offered as clinically indicated](#).
- [Reference to](#) additional information and details about recommended laboratory testing in the CDC's [PrEP for the Prevention of HIV Infection in the United States 2021 Update](#), as needed.

## ***Time to Protection***

High adherence to daily pills is required to achieve effective drug concentrations of TDF and FTC in vaginal and cervical tissues. Studies in nonpregnant women demonstrate that it may take up to 20 days to reach maximum intracellular concentrations of tenofovir and/or FTC in cervicovaginal tissue, compared to only 7 days in anal tissues.<sup>22-24</sup> Although pharmacokinetic (PK) data are limited in pregnant women, they suggest that pregnant women taking daily PrEP experience lower tenofovir drug levels.<sup>25,26</sup> Given the increased volume of distribution and concomitant lower levels of TDF/FTC in plasma, the Panel recommends continued use of other prevention strategies until PrEP has been taken for at least 20 days and protection against transmission can be assumed in pregnant or postpartum PrEP users. Six or seven doses per week (or daily dosing) are needed to maintain drug levels in cervicovaginal tissue in nonpregnant women.<sup>27</sup> When people initiate PrEP and have not yet reached protective drug levels or struggle with daily adherence, other strategies (e.g., condoms) should be used to prevent HIV.

For people planning to discontinue daily oral PrEP, ongoing use for 7 to 28 days after last HIV exposure is recommended. This time frame aligns with recommendations for post-exposure prophylaxis.<sup>28</sup>

## ***Adherence Support***

Before initiating PrEP, providers should assess barriers to PrEP adherence and address concerns regarding PrEP use during the periconception, antepartum, and postpartum periods. Opportunities to promote adherence and mitigate barriers to adherence should be addressed at each visit. Data suggest that some adherence challenges stem from adherence fatigue, low perceptions of personal risk, stigma, cost, misinformation about PrEP, peer perspectives, mental health challenges, and intimate partner violence.<sup>29-31</sup> Based on barriers, providers can discuss strategies tailored to each patient's needs to promote adherence and maximize benefits. Approaches include providing accurate information about the risks and benefits of PrEP, developing reminder strategies, and identifying supportive individuals as part of the health care team or the patient's social network who can provide social support toward PrEP adherence. PrEP services are ideally delivered in a comprehensive manner and address social determinants of health—including how clients will access PrEP and related services—and address housing instability, access to health insurance, and transportation because these factors have been shown to interfere with adherence. The CDC provides a [PrEP webpage](#) and a [PrEP chapter](#).

## ***Contraception***

Contraception is an important component of reproductive health care for people receiving PrEP who do not want to become pregnant.<sup>16</sup> No known significant drug–drug interactions exist between TDF and different modes of hormonal contraception used during periconception and the postpartum period.<sup>32-34</sup> For additional information, refer to CDC's [U.S. Medical Eligibility Criteria for Contraceptive Use, 2016](#) and [Update to U.S. Medical Eligibility Criteria for Contraceptive Use, 2016: Updated Recommendations for the Use of Contraception Among Women at High Risk for HIV Infection](#).

## Background on Use of PrEP During Periconception, Antepartum, and Postpartum Periods

Women account for nearly 20% of new HIV diagnoses in the United States yet only account for 7% of people prescribed PrEP.<sup>35,36</sup> PrEP is recommended for all people with potential exposure to HIV.<sup>3,37</sup> Although data about the use of PrEP among periconception, pregnant, and postpartum people are less robust than for nonpregnant people,<sup>38</sup> PrEP is highly efficacious for women, and a large body of data from pregnant women using TDF/FTC as treatment for HIV and HBV suggests these agents are safe for pregnant and breastfeeding women and their infants.<sup>39-42</sup>

Susceptibility to HIV acquisition is greater during periconception, antepartum, and early postpartum periods through 6 months. Data suggest that people trying to conceive are at higher risk for HIV acquisition, likely due to increased condomless sex.<sup>43,44</sup> The increase in HIV acquisition risk continues in pregnancy and is likely due to a combination of behavioral factors—such as no longer needing to use condoms for contraception—and biological factors that include increased innate and suppressed adaptive immunity, increased genital tract inflammation, alterations in the vaginal microbiome, decreased integrity of the vaginal epithelium, and both gross trauma and microtrauma to the genital tract during delivery.<sup>45-47</sup> HIV incidence among women during pregnancy and postpartum is two to six times greater than **HIV incidence** outside of pregnancy.<sup>47-51</sup> Two large HIV prevention studies conducted in African countries demonstrated that the probability of HIV acquisition per condomless sex act increases beginning in early pregnancy and peaks in the early postpartum period (in data analyzed from birth through 24 weeks postpartum in most studies). After adjustment for age, use of PrEP, and male partner HIV viral load, the probability of HIV acquisition was significantly higher throughout pregnancy and the postpartum period (adjusted relative risk 2.76; 95% **confidence interval** [CI], 1.58–4.81).<sup>52</sup> In addition, people who acquire HIV while pregnant or breastfeeding are more likely to transmit HIV to their infant.<sup>53-55</sup>

For people who become pregnant while receiving PrEP, including drugs not yet approved for PrEP during pregnancy (e.g., long-acting injectable CAB [CAB-LA], TAF), clinicians are strongly encouraged to register them with the [Antiretroviral Pregnancy Registry](#) as early in pregnancy as possible.

## Efficacy of **Tenofovir Disoproxil Fumarate/Emtricitabine** as PrEP During Periconception, Pregnancy, and Postpartum Periods

Data from two randomized controlled trials that enrolled heterosexual-identifying men and women demonstrated the efficacy of TDF/FTC as PrEP to be 63% to 75%. In women with detectable drug levels (or taking PrEP), PrEP protected against 90% of incident transmissions.<sup>56</sup> In a meta-analysis of all available clinical trial data, modeling suggested that if women adhere to at least 75% of doses, PrEP decreases HIV acquisition by 61% (relative risk 0.39; 95% CI, 0.25–0.60).<sup>57</sup>

Although people planning for pregnancy were not enrolled in these clinical trials, subsequent data suggest that PrEP uptake and adherence are high during periconception periods.<sup>58-61</sup>

## ***Safety of [Tenofovir Disoproxil Fumarate/Emtricitabine](#) as PrEP for Women, Including Those Who Are Pregnant or Breastfeeding***

Currently available data suggest that the benefits of TDF/FTC as PrEP to prevent HIV [during periconception, pregnancy, and breastfeeding periods](#) outweigh any potential toxicities. PrEP should be promoted as an HIV prevention strategy during periconception, pregnancy, and postpartum periods.<sup>39,62</sup> Additional data and primary sources describing what is known about TDF and FTC on birth outcomes, renal and bone effects for women, and renal and bone effects for infants exposed to TDF/FTC *in utero* or while breastfeeding are available in the [Tenofovir Disoproxil Fumarate](#) and [Emtricitabine](#) sections of these guidelines.

### **What Is Known About Other PrEP Agents During Periconception, Antepartum, and Postpartum Periods?**

Efficacy studies evaluating TAF/FTC as PrEP in people with vaginal exposure have not been completed. Therefore, the Panel does not recommend TAF/FTC as PrEP for this population, including during pregnancy and postpartum. Additionally, TDF/FTC PK data cannot be readily extrapolated to TAF/FTC.<sup>5,6</sup>

Long-acting injectable CAB-LA is FDA-approved for use as PrEP in adults and adolescents. Data on the PK of CAB injections initiated or continued during pregnancy are not available; thus, the optimal dose and dosing interval during pregnancy are unknown. Limited PK tail data and safety data are reassuring for individuals who became pregnant on CAB-LA<sup>63-69</sup> (see [Cabotegravir section](#)). For people with PrEP indications who are planning for pregnancy, the optimal time to conceive after stopping injections is unknown.<sup>69,70</sup>

CDC guidance notes that CAB for PrEP may be initiated or continued in people who become pregnant while receiving injections when anticipated benefits outweigh the risks. For people with PrEP indications in pregnancy, as CAB dosing, efficacy, and other details are still unknown, TDF/FTC is preferred for initiation during pregnancy given the more robust safety and efficacy data.<sup>39,42,71,72</sup> If a person receiving CAB for PrEP becomes pregnant, the limited available safety data and long half-life of CAB should be discussed, and the patient and provider should engage in shared decision-making about whether to continue CAB or switch to TDF/FTC. Expert consultation may be beneficial to make the best decision about continuing or discontinuing CAB for PrEP in light of evolving data and knowledge. Important considerations include the following:

- Given the long half-life of injectable CAB, exposure from dosing during pre-pregnancy/early pregnancy is likely to continue throughout the pregnancy; thus, the benefit of stopping CAB at pregnancy is uncertain.
- CAB has structural similarities to other ARV drugs (e.g., dolutegravir) for which there are reassuring safety profiles in pregnancy.
- If CAB is stopped during pregnancy and HIV exposure is ongoing, TDF/FTC as PrEP and additional strategies for HIV prevention should be offered.

The dapivirine vaginal ring also reduces the risk of HIV acquisition via receptive vaginal exposure but has been permanently withdrawn from the FDA approval process.<sup>73</sup> Oral TAF/FTC has not yet been demonstrated to be effective for HIV prevention in people with receptive vaginal exposure.

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