Pre-Exposure Prophylaxis (PrEP)

July 2012

For more basic fact sheets in this series on emerging HIV prevention strategies visit www.avac.org

What is PrEP?

Pre-exposure prophylaxis, or PrEP, is a strategy that involves use of antiretroviral medications (ARVs) to reduce the risk of HIV infection via sexual exposure. All of the current effectiveness and follow-on trials are testing tenofovir-based regimens—using either TDF/FTC (an antiretroviral containing tenofovir (TDF) and emtricitabine (FTC) that is sold under the brand name Truvada) or TDF (an antiretroviral pill marketed under the brand name Viread). *Based on the data that have been collected to date the US Food and Drug Administration (FDA) announced its approval of daily oral TDF/FTC for PrEP. This is the first ARV to be approved for HIV prevention in HIV-negative adults.*

What are the data from efficacy trials of tenofovir-based PrEP[1]?

To date, three trials have found evidence of HIV prevention benefit using tenofovir-based PrEP:[2]

- The multi-country iPrEx trial showed that once-daily oral TDF/FTC reduced risk of HIV by 42 percent overall in gay men and transgender women.
- The Partners PrEP trial discontinued the placebo arm of the study after an interim review of trial data by its independent data and safety monitoring board (DSMB) showed that both once-daily oral TDF/FTC and once-daily oral TDF are effective at reducing risk of HIV infection for the HIV-negative partner in the heterosexual HIV-serodiscordant couples enrolled in the trial (one partner is HIV-negative and one HIV-positive)—TDF/FTC by 73 percent overall and TDF by 62 percent overall. Data collection is ongoing through the end of 2012.
- The TDF2 trial in heterosexual men and women in Botswana showed that once-daily oral TDF/FTC reduced risk of HIV infection by 63 percent overall.

To date, two trials have found no evidence of benefit using tenofovir-based PrEP:

- FEM-PrEP, which evaluated once-daily oral TDF/FTC in women in east and southern Africa found that while the product was safe, there was no evidence of benefit and halted early based on a recommendation from the trial's independent DSMB. In early 2012, the FEM-PrEP trial team presented analysis suggesting that, in FEM-PrEP, low levels of adherence could explain the trial outcome.
- VOICE (launched as a five-arm trial of once-daily oral TDF/FTC, once-daily oral TDF and daily 1% tenofovir gel) halted its oral TDF arm after its independent DSMB determined that while the product was safe, there was no possibility that TDF would reduce HIV risk in the context of the trial. The 1% tenofovir gel arm was halted for the same reason. The TDF/FTC arm is ongoing and results could be available in 2013.

Follow-up research is ongoing to learn more about the results in all of the trials described above:

- The iPrEx Open-Label Extension (iPrEx OLE) study provides daily TDF/FTC to HIV-negative iPrEx trial participants in the context of less intensive monitoring and follow-up. This trial has completed enrollment. Results from data analysis may be available in 2014.
- The Partners PrEP trial has randomized all HIV-negative placebo recipients who gave informed consent to receive either TDF/FTC or TDF—the trial is expected to end in late 2012/early 2013.
- TDF2 is planning a follow-on trial of once-daily oral TDF/FTC in men and women that will learn more about the effect of the intervention in the context of less intensive real-world monitoring.
- VOICE and FEM-PrEP trial teams are continuing to analyze data on adherence, risk behavior and other factors that might have affected the effectiveness of TDF and TDF/FTC, respectively. A peer-reviewed publication with data from FEM-PrEP was released in July 2012.

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[1] Please visit *www.avac.org/prep* and *www.avac.org/pxrd* for up-to-date timelines tracking ongoing research.

[2] All of the safety and effectiveness trials described here offered participants PrEP or an identical placebo pill plus a standard prevention package. For more on HIV prevention trial design and standard of prevention see *www.avac.org/trials*.

There is an ongoing efficacy study in injecting drug users in Thailand. A range of additional trials are ongoing including research on intermittent, less-frequent dosing strategies (all of the efficacy trials to date evaluated once-daily regimens) and other medications. For a comprehensive review of completed and ongoing PrEP trials, visit *www.avac.org/trials/prep*.

What are some key developments or conclusions from PrEP effectiveness trials so far?

- There were no significant side effects observed in trials of tenofovir-based PrEP in any of the trials.
- Adherence is essential. Each of the trials that found benefit also found that people who had high levels of adherence had high levels of protection. Lower adherence was associated with low or no protection.
- HIV drug resistance to PrEP medications was observed, but primarily in participants who were HIV-positive and in the "window period" of early infection when they began taking PrEP. These individuals tested HIV-negative on the trials' screening tests. This reinforces the importance of regular testing for anyone initiating or taking PrEP.
- TDF/FTC and TDF are both key drugs for treating HIV in HIV-positive people. Access to tenofovir-based PrEP can only be explored in the context of sustained ART access for HIV-positive people worldwide.

What is happening now?

Regulatory and guidance activities: On July 16, the US FDA announced its approval of Gilead Science Inc.'s application for approval of daily oral TDF/FTC as PrEP. The US CDC is developing US Public Health Service (PHS) guidelines for the use of TDF/FTC as PrEP, which are expected late 2012/early 2013. These will update the interim guidance on PrEP in gay men and other MSM released by CDC in 2011. They will be posted for public comment prior to publication. The Southern African HIV Clinicians Society issued guidance in June 2012 for use of TDF/FTC as PrEP in gay men and other men who have sex with men. The World Health Organization (WHO) is expected to release rapid advice guidance on PrEP in July 2012. The European Medicines Agency (Europe's regulatory body) is updating its concept paper on the development of medicines to prevent HIV infection. Some groups have chosen a slower approach. The British HIV Association and the British Association for Sexual Health and HIV have stated that, based on available data, PrEP should only be prescribed in the context of a clinical trial until more data are available.

Demonstration Projects: Much more needs to be learned about the safety and effectiveness of PrEP in the real world. Demonstration projects are designed to gather information on safety, efficacy and program design for new interventions. They help guide subsequent larger-scale introduction. Such projects are planned or underway for the US, Kenya, Nigeria and Uganda.

What is in the PrEP pipeline?

NEXT-PrEP (HPTN 069) is recently-launched Phase II safety and tolerability study comparing oral Maraviroc (MVC) alone, MVC/FTC, MVC/TDF and TDF/FTC for PrEP amongst men who have sex with men in the US. Next-generation strategies will use longer-acting drugs, focusing on those that are not widely used for HIV treatment. These include TMC278LA formulated as a long-acting injectable, a vaginal ring containing dapivirine and a vaginal ring combining dapivirine and maraviroc formulated as a vaginal ring.

Priorities for 2012

AVAC's *Playbook 2012* sets out top strategic goals and priorities in HIV prevention for ourselves—and for the world. Here's what we have to say about PrEP. For more, visit *www.avac.org/playbook*.

Global Goals	AVAC Priorities
▪ Swift implementation of pilots and phased implementation in countries and communities where oral TDF/FTC-based PrEP is relevant; clear action on evaluating PrEP and developing policies in countries where it might be introduced over the long-term. ▪ Expanded pipeline of other active agents, dosing regimens and delivery mechanisms.	▪ Ensure that PrEP demonstration projects are launched for relevant populations. ▪ Mobilize partners to engage in US FDA regulatory process.

For more resources on HIV prevention research and for information on AVAC programs, visit www.avac.org.