



**Practical PrEP Priorities, or Profound Problems:
U.S. Pricing and Access Issues in the wake of iPrEx
PLUS FEM-PrEP and UN UPDATE!**

Our Webinar will begin shortly.

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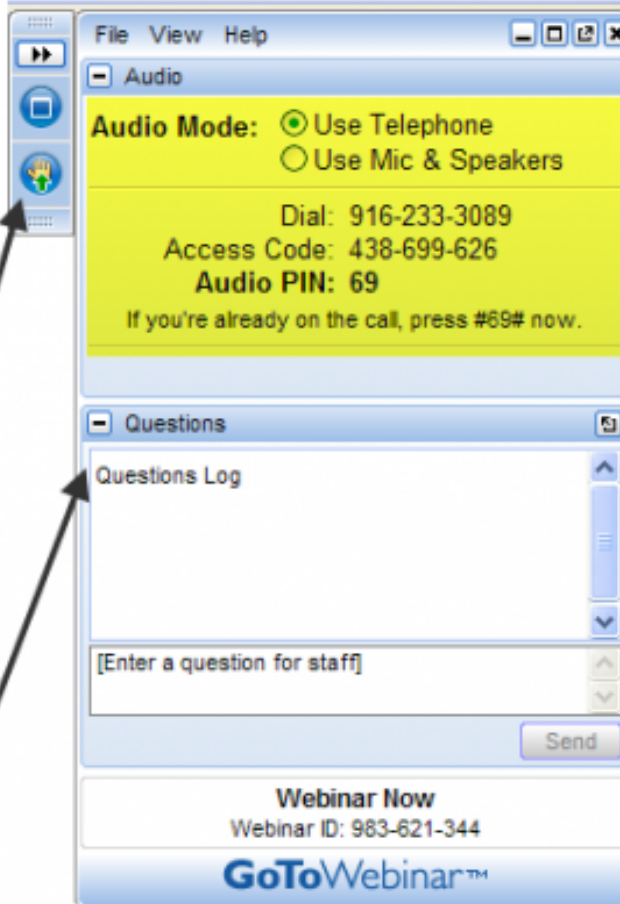
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Today's Agenda (all times eastern)

FEM-PrEP Trial Closure Update and Discussion

3:40-3:45 – Introduction

Keith Green, AIDS Foundation of Chicago

3:45-4:00 – FEM-PrEP Closure: What Happened and What it Means

Dr. Tim Mastro, FHI (Trial Sponsors)

4:00-4:05 – Q & A w/ Dr. Mastro

Today's Agenda (all times eastern)

Practical PrEP Priorities, or Profound Problems: U.S. Pricing and Access Issues in the wake of iPrEx

4:05-4:20 – Pricing Options for TDF/FTC for PrEP Use
Kevin Fisher, AVAC

4:20-4:45 – FDA Review of Oral PrEP
Robert Reinhard, Public and Global Health Consultant

4:45-5:10 – Ensuring Access for the Most Vulnerable Communities
Keith Green, AIDS Foundation of Chicago

5:10-5:20 – Q & A with Panelists

Today's Agenda (all times eastern)

UN High Level Meeting on HIV/AIDS

5:20-5:30 p.m.

Matt Kavanagh, Health GAP



Part 1: FEM-PrEP Trial Closure Update and Discussion

Dr. Tim Mastro

Vice President for Health and Development
Sciences at FHI (sponsors of the trial)



Part 1: FEM-PrEP Trial Closure Update and Discussion

Question and Answer Session

- To ask over the phone, click the 'Raise Hand' button and wait to be called upon.
- Anyone can ask via the chat/question function at anytime.



**PART 2: Practical PrEP Priorities, or
Profound Problems: U.S. Pricing and Access
Issues in the wake of iPrEx**

Kevin Fisher, AVAC

Robert Reinhard,

Public and Global Health Consultant

Keith Green, AIDS Foundation of Chicago

AVAC

Global Advocacy for HIV Prevention

Pricing Options for TDF/FTC for PrEP Use

Kevin Fisher

HIV PJA Strategy Webinar

20 April 2011

What Does Truvada Cost?

- “Product prices in the wealthiest nations of the world are based on the product’s full value.” Gilead Sciences
- US Annual Price (\$10,000 - \$14,000)
- ADAP Annual Price (Unk. - Possible \$5,000-\$7,000)
- And the price is increasing. Truvada price just increased approximately 8%.

Outside The US

- As low as \$140/year.
- Provides TDF and TDF/FTC at reduced cost in 130 low- and lower middle-income countries
 - Low-income countries (GNI \leq \$1000 and/or an extremely high burden of HIV)
 - Lower middle-income countries (GNI between \$1000 and \$3,000)
 - Truvada and Viread provided at cost (no profit) to low-income countries and near cost to lower middle-income countries

Making PrEP More Affordable

- Lowering Price of TDF/FTC
- Improving Insurance Reimbursement for PrEP Use
- Public Funding for PrEP Use
- Reducing PrEP Related Costs.
 - Doctor visits.
 - HIV testing.
 - Supportive Counseling and Testing
 - Renal or Bone Density Testing?

US Options for Lowering Price

- Adjusting Price for Truvada to Point At Which PrEP is Affordable (\$100/month)
- Dual Pricing (Ethical and Logistical Issues)
- ADAP Pricing for PrEP (340B Drug Pricing)
- Waiting for generic Truvada (Patent for both active ingredients in Truvada expire by 2017. But combination may be 2021 or 2018 in Europe)
- Gilead Patient Assistance Program (PEP Covered)
- Reducing the Required Dosage.

Price in Resource Poor Settings

- Price is lower (\$140/month) but so individual's ability to pay in low resource settings.
- Cost effectiveness in supporting country HIV program by reducing incidence and demand for treatment.
 - Model estimated \$257/year PrEP cost in South Africa was not deemed cost effective unless the cost of PrEP could be halved (Walensky).

Third Party Payment in US

- Private Insurance
- Medicare after 2014
- PrEP Programs
 - CDC HIV Prevention Funding
 - State Health Authorities

Private Insurance in US

- Some insurance plans may cover Truvada.
- Recent CDC meeting Kaiser covering PrEP. AETNA and Wellpoint thought they might too.
- Self Insured Employers may be less likely to (eg Levi).
- Truvada may still be subject to Co-Payment under a Tiered System. Some tiered drug plans can require 30% of cost.

Medicare After 2014

- Medicaid coverage to all nonelderly individuals with incomes below 133% of the Federal Poverty Level in 2014 .
- Prevention measures that receive a grade A or B from the US Preventive Services Task Force will automatically be covered by Medicare.

CDC and Health Departments

- Very limited CDC and State/Local Health Department HIV prevention funding in near term.
- Cost of covering persons indicated for PrEP would exceed all CDC prevention funds.

Way Forward on Pricing in US

- Negotiate ADAP level pricing under 340B mechanism.
- Test targeted PrEP programming in demonstration projects that will show cost effectiveness to CMS and USPSTF.
- Develop a patchwork system of coverage in individuals facing higher HIV risk through private insurance and Medicare for lower income individuals.

FDA Review Oral PrEP

Robert Reinhard
April 20, 2011

“NEW DRUG” APPROVAL (NEW “INDICATIONS” FOR APPROVED DRUGS)

- IT IS UNLAWFUL TO MARKET A DRUG WITHOUT PRIOR FDA REVIEW AND APPROVAL OF AN APPLICATION SHOWING THAT THE DRUG IS SAFE, EFFECTIVE, AND APPROPRIATELY LABELED FOR ITS APPROVED INDICATION(S), I.E., INTENDED USE(S).

- A DRUG MAY BE APPROVED FOR MORE THAN ONE USE

- EACH USE REQUIRES SEPARATE APPROVAL

- WHEN A DRUG HAS AT LEAST ONE APPROVED USE, OTHER NON-APPROVED USES ARE “OFF LABEL”

OFF LABEL USE VS. APPROVED USE

- COMPANY CANNOT MARKET OFF LABEL USE OF ITS DRUG
- FDA REGULATES MARKETING OF DRUGS, NOT THE PRACTICE OF MEDICINE BY PHYSICIANS
- A LICENSED PHYSICIAN MAY PRESCRIBE AN OFF-LABEL USE.
- TRUVADA IS CURRENTLY FDA APPROVED FOR TREATMENT OF HIV NOT ANY PREVENTION OF HIV
- PURPOSE OF APPLICATION FOR A NEW USE OF TRUVADA WOULD BE TO PERMIT ITS MARKETING FOR A NEW PREVENTION USE.

SCOPE OF NEW USE OF TRUVADA

SCOPE OF A NEW HIV PREVENTION USE WOULD BE BASED ON SPECIFIC APPLICATION TO FDA

- POPULATION – E.G. MSM AND TRANSGENDER WOMEN BUT NOT IDU OR HETEROSEXUALS? (RELEVANCE OF INCOMPLETED TRIALS AND THE FEM-PrEP TRIAL)
- BEHAVIORS – FREQUENCY OF UAI AND MULTIPLE PARTNERS?

USE OUTSIDE OF SCOPE WOULD BE OFF LABEL REQUIRING A NEW APPLICATION. ADDING SCOPE SEQUENTIALLY IS COMMON IF JUSTIFIED (E.G. GARDASIL)



WHAT FDA DOES NOT DECIDE/RECOMMEND

FDA does not decide/recommend:

- Individual prescribing for patients within scope of indication or decisions *not* to prescribe
- Who should or how to pay for use
- How public health programs should or should not implement, adopt, fund, prioritize or integrate into strategy
- Approval for use outside the United States

WHAT DOES FDA DO WHEN IT REVIEWS FOR APPROVAL?

Collection of data
from applicant-
step 1

- All relevant data –(preclinical, animal, human) are reviewed for quality and adequacy. Labeling also submitted.
- Weight given to different data depends on its quality and completeness; burden of proof is on the applicant
- Cost is not a criterion for approval.

Advisory Committee
– optional step 2

- In some cases, an outside panel may review data publicly and make recommendations. That would be likely if oral PrEP goes to FDA for review
- FDA is not bound by the recommendations. It acts independently.

Decisions Made by
FDA- step 3

- Approve
- Approve with conditions
- Disapprove

FDA REVIEW AFTER APPROVAL OR APPROVAL WITH CONDITIONS

Safety/toxicity and other measures are reported by:

- Significant adverse event (SAE) reports
- Reporting from clinical practice or from patients
- FDA initiatives such as “Sentinel” program
- An agreed upon or required program of study or trial known as Phase IV or postmarketing reports/commitment - new guidance at:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM172001.pdf>

LABELS MATTER

THEY CLARIFY INDICATED USE

[ORAL PrEP IS NOT SIMPLY A PILL]



- SAFETY/TOXICITY WARNINGS
- DOSE/ADHERENCE
- MONITORING FOR DRUG RESISTANCE
- RISK COMPENSATION
- OTHER SOCIAL/BEHAVIORAL ISSUES POSSIBLE

CONSEQUENCES OF APPROVAL AND LABELING OR WITHHOLDING APPROVAL - I

- Approved use is more easily reimbursed by public and private mechanisms and often required.
- Off label use reimbursement is rarely available from public funds and is not required, except by some standards or laws- e.g cancer treatments. Private reimbursement discretionary.
- If off label use is reimbursed, it may be ad hoc or geographically limited. Patchwork contributes to population wide inequity.
- CDC: “ Concerns exist that without early guidance, various unsafe and potentially less effective PrEP-related practices could develop among health-care providers and MSM beginning to use PrEP .”

CONSEQUENCES OF APPROVAL AND LABELING OR WITHHOLDING APPROVAL - II

- Some physicians may be unwilling to prescribe off label based – not on medical criteria – but on other factors such as liability concerns or absence of complete label instructions. A liability “waiver” by patient may erode confidence and interfere with doctor/patient trust needed for health decisions.
- Permission to market and promote offers a professional gateway information exchange between manufacturer and clinicians.
- PrEP “real world” demonstration projects would be thwarted w/o approval but may be facilitated by approval w/conditions.

**Q: DOES ORAL PrEP MEET FDA
APPROVAL (WITH CONDITIONS) CRITERIA?
A: YES, NO, YOU DECIDE**

Specific use example: men and transgender women who have UAI with other men

Available data or events:

- Human trials in this population: CDC safety trial and iPrEX
- Other completed data: preclinical, animal and perhaps data from CAPRISA 04 if it is relevant, biological models (e.g. PMTCT)
- Relevance of other incomplete information: is FEM-PrEP relevant ???

BRIEF COMPARISON OF iPrEX and FEM-PrEP - I

	iPrEX	FEM-PrEP
Population studied in a Phase III blinded RCT- ½ receiving Truvada, ½ receiving placebo. Dose of Truvada = dose used in treatment	2,499 men and transgender women who have sex with men (>18 years of age, 69% were between 18-29). Primary sexual behavior is anal sex, UAI	Planned: 3900 women. (ages 18-35) Primary sexual behavior is vaginal sex # Enrolled at time study was discontinued: 1951
Study drug regimen	Daily oral use of Truvada	Daily oral use of Truvada
Other Rx drugs	n/a	Oral(1/3 of participants) or injectable (2/3) contraception was provided and used, adherence ??
Selected safety/toxicity of concern	Some measurable bone and renal values with limited clinical significance. BMD in young men may be of concern	Not yet fully reported-preliminary finding: “not serious”; no observed effects yet on children of women who became pregnant and delivered
Adherence to study drug - based on self report	Up to 95%; however, as measured by detection of drug in blood samples of those who received Truvada - ~50%	Preliminary findings by self report -95%; as measured by detection in blood samples- unknown

BRIEF COMPARISON OF iPrEX and FEM-PrEP - II

	iPrEX	FEM-PrEP
Efficacy result	44% fewer infections (95% CI 15.4 to 62.6%; P=0.005) in those who received Truvada compared to those who received placebo; efficacy results were higher in those who achieved highest rates of adherence to Truvada	<p>“Following a scheduled interim review of the FEM-PrEP study data, the Independent Data Monitoring Committee (IDMC) advised that the FEM-PrEP study will be highly unlikely to be able to demonstrate Truvada’s effectiveness in preventing HIV infection in the FEM-PrEP study population even if it continued to its originally planned conclusion. . . The final analyses have not yet been conducted. <u>At this time, it cannot be determined whether or not Truvada works to prevent HIV infection in women.</u>”</p> <p>At the time of discontinuance, HIV infections occurred at 5%/year in all participants</p>

WHAT LEVEL OF EFFICACY IS REQUIRED FOR FDA APPROVAL?

- Required level of efficacy in this case has little or no precedent. PrEP equation is not like malaria drugs, statins or other examples.
- FDA has few experiences to draw upon. Experts matter.
- Efficacy is a factor of adherence, warnings and systems and depends on how well label or conditions of approval promote, inhibit or ignore those factors.
- Efficacy is in a context of approval conditions, label and physician/patient/social setting relationships
- Efficacy is balanced with safety risks considering the seriousness of potential HIV infection in a specific population

WHAT SHOULD FDA DO or NOT DO?

- Identify good quality data
- Convene impartial experts
- Listen
- Base decisions on good science
- Don't politicize
- Don't stigmatize
- Fulfill its mandate



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Issues in the wake of iPrEx**

**Ensuring Access for the Most Vulnerable
Populations**

Keith Green, AIDS Foundation of Chicago



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Question and Answer Session

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PART 3: UN High-Level Meeting on HIV/AIDS

Matt Kavanagh – Health GAP



Thanks for joining us today!

A recording and slides will be available on preventionjustice.org shortly.

Our next call will be on May 18, 2011 at 3:30 p.m.ET. – stay tuned for details!