

Provider Information Sheet – PrEP During Conception, Pregnancy, and Breastfeeding

Information for Clinicians

Counseling Patients about PrEP Use During Conception, Pregnancy, and Breastfeeding

PrEP use may be one of several options to help protect the HIV-negative male or female partner in a heterosexual HIV-discordant couple during attempts to conceive^{1,2}.

DHHS Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission

Panel's Recommendations on Reproductive Options for HIV-Concordant and Serodiscordant Couples

- For serodiscordant couples who want to conceive, expert consultation is recommended so that approaches can be tailored to specific needs, which may vary from couple to couple (**AIII**). It is important to recognize that treatment of the infected partner may not be fully protective against sexual transmission of HIV.
- Partners should be screened and treated for genital tract infections before attempting to conceive (**AII**).
- For HIV-infected females with HIV-uninfected male partners, the safest conception option is artificial insemination, including the option of self-insemination with a partner's sperm during the peri-ovulatory period (**AIII**).
- For HIV-infected men with HIV-uninfected female partners, the use of sperm preparation techniques coupled with either intrauterine insemination or *in vitro* fertilization should be considered if using donor sperm from an HIV-uninfected male is unacceptable (**AII**).
- For serodiscordant couples who want to conceive, initiation of antiretroviral therapy (ART) for the HIV-infected partner is recommended (**AI** for CD4 T-lymphocyte (CD4-cell) count ≤ 550 cells/mm³, **BIII** for CD4-cell count > 550 cells/mm³). If therapy is initiated, maximal viral suppression is recommended before conception is attempted (**AIII**).
- Periconception administration of antiretroviral pre-exposure prophylaxis (PrEP) for HIV-uninfected partners may offer an additional tool to reduce the risk of sexual transmission (**CIII**). The utility of PrEP of the uninfected partner when the infected partner is receiving ART has not been studied.

Rating of Recommendations: **A** = Strong; **B** = Moderate; **C** = Optional

Rating of Evidence: **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

The following information is provided to help you inform your patients of current information about potential risks and benefits of PrEP use so that you and your patients can make an informed decision.

Key Points

- Provide education about PrEP and other methods of conception that minimize the risk of HIV transmission to both members of an HIV-discordant couple whenever possible.
- During counseling, include discussion of what is currently known and unknown about
 - » Potential benefits
 - » Potential risks
- If you prescribe PrEP, include the following in counseling:
 - » Importance of adherence to daily doses of medication
 - » Importance of continuing condom use after conception to protect against sexually transmitted infections and to add protection against HIV infection
 - » Signs and symptoms of acute HIV infection and the need for urgent HIV testing if HIV infection is suspected

For an HIV-negative man planning pregnancy with an HIV-positive female partner

Options

Reducing the risk of HIV acquisition by an HIV-negative man during conception can be achieved by use of the following, singly or ideally in combination^{3,4}:

- Antiretroviral treatment of the HIV-positive female partner to achieve an undetectable viral load⁵
- STI diagnosis and any indicated treatment for both partners before conception attempts
- Daily, oral doses of TDF/FTC beginning 1 month before a conception attempt and continuing for 1 month after a conception attempt
- Intravaginal insemination⁶ (either at home or in the clinic) with a fresh semen sample

OR

- Limit sex without a condom (natural conception) to peak fertility times identified by home or laboratory tests for ovulation.

Potential Benefits of PrEP use

In clinical trials with heterosexually active adults, daily oral PrEP with TDF/FTC was safe and reduced the risk of HIV acquisition by an average of 63%–75%. Higher levels of protection ($\geq 90\%$) were found among persons whose drug levels in their blood indicated that they had consistently taken the medication^{7,8}.

Potential Risks of PrEP use

In PrEP trials, follow-up with persons taking medication has been conducted for an average of 1–4 years. Although no serious health risks were associated with PrEP use by HIV-uninfected adults, the long-term safety of PrEP has not yet been determined.

For an HIV-negative woman planning pregnancy with an HIV-positive male partner

Options

Reducing the risk of HIV acquisition by an HIV-negative woman during conception can be achieved by use of the following, singly or ideally in combination^{3,4}:

- Antiretroviral treatment of the HIV-positive male partner to achieve an undetectable viral load⁵
- STI diagnosis and any indicated treatment for both partners before conception attempts
- Daily, oral doses of TDF/FTC beginning 1 month before a conception attempt and continuing for 1 month after a conception attempt
- Intravaginal⁶ or intrauterine insemination, or intracytoplasmic sperm injection with a semen sample processed by “sperm washing” and confirmed to have a negative test result for the presence of remnant HIV⁹

OR

- Limit sex without a condom (natural conception) to peak fertility times identified by home or laboratory tests for ovulation in the female partner¹⁰.

Potential Benefits of PrEP use

In clinical trials with heterosexually active adults, daily oral PrEP with TDF/FTC was safe and reduced the risk of HIV acquisition by an average of 63%–75%. Higher levels of protection ($\geq 90\%$) were found among persons whose drug levels in their blood indicated that they had consistently taken the medication^{7,8}.

The risk of HIV acquisition increases during pregnancy¹¹, as does the risk of HIV transmission to an infant born to a mother who becomes infected during pregnancy or breastfeeding¹² Therefore, an HIV-negative woman whose sexual partner/spouse has HIV infection may benefit from continuing PrEP use throughout her pregnancy and breastfeeding to protect herself and her infant.

Potential Risks of PrEP use

In PrEP trials, follow-up with persons taking medication has been conducted for an average of 1–4 years. Although no serious health risks were associated with PrEP use by HIV-uninfected adults, the long-term safety of PrEP has not yet been determined.

In PrEP trials women were taken off medication as soon as pregnancy was detected. During these trials, no health problems have been associated with PrEP use by women in early pregnancy or for their offspring. However, the long-term safety of PrEP taken HIV-uninfected women after fetal (during pregnancy) or infant (during breastfeeding) exposure is not yet determined.

No adverse effects have been found among infants exposed to TDF/FTC when the medications were taken as part of a treatment regimen for HIV-infected women during pregnancy¹³⁻¹⁵ or during breastfeeding (for which data suggest limited drug exposure^{16,17}).

If you prescribe PrEP to a woman while pregnant, you are encouraged to prospectively and anonymously submit information about the pregnancy to the Antiretroviral Use in Pregnancy Registry (<http://www.apregistry.com/>).

References

1. Centers for Disease C, Prevention. Interim guidance for clinicians considering the use of preexposure prophylaxis for the prevention of HIV infection in heterosexually active adults. *MMWR. Morbidity and mortality weekly report*. Aug 10 2012;61(31):586-589.
2. Panel on treatment of HIV-infected pregnant women and prevention of perinatal transmission. Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States. 2012. <http://aidsinfo.nih.gov/ContentFiles/PerinatalGL.pdf>. Accessed 14 September 2012.
3. Lampe MA, Smith DK, Anderson GJE, Edwards AE, Nesheim SR. Achieving safe conception in HIV-discordant couples: the potential role of oral preexposure prophylaxis (PrEP) in the United States. *Am J Obstet Gynecol*. Jun 2011;204(6).
4. Matthews LT, Smit JA, Cu-Uvin S, Cohan D. Antiretrovirals and safer conception for HIV-serodiscordant couples. *Current Opinion in HIV and AIDS*. 2012;7(6):569-578.
5. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med*. Aug 11 2011;365(6):493-505.
6. Mmeje O, Cohen CR, Cohan D. Evaluating safer conception options for HIV-serodiscordant couples (HIV-infected female/HIV-uninfected male): a closer look at vaginal insemination. *Infectious diseases in obstetrics and gynecology*. 2012;2012.
7. Baeten JM, Donnell D, Ndase P, et al. Antiretroviral Prophylaxis for HIV Prevention in Heterosexual Men and Women. *New England Journal of Medicine*. 2012;367(5):399-410.
8. Thigpen MC, Kebaabetswe PM, Paxton LA, et al. Antiretroviral Preexposure Prophylaxis for Heterosexual HIV Transmission in Botswana. *New England Journal of Medicine*. 2012;367(5):423-434.
9. Semprini AE, Macaluso M, Hollander L, et al. Safe conception for HIV-discordant couples: insemination with processed semen from the HIV-infected partner. *Am J Obstet Gynecol*. 5// 2013;208(5):402.e401-402.e409.
10. Vernazza PL, Graf I, Sonnenberg-Schwan U, Geit M, Meurer A. Preexposure prophylaxis and timed intercourse for HIV-discordant couples willing to conceive a child. *Aids*. Oct 23 2011;25(16):2005-2008.
11. Mugo NR, Heffron R, Donnell D, et al. Increased risk of HIV-1 transmission in pregnancy: a prospective study among African HIV-1-serodiscordant couples. *Aids*. Sep 24 2011;25(15):1887-1895.
12. Johnson LF, Stinson K, Newell M-L, et al. The contribution of maternal HIV seroconversion during late pregnancy and breastfeeding to mother-to-child transmission of HIV. *Journal of Acquired Immune Deficiency Syndromes (1999)*. 2012;59(4):417.
13. Foster C, Lyall H, Olmscheid B, Pearce G, Zhang S, Gibb DM. Tenofovir disoproxil fumarate in pregnancy and prevention of mother-to-child transmission of HIV-1: is it time to move on from zidovudine? *HIV medicine*. Aug 2009;10(7):397-406.
14. Gibb DM, Kizito H, Russell EC, et al. Pregnancy and Infant Outcomes among HIV-Infected Women Taking Long-Term ART with and without Tenofovir in the DART Trial. *Plos Med*. 2012;9(5):e1001217.
15. The Antiretroviral Pregnancy Registry. Interim REport: 1 January 1989 through 31 January 2013. 2013; http://www.apregistry.com/forms/interim_report.pdf. Accessed 30 September 2013.
16. Benaboud S, Pruvost A, Coffie PA, et al. Concentrations of tenofovir and emtricitabine in breast milk of HIV-1-infected women in Abidjan, Cote d'Ivoire, in the ANRS 12109 TEmAA Study, Step 2. *Antimicrobial agents and chemotherapy*. Mar 2011;55(3):1315-1317.
17. Mirochnick M, Best BM, Clarke DF. Antiretroviral pharmacology: special issues regarding pregnant women and neonates. *Clinics in perinatology*. Dec 2010;37(4):907-927.