

# **Gilead Update on PrEP**

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**London, Sept 2013**

# PrEP Indication

- Truvada is indicated in combination with safer sex practices for pre-exposure prophylaxis to reduce the risk of sexually acquired HIV-1 infection in adults at high risk
- This indication is based on clinical trials in MSM at high risk for HIV-1 infection and in heterosexual serodiscordant couples

# Factors to Help Identify Individuals at High Risk

- Has a partner known to be HIV-1 infected, *or*
- Engages in sexual activity within a high prevalence area or social network and one or more of the following:
  - Inconsistent or no condom use
  - Diagnosis of sexually transmitted infections
  - Exchange of sex for commodities (such as money, food, shelter, or drugs)
  - Use of illicit drugs or alcohol dependence
  - Incarceration
  - Partner(s) of unknown HIV-1 status with any of the factors listed above

# When Prescribing Truvada for a PrEP Indication, Healthcare Providers must:

- Prescribe Truvada as part of a **comprehensive prevention strategy**
- Counsel individuals to strictly adhere to a **daily dosing schedule**
- **Confirm a negative HIV-1 test** immediately prior to initiating PrEP
  - If clinical signs or symptoms consistent with acute viral infection are present and recent (<1 month) exposures are suspected,
    - Delay starting PrEP for at least one month and reconfirm HIV-1 status *or*
    - Use a test approved by the FDA as an aid in the diagnosis of HIV-1 infection, including acute or primary HIV-1 infection
- While using Truvada for PrEP, HIV-1 screening tests should be repeated **at least every 3 months**
  - If symptoms consistent with acute HIV-1 infection develop following a potential exposure event, PrEP should be discontinued until negative infection status is confirmed using a test approved by the FDA as an aid in the diagnosis of HIV-1, including acute or primary HIV-1 infection

# What is a REMS?

- Risk Evaluation and Mitigation Strategy
- FDA program to manage a known or potential risk associated with a drug
  - Designed to ensure the benefits of a drug outweigh its risks
- Goals of REMS for Truvada for PrEP is to educate prescribers and individuals about
  - The importance of adherence
  - The importance of regular monitoring of HIV-1 serostatus
  - Truvada for PrEP must be part of a comprehensive prevention strategy

# REMS Materials

Available at [www.truvadapreprems.com](http://www.truvadapreprems.com)

- Dear Healthcare Provider Letter
- Training Guide for Healthcare Providers
- Important Safety Information for Healthcare Providers
- Safety Information Fact Sheet
- Agreement Form
- Checklist for Prescribers
- Medication Guide
- Important Safety Information for Uninfected Individuals
- Full Prescribing Information

# Additional Non-REMS Measures

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- Free HIV & HBV testing for qualified individuals
- Free condoms
- Subsidized HIV-1 viral resistance testing to individuals who seroconvert
- Opt-in reminder service regarding regular testing for HIV and other STDs
- Support for community education activities on PrEP
- Support for demonstration projects
- Truvada Medication Assistance Program for PrEP for uninfected individuals who lack insurance coverage

# How will PrEP be made available in clinical practice?

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- ◆ Drugs will be the same as for HIV treatment (Truvada (FTC/TDF), Viread (TDF), and generic versions)
- ◆ Guidance could be normative, regulatory (by labeling), or both. Process may vary by country.
  - CDC has issued guidance for PrEP for high risk MSM, serodiscordant couples, and IDUs in the US based upon the iPrEx, Partners PrEP, CDC Bangkok TDF and other studies
  - Guidelines being drafted by other groups (UK, France, South Africa, WHO, etc.)
  - Regulatory filings planned for developing world
- ◆ Access to medication remains to be determined at the local level (same sites as for HIV treatment or other venues??) but Gilead Access Program will support both treatment and prevention. PEPFAR, Global Fund, WHO interested but decisions regarding the use of PrEP not yet established



# Gilead Access Program

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- ◆ Registration for TDF and FTC/TDF for HIV treatment in over 100 countries globally including all of Africa
- ◆ Partnership with distributors to make branded Truvada and Viread available locally
- ◆ Partnership with over a dozen generic manufacturers in India and Africa to make generic versions of TDF and FTC in combination with other products. Able to brand and price flexibly. Has driven the price of TDF from \$1.35 per day to \$0.14 per day over 5 years. Current lowest price of TVD is \$0.20 per day.
- ◆ Over 3 million patients in the developing world are now on a TDF containing regimen; more than 90% on generic drug

# Support for ongoing research

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- ◆ Ongoing Phase 3 studies
  - IPERGAY study
- ◆ Phase 3 study extensions and rollovers
  - Partners PrEP
  - iPrEx OLE
  - TDF2
  - CDC Bangkok IDU study
- ◆ Demonstration projects
  - CDC demonstration project in US
  - San Francisco/Miami/Washington DC demonstration project
  - PROUD study in London

# Support for ongoing research

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- ◆ Phase 1 and 2 studies of alternative dosing strategies and regimens and populations
  - Intermittent dosing
    - HPTN 066, 067 (ADAPT)
  - Alternative regimens
    - HPTN 069 (miraviroc+/- TDF or FTC)
  - Alternative populations
    - Adolescent studies in young MSM ages 15-22 (ATN)
- ◆ PrEPception??!!
- ◆ Support for microbicide gel research; vaginal, rectal, new formulations and patient populations, safety and efficacy trials
- ◆ New drugs; new prodrug of tenofovir GS 7340; new prevention specific ARVs?

# Ongoing and Planned Phase 3/4 Research, Including Demonstration Projects

- ◆ Phase 3 studies are continuing to evaluate PrEP in various demographic groups
- ◆ Gilead is committed to post-marketing demonstration studies in the U.S. and globally
- ◆ Collaborators: ANRS, CDC, FHI, MRC, NIAID (DAIDS), NICHD (ATN), SFDPH, U. Washington, and Gilead Sciences

Population	Studies	Participants
MSM	17	14,100
Heterosexual Men & Women Serodiscordant Couples	8	10,201
<b>Total</b>	<b>25</b>	<b>24,301</b>

# Phase 3/4 Research and Demonstration Projects in MSM

Study	N	Duration	Location
<b>Ongoing Phase 3 Studies</b>			
IPERGAY	1900	24 months	France, Canada
<b>Demonstration Projects and Open-Label Extensions (planned and ongoing)</b>			
iPrEx OLE	1770	72 weeks	Americas, Thailand, S. Africa
DAIDS PrEP MSM Demo	500	12 months	U.S.
CDC PrEP Demo*	600	12 months	U.S.
PROUD	5000 (500 as pilot)	12 months on tx, 12 month follow-up	U.K.
Project PrEPare 110	200	48 weeks	U.S.
SFDPH EPIC PrEP	300	12 months	U.S.
ALERT	400	12 months+	U.S.
Los Angeles PATH	300	48 weeks	U.S.
Seattle PrEP	300	48 weeks	U.S.
NYC PrEP	200	12 months	U.S.
Brazilian PrEP	400	12 months	Brazil
Rio PrEP	65	12 months	Brazil
HPTN 073	225	12 months	U.S.
HPTN 069**	400	48 weeks	U.S.
HPTN 067**	540	34 weeks	U.S., Thailand, S. Africa
HVTN 505	1000	5 years	U.S.
<b>TOTAL: 17</b>	<b>14,100</b>		

\*CDC PrEP Demo includes both MSM and heterosexual men and women (1200 participants total)

\*\*Includes both MSM and heterosexual women (estimated 50% MSM, 50% heterosexual women)

# Phase 3/4 Research and Demonstration Projects in Heterosexual Women and Men

Study	N	Duration	Location
<b>Ongoing Phase 3 Studies</b>			
Partners PrEP (discordant couples)	4758 couples	12 month extension	Kenya, Uganda
CDC Bangkok TDF (IVDU)	2413	Endpoint driven	Thailand
<b>Demonstration Projects and Open-Label Extensions (planned and ongoing)</b>			
CDC PrEP Demo* (men and women)	600	12 months	U.S.
HPTN 069**	200	48 weeks	U.S.
HPTN 067**	~180	34 weeks	U.S., Thailand, S. Africa
TDF2 Open-Label Extension (men and women)	900 (all rollover)	12 months	Botswana
CHAMPS (men and women)	150	12 months	South Africa
UW Partners PrEP Demo (discordant couples)	1000	24 months	Kenya, Uganda
<b>TOTAL: 8</b>	<b>10,201+</b>		

\*CDC PrEP Demo includes both MSM and heterosexual men and women (1200 participants total)

\*\*Includes both MSM and heterosexual women (estimated 50% MSM, 50% heterosexual women)

+Excluding rollover participants

# Challenges to Implementation of PrEP in the US

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- ◆ Initial uptake of PrEP in the US has been slow but is increasing
- ◆ Limited provider experience. Small number of patients enrolled in clinical trials in US ( only 3 US sites and < 1000 subjects out of ~10,000 in pivotal studies).
- ◆ New strategy with no clear template for administration (many practical questions re implementation) and no PrEP “protocol” in place. Many (most?) LGBT centers in the US do not yet have an active PrEP program in place
- ◆ Separation of HIV prevention and treatment services in the US

# Challenges to Implementation of PrEP in the US

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- ◆ Reimbursement for drug and services not clear
- ◆ Low level of awareness amongst subjects and providers
- ◆ Eligible subjects not clearly defined
- ◆ Good news: many of the above issues can be addressed with additional experience/data



# Assessment of Truvada for PrEP Utilization in the US

The study is a prospective three year observational study to describe drug utilization among uninfected individuals who initiate TVD for PrEP. All subjects who started therapy after Jan 1 2011 were included in the study.

The study used an electronic source of nationally representative de-identified patient level data, with drug information from dispensed retail prescriptions for approximately 55% of all US pharmacies

An algorithm was developed to identify the use of TVD for the PrEP indication which excluded use for HIV treatment, post-exposure prophylaxis and off-label chronic Hepatitis B treatment

## Results

**1,774 individuals received Truvada for PrEP between 2011 and March 2013**

**Median age 37 years old**

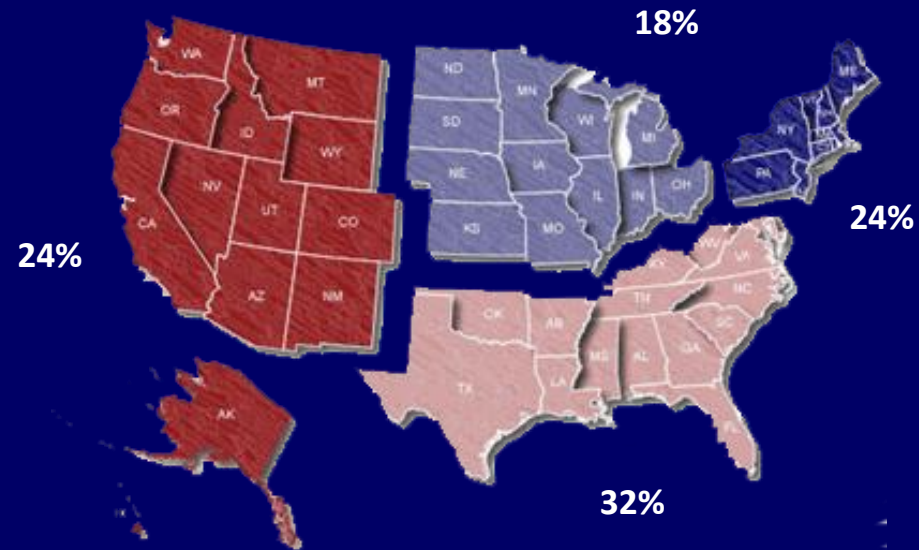
**48 % women**

**1674 unique prescribers**

<sup>a</sup> multivariate logistic model <sup>b</sup>  $p < 0.01$

# Assessment of Truvada for PrEP Utilization in the US

- Geographically prescribers of TVD for PrEP are located in 49 states and distributed across approximately 700 cities
- Only 37% also prescribed Truvada for HIV treatment
- Overall 6 specialties initiated 75.6% of PrEP prescriptions
  - Family Practice 16%
  - Internal Medicine 15%
  - Emergency Medicine 14%
  - Infectious Diseases 12%
  - Nurse Practitioners 9%
  - Physician Assistants 8%
- When compared to HIV positive patients<sup>a</sup>, uninfected individuals receiving TVD for PrEP were:
  - 1.4 times more likely to be from the South (95% CI 1.3 – 1.6)<sup>b</sup>
  - 1.8 times more likely to be female (95% CI 1.7 – 2.0)<sup>b</sup>
  - 1.4 times more likely to be younger than 25 years old (95% CI 1.2 – 1.6)<sup>b</sup>
  - 3.8 times more likely to be treated by a non-ID physician (95% CI 3.3 – 4.2)<sup>b</sup>



# Conclusions

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- ◆ Truvada has been approved for a pre-exposure prophylaxis indication in the US
- ◆ A REMS program is in place to ensure the safe and appropriate use of PrEP
  - Educate healthcare providers and uninfected individuals
  - REMS materials are available at [www.truvadapreprems.com](http://www.truvadapreprems.com)
- ◆ Ongoing demonstration projects will yield important information on the use of TVD for PrEP when given in an open label fashion

# Conclusions

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- ◆ Gilead is committed to supporting a comprehensive prevention program via education but is not actively promoting the indication
- ◆ TVD for PrEP is now being implemented in the US. Initial uptake has been slow but should improve with additional experience in the field and data from ongoing demonstration projects.
  - Similar to a product launch but is a “new strategy” launch
  - Will take 5-10 years to realize the potential of the strategy
- ◆ Phase 3b/4 studies are ongoing evaluating TVD, TDF, various dosing strategies, and other ARV combinations for prevention of HIV infection

