New Guidance on Daily Oral PrEP: What's out there and what does it mean for advocates?

AVAC
Global Advocacy for HIV Prevention

September 18, 2012

FDA approves first drug for reducing the risk of sexually acquired HIV infection

http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm312210.htm

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FDA NEWS RELEASE

For Immediate Release: July 16, 2012
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En Español

FDA approves first drug for reducing the risk of sexually acquired HIV infection

Evidence-based approach enhances existing prevention strategies

Today, the U.S. Food and Drug Administration approved Truvada (emtricitabine/tenofovir disoproxil fumarate), the first drug approved to reduce the risk of HIV infection in uninfected individuals who are at high risk of HIV infection and who may engage in sexual activity with HIV-infected partners. Truvada, taken daily, is to be used for pre-exposure prophylaxis (PrEP) in combination with safer sex practices to reduce the risk of sexually-acquired HIV infection in adults at high risk.

The FDA previously approved Truvada to be used in combination with other antiretroviral agents for the treatment of HIV-infected adults and children 12 years or older.

As part of PrEP, HIV-uninfected individuals who are at high risk will take Truvada daily to lower their chances of becoming infected with HIV should they be exposed to the virus. A PrEP indication means Truvada is approved for use as part of a comprehensive HIV prevention strategy that includes other prevention methods, such as safe sex practices, risk reduction counseling, and regular HIV testing.

"Today's approval marks an important milestone in our fight against HIV," said FDA Commissioner Margaret A. Hamburg, M.D. "Every year, about 50,000 U.S. adults and adolescents are diagnosed with HIV infection, despite the availability of prevention methods and strategies to educate, test, and care for people living with the disease. New treatments as well as prevention methods are needed to fight the HIV epidemic in this country."

As a part of this action, the FDA is strengthening Truvada's Boxed Warning to alert health care professionals and uninfected individuals that Truvada for PrEP must only be used by individuals who are confirmed to be HIV-negative prior to prescribing the drug and at least every three months during use. The drug is contraindicated for PrEP in individuals with unknown or positive HIV status. The FDA strongly recommends against such use.

Truvada for PrEP is being approved with a Risk Evaluation and Mitigation Strategy (REMS) to minimize the risk to uninfected individuals of acquiring HIV infection and to reduce the risk of development of resistant HIV-1 variants. The central component of this REMS is a training and education program to assist prescribers in counseling individuals who are taking or considering Truvada for PrEP. The training and education program will not restrict distribution of Truvada but will provide information about the importance of adhering to the recommended dosing regimen and understanding the serious risks of becoming infected with HIV while taking Truvada for the PrEP indication.

"The REMS for Truvada for the PrEP indication is aimed at educating health care professionals and uninfected individuals to help ensure its safe use for this indication without placing an unnecessary burden on health care professionals and patients," said Janet Woodcock, M.D., director of the FDA's Center for Drug Evaluation and Research.

Truvada's safety and efficacy for PrEP were demonstrated in two large, randomized, double-blind, placebo-controlled clinical trials. The iPrEx trial evaluated Truvada in 2,499 HIV-negative men or transgender women who have sex with men and with evidence of high risk behavior for HIV infection, such as inconsistent or no condom use during sex with a partner of positive or unknown HIV status, a high number of sex partners, and exchange of sex for commodities. Results showed Truvada was effective in reducing the risk of HIV infection by 42 percent compared with placebo in this population. Efficacy was strongly correlated with drug adherence in this trial.

The Partners PrEP trial was conducted in 4,758 heterosexual couples where one partner was HIV-infected and the other was not (serodiscordant couples). The trial evaluated the efficacy and safety of Truvada and tenofovir versus placebo in preventing HIV infection in the uninfected male or female partner. Results showed Truvada reduced the risk of becoming infected by 75 percent compared with placebo.

No new side effects were identified in the clinical trials evaluating Truvada for the PrEP indication. The most common side effects reported with Truvada included diarrhea, nausea, abdominal pain, headache, and weight loss. Serious adverse events in general, as well as those specifically related to kidney or bone toxicity, were uncommon.

As a condition of approval, Truvada's manufacturer, Gilead Sciences, Inc., is required to collect viral isolates from individuals who acquire HIV while taking Truvada and to evaluate these isolates for the presence of resistance. Additionally, the company is required to collect data on pregnancy outcomes for women who become pregnant while taking Truvada for PrEP and to conduct a trial to evaluate drug adherence and its relationship to adverse events, risk of seroconversion, and resistance development in seroconverters. Gilead has committed to provide national drug utilization data in order to better characterize individuals who utilize Truvada for a PrEP indication and to develop an adherence questionnaire that will assist prescribers in identifying individuals at risk for low compliance.

Gilead Sciences, Inc. is based in Foster City, Calif.

For more information:

- FDA: Consumer Update - FDA Approves First Medication to Reduce HIV Risk
- FDA: HIV and AIDS Activities
- CDC: Pre-Exposure Prophylaxis (PrEP)
- NIH: AIDS Information
- HHS: AIDS News and Resources
- Truvada for PrEP Fact Sheet

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

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Interim guidance for clinicians considering the use of preexposure prophylaxis for the prevention of HIV infection in heterosexually active adults

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6131a2.htm?s_cid=mm6131a2_w

Interim Guidance: Preexposure prophylaxis for the prevention of HIV infection in men who have sex with men

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6003a1.htm

World Health Organization

Guidance on pre-exposure oral prophylaxis (PrEP) for serodiscordant couples, men and transgender women who have sex with men at high risk of HIV

http://www.who.int/hiv/pub/guidance_prep/en/index.html

SA PrEP Guidelines

- Recognises
  - MSM a significant key population at risk for HIV in RSA
  - Evidence for an effective biomedical prevention
  - Must be combined with other behavioural and structural interventions
  - Can be formulated as a part of "package for MSM"
  - Truvada available in pharmacies in RSA.
  - Have an ethical and moral obligation to make sure guidance available for this to be prescribed for this indication safely.
  - Complete and on line….. saj**hiv**med.org.za

The British HIV Association/British Association for Sexual Health and HIV position statement on pre-exposure prophylaxis in the UK

http://www.bhiva.org/documents/Publications/PrEP2012.pdf

GUIDELINE

The British HIV Association/British Association for Sexual Health and HIV Position Statement on pre-exposure prophylaxis in the UK

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Keywords: HIV, PrEP, pre-exposure prophylaxis, HIV prevention, guideline, UK

PURPOSE OF STATEMENT

The intention of this Position Statement is to inform UK healthcare workers on the role of antiretroviral pre-exposure prophylaxis (PrEP) in the setting of the UK HIV epidemic, so that they can have an informed discussion with their patients. Recent results from clinical trials of PrEP have made it imperative to investigate whether this biomedical tool will have a useful part to play in HIV prevention in the UK. However, it is not possible to review the evidence for this biomedical intervention in isolation, as PrEP (systemic and topical) is one of several methods in the prevention package, and one of four biomedical tools available; the other three being medical male circumcision, postexposure prophylaxis following sexual exposure and early treatment of the positive partner.

We have therefore broadened the scope of the Position Statement to attempt to put the evidence for PrEP in context, both in terms of the characteristics of the UK epidemic and in terms of the evidence for other biomedical interventions. We took note of the current guidelines on the topic of HIV prevention, including those that are out for consultation.

METHODS

Feedback was obtained at the British HIV Association (BHIVA) annual conference, and subsequently through the UK PrEP Working eGroup, to which there is an open invitation to join. Two conference calls were arranged to solicit the opinions of organizations based in the community, and a meeting of stakeholders drawn from the eGroup was held on the 5 May 2011. Comments were solicited on the tables, and then the consensus statements. A further call was held on the 13 July 2011 to discuss the design of a randomized controlled trial (RCT). The tables and statements were updated to reflect new evidence that emerged in July, September and November 2011.

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CONSENSUS STATEMENTS

- HIV remains an infectious disease of major public health importance in the UK with an estimated 91,500 individuals living with HIV at the end of 2010.[1] The epidemic most affects Black African, gay and other men who have sex with men (MSM) communities. In 2010, 3000 new infections were diagnosed in MSM (the highest ever total) and 2440 (81%) of these were judged to have been acquired within the UK;[1]
- The majority of HIV prevention efforts in the UK have focused on behaviour change, mainly the use of condoms and, more recently, testing behaviour. There is limited funding for initiatives to be implemented in accordance with national guidelines, and increasing pressure to make savings. While cross-sectional data-sets of outcomes and impact provide some insight, there has been no systematic approach to the evaluation of behavioural interventions on a national basis;
- Four randomized, placebo-controlled trials have now reported on the use of PrEP, providing evidence for the effectiveness of daily oral Truvada (tenofovir and emtricitabine) in MSM,[2] serodiscordant couples who were predominantly heterosexual,[3] young heterosexual adults[4] and coital tenofovir 1% vaginal gel in women.[5] A fifth trial of daily oral Truvada in women is conducting an orderly closure following an interim analysis which revealed equal numbers of HIV infections in the Truvada and placebo groups.[6] A sixth trial in women is similarly to discontinue daily oral tenofovir (September 2011) and daily tenofovir 1% vaginal gel (November 2011), but will continue daily oral Truvada and their respective placebo.[7] Other trials are underway or planned, one of these in the UK (Table 1), available online only at: http://www.ijsa.rsmjournals.com/cgi/content/full/23/1/1/DC1;
- The momentum following these clinical trials creates the opportunity to re-think our overall strategy for HIV prevention at a time when the NHS is undergoing change. The continued increase in infections being identified in MSM acquired within the UK underscores the urgent need to do so. Central to the prevention strategy is full engagement of the most affected communities;

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Gilead Sciences: Beyond FDA Approval

- Discussions are ongoing with regulatory agencies in other countries including Europe, Canada and Australia, but specific plans for filing have not yet been finalized
- Dossier for Truvada for treatment submitted in Peru during IAS
- Corporate grants program launched mid-September
- Support for demonstration projects ongoing

Truvada PrEP Educational Website

Truvada®
200 mg emtricitabine - 300 mg tenofovir disoproxil fumarate

Prescribing Information | Medication Guide
Important Safety Information and Boxed WARNINGS | REMS Resources

TRUVADA for a Pre-Exposure Prophylaxis (PrEP) Indication

TRUVADA is indicated, in combination with safer sex practices, for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults at high risk.

Click here for factors that place an uninfected adult at high risk →

Click here for factors to consider before prescribing TRUVADA for PrEP →

View Full Prescribing Information including Boxed Warnings →

View Medication Guide →

Resources for Healthcare Providers

REMS Resources

Download important Risk Evaluaton Mitigation S
healthcare providers before prescribing TRUVA
uninfected individuals at high risk of sexually ac

Read important REMS materials →

HIV Testing

Read important information about safely prescribing TRUVADA for a PrEP indication, and answer a post-training questionnaire to qualify to offer HIV testing at no cost to uninsured or financially needy individuals.

Qualify to offer HIV testing at no cost to uninsured or financially needy individuals

Medication Assistance Program

Help eligible uninfected individuals taking TRUVADA for a PrEP indication receive assistance paying for the medication.

Free HIV testing

For Uninfected Individuals

Condoms

If you are an uninfected individual at high risk taking TRUVADA for a PrEP indication, you can obtain condoms at no cost.

Open condom ordering form →

Safety Information for Uninfected Individuals

Review information for uninfected individuals at high risk.

Review material for uninfected individuals

Free condoms

Q&A

Thank you for joining today's webinar. To ask a question you can:

- Email your question to avac@avac.org
- Ask your question in the chatbox on the web interface if you're listening online
- Once the facilitator has opened the line for questions, press *7 to unmute yourself

Join us on October 3rd for another webinar —
Beyond Daily TDF/FTC as PrEP: Exploring new drugs and regimens for PrEP.

Register here: http://bit.ly/Uhqh7i