FDA's Advisory Committee Review of Daily Oral Truvada as Pre-Exposure Prophylaxis (PrEP) to Reduce the Risk of HIV Infection

An Advocate's Primer for Public Participation

On February 13, 2012, FDA granted priority review to consider Gilead Sciences, Inc.'s application for approval of once-daily emtricitabine/tenofovir disoproxil fumarate (Truvada®) to reduce the risk of HIV infection among uninfected adults (an approach known as oral pre-exposure prophylaxis, or PrEP). Priority review speeds up the process, and the FDA set June 15, 2012 as the target approval decision date for Gilead's application. Seeking outside expert opinions about the application, FDA will put several issues before members of its Antiviral Drugs Advisory Committee ("Committee"), scheduled to meet in open public session on May 10, 2012.

Expert opinions, public comment, available clinical data and the recommendations of the committee provide FDA with information to make its independent decision whether to approve once-daily Truvada as PrEP, balancing benefits and safety risks and considering the degree of seriousness for HIV infection and prevention. FDA is not bound by the recommendations of its committees, but often follows their advice. This primer offers a guide to the workings of the committee and ways to participate in its review.

Who are members of the Advisory Committee?
Voting committee membership consists of about a dozen regular and temporary member experts in the field. A consumer or patient representative (a person with the ability to effectively communicate patient concerns) is also a member of the committee. Each member is required to disclose financial or other conflicts of interest and may require that he/she recuse him/herself from voting.

What will the committee see in advance and be asked to do?
Two or three weeks in advance of the meeting, the FDA will provide committee members with a formal set of briefing materials consisting of:

1) Gilead's submitted data about safety and effectiveness for once-daily Truvada as PrEP, proposed drug labeling (including intended population users and warnings or cautions) and other technical support items, and
2) FDA staff's own initial evaluation.

This full material set may contain some protected private information that the public will not see. The committee will also later receive materials that the public submits.

Two days before the meeting, FDA provides the public a web accessible copy of briefing materials that can be publically disclosed. The public will also see a set of specific questions that the FDA will ask the committee to answer by voting or opinion. These questions will most likely address areas of special FDA concern about once-daily Truvada as PrEP such as its overall benefit in relation to known risks, the need for other studies or conditions of proper use in different populations, and the best ways for individuals to use it. Public input

to the committee should address these questions when providing oral comments to have greatest impact.

Will the committee accept input before and/or during the day of the meeting?
The open meeting will consist mostly of formal and invited presentations by Gilead, other experts and FDA staff to review the specific questions under review.

The public has two opportunities for input:

1) Written comments submitted approximately two weeks in advance, and

2) Five- to ten-minute oral remarks (outlined and mailed to the FDA approximately three weeks in advance, even if they are not in final form,) presented during a one-hour or extended meeting time slot after formal presentations. Permission to deliver oral remarks must be requested, and the FDA may limit public presentations by conducting a lottery among those requesting time. Groups may wish to join together to present combined input. Those who have not registered before the meeting will only be invited to speak at the discretion of the Chair and should submit their request to FDA officials at the registration desk on the day of the meeting.

The tight deadlines require the public to be aware of the schedules FDA provides for submitting materials. A notice announcing the meeting and submission instructions appeared in the Federal Register on March 14, 2012. A table of the deadlines for submissions and instructions on what must be included in requests to speak is below and available on the AVAC website (www.avac.org). Because FDA may change the dates, monitoring announcements is also useful.

FDA Action	Dates
FDA announces the Committee meeting in the Federal Register and on its Advisory Committee website	March 14, 2012
Requests to present formal oral presentations at the meeting must be sent to Committee contact person; FDA notification to speakers follows shortly after	April 18, 2012
Written submissions must be sent to the Committee contact person to be given to the Committee	April 26, 2012
FDA posts publicly available briefing materials and questions posed to the Committee for review	May 7, 2012
The Committee meeting	May 10, 2012
Written comments may be sent to the Committee (earlier submissions will be given to the Committee before the May 10 meeting)	May 17, 2012
FDA issues decision on Gilead application	June 15, 2012

How can public participation be most effective?

The Committee meeting is expected to generate a wide variety of public responses. Here are tips for providing effective comments either in written or oral format:

- If you are presenting oral remarks, consult the posted briefing materials (made available approximately two days before the meeting) and take the specific committee questions into account.
- Focus your remarks on decisions that FDA is charged with making, such as the relative safety and efficacy of once-daily Truvada as PrEP for HIV prevention in specific populations. Explain your views about the level of efficacy appropriate for this use based on the risks of HIV infection populations face. ***FDA does not weigh issues related to rollout, payment and reimbursement by public or private insurance or use outside the US—comments on those subjects will not affect the outcome.***
- The committee may be interested in how to mitigate safety risks or issues of adhering to once-daily Truvada as PrEP by means of labeling changes that provide patient guidance, educational materials or other conditions. Evaluate for your communities how those might best be presented, received or disseminated if those are effective and you think mitigation is useful. Committee members will want to know if risks are acceptable if properly managed.
- Keep written submissions brief and to the point. The committee has very little time to read long presentations. The committee has little patience for comments that go beyond allotted time or that they consider disruptive.
- Gilead will present all of the public details of the clinical trial data so you can assume the committee is aware of this information.
- The presence of an unmet need is often not enough of an argument on its own to persuade committees a new use should be approved. Rationale for or against approving the drug that is specific to the populations you represent and their HIV prevention needs may provide additional and compelling guidance to the advisory committee, but it must take safety and efficacy into account.

What happens after the Advisory Committee meeting?

On May 10th the Committee will vote publicly on the questions that the FDA has submitted in the briefing materials released to the public two days before. The record of the committee votes on those questions will be submitted to the FDA for its decision, which is expected to occur one month later on June 15, 2012.

Resources

Related to the FDA:

- FDA's Advisory Committee Webpage and announcements: http://www.fda.gov/AdvisoryCommittees/WhatsNew/default.htm
- Guidance for Industry Advisory Committee Meetings —Preparation and Public Availability of Information Given to Advisory Committee Members: http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM125650.pdf

- Guidance for the public, FDA Advisory Committee Members, and FDA Staff: The Open Public Hearing at FDA Advisory Committee Meeting: http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM236144.pdf
- Patient Representatives to FDA Advisory Committees: http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/PatientInvolvement/ucm123861.htm
- Example of FDA questions submitted to an advisory committee: http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/AntiviralDrugsAdvisoryCommittee/UCM254082.pdf
- FDA and the Regulation of Healthcare Interventions - A Spotlight Session http://us.cochrane.org/fda-and-regulation-healthcare-interventions-spotlight-session
- AVAC Webinar on Navigating the FDA Review process, February 29, 2012. This webinar was designed as an advocates' guide FDA review of data regarding TDF/FTC for HIV prevention. Advocates discussed steps for involvement in the process; download the audio (mp3) and the slides (pdf).

Related to oral PrEP

- Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. N Engl J Med 2010; 363:2587– 2599.
- Baeten J, Celum C. Antiretroviral pre-exposure prophylaxis for HIV-1 prevention among heterosexual African men and wo- men: the Partners PrEP study. In: 6th IAS Conference on HIV Pathogenesis, Treatment, and Prevention. Rome, Italy; 2011.
- CDC trial and another major study find PrEP can reduce risk of HIV infection among heterosexuals. In: Centers for Disease Control and Prevention; 2011.
- FHI statement on the FEM-PrEP HIV prevention study: FHI to initiate orderly closure of FEM-PrEP. In: FHI; 2011.
- Microbicide trials network statement on decision to discontinue use of oral Tenofovir tablets in VOICE, a major HIV prevention study in women. In: Microbicide Trials Network; 2011.
- AVAC PrEP Fact Sheet, Primer and other resource materials at http://www.avac.org/prep.
- Cascade of Hope and Questions, www.avac.org/series
    - Cascade of Hope and Questions, Vol 2: Understanding the results of CAPRISA 004 (July 2010)
    - Cascade of Hope and Questions, Vol 1: Anticipating results of ARV-based HIV prevention trials (August 2010)
- CDC Interim Guidance document (January 2011): www.cdc.gov/mmwr/pdf/wk/mm6003.pdf
- New Prevention Technologies: What are they and what is their relevance for people living with HIV?, Global Network of People Living with HIV (2010): www.gnpplus.net/images/stories/PHDP/NPT_Toolkit_ENG_web.pdf
- Planning for pre-exposure prophylaxis to prevent HIV transmission: challenges and opportunities, Journal of the International AIDS Society (12 July 2010): www.jiasociety.org/content/13/1/24.