



Summary from the AVAC Think Tank on PrEP Financing in the US

Wednesday, 14 January, 2009, San Francisco

Colleagues from multiple disciplines met at the San Francisco AIDS Foundation for a one-day, AVAC-sponsored think tank examining how pre-exposure prophylaxis (PrEP) for HIV prevention might be funded or reimbursed through insurance mechanisms in the United States should it prove safe and effective. The think tank took forward discussions on PrEP implementation strategies by identifying key regulatory, legal and financial challenges to PrEP implementation.

Multiple PrEP clinical trials are currently planned or underway looking at the safety and efficacy of PrEP with planned completion dates in 2009 and beyond. Yet there is no clear pathway to broad access to PrEP in the US should these trials demonstrate safety and effectiveness.

In its *Anticipating the Results of PrEP Trials* report published August 2008, AVAC stressed the urgent need for an informed and sustained investment in PrEP research and identified various priorities for researchers, policy makers and advocates. In addition to ensuring the current clinical trials of TDF (tenofovir disoproxil fumarate) and TDF/FTC (tenofovir disoproxil fumarate and emtricitabine) have the best chance of producing decisive results, the report emphasized the need to plan for access to PrEP should it prove safe and effective. Stakeholders need to begin creating and supporting health systems capable of delivering PrEP to those at risk in the United States.

The objectives of the think tank were to:

1. Review US regulatory approval and indication scenarios for PrEP.
2. Review the feasibility of possible PrEP financing/reimbursement models using existing health care funding mechanisms and government programs in the US.
3. Review the possible impact of PrEP access on different funding mechanisms.
4. Define early messaging and advocacy goals for PrEP access in the US.

Discussion

Currently, there are five ongoing PrEP trials in humans, two planned and one completed. As early as 2010 we expect the first PrEP efficacy trial results. Results could

come earlier if interim analyses show a proof of concept before scheduled trial completion. In fact, eighty percent of earlier perinatal ARV prevention studies (MTCT and breastfeeding) stopped prematurely due to evidence of benefit. If this trend is any indication of what's to come with PrEP, then the need to prepare for PrEP demands urgent attention to its financing and programming.

Presentations revealed that there are no PrEP funding/reimbursement mechanisms in place which are likely to be affordable for most of those for whom it could be prescribed, and no plans by Gilead Sciences, Inc., the manufacturer of the TDF-based drugs used in the trials, to seek FDA approval or label indication changes for prevention use. An approved label indication for prevention would be a significant boost to funding and reimbursement since many insurance mechanisms rely on approved uses to agree to cover prescriptions. There is little awareness of this prospective prevention method among potential providers and consumers.

“The clinical trials are not enough to make an impact on the epidemic,” said one participant underscoring the need to prepare for rollout. “Technologies get discovered and then under-implemented and under-utilized.” Because the PrEP drugs are used for AIDS treatment and thereby already manufactured at large scale and publicly available, PrEP use may be taken up before programs are in place. This could pose hurdles for the necessary monitoring and evaluation of PrEP use in the real world.

Viread and Truvada label indication and regulatory scenarios for PrEP

Gilead Sciences, Inc., the patent holder of the antiretrovirals Viread (TDF) and Truvada (TDF/FTC), has not declared its intention to seek an FDA label for a prevention indication. Possible concerns by Gilead may include fear of liability for HIV seroconversion while on PrEP and drug toxicity or public perceptions about encouraging risk behavior. If these drugs prove effective for PrEP, doctors in the US on an individual basis could still prescribe their off-label use.

Gilead could also risk liability and regulatory sanctions for directly or indirectly marketing off-label use of its drugs for PrEP, even by seemingly modest means. Limiting PrEP to off-label use would have a ripple inhibitory effect on government and private insurance reimbursements, which disfavor such use. (Though there are state laws compelling insurance to pay for off-label use—typically for cancer treatment—these have not been applied to healthy populations.) The absence of a prevention label could also discourage doctors from prescribing PrEP.

If TDF and/or TDF/FTC are shown to be safe and effective for PrEP, Gilead, its shareholders, and PrEP consumers could benefit from labeling and pricing Truvada and Viread for HIV prevention.

- An FDA-approved label change indicating TDF and TDF/FTC's use as PrEP—in addition to its current FDA-approved use for the treatment of HIV/AIDS—would significantly reduce or eliminate regulatory risks to Gilead; increase physician confidence in prescribing; establish the safety and efficacy of the intervention more completely; and open doors to US and international reimbursement programs that are wholly or partially conditioned on US FDA approval.

- Gilead, as the New Drug Application (NDA) owner, controls the exclusive right to market TDF and TDF/FTC for use in the US. Since these drugs are FDA approved only for treatment use, another company may not file an Abbreviated New Drug Application (ANDA) for generic use for prevention once they go off patent protection. (Viread and Truvada come off patent in 2018 and 2021, respectively.)
- Manufacture of these drugs for prevention will require that an NDA be filed for a prevention indication. If Gilead decides not to proceed with an NDA, another company or organization could sponsor these drugs as PrEP-indicated products under an NDA, using section 505(b)(2) of the Federal Drug and Cosmetic Act (FDCA). A Section 505(b)(2) NDA may be filed without Gilead, however the applicant would need access to Gilead's data. The viability of this option would depend upon cooperation from Gilead.
- Physicians are free to prescribe TDF and TDF/FTC for off-label use; however, Gilead cannot market or promote the drugs' off-label use. Drug manufacturers cannot advertise off-label use, or they run the risk of regulatory action for "misbranding," which can incur criminal actions and significant fines. The FDA can also impose interruptions or sanctions against Gilead's other products. Advertising /marketing includes a broad set of activities not just limited to direct to consumer messages.
- Without a label change, the restrictions on private insurance and government reimbursement for off-label use will make PrEP use unaffordable for most. Off-label use [or approved use too] will make it imperative that prices for TDF and TDF/FTC be lower to guarantee access for those paying out of pocket.
- Many private insurance companies follow Medicare/Medicaid coverage determinations. As of July 2006, all Medicare/Medicaid plans covered TDF and TDF/FTC for use in HIV/AIDS treatment. Although the Centers for Medicaid and Medicare Services (CMS) provides limited coverage of off-label use, CMS does not have the authority to require that Part D (Medicare drug coverage) cover off-label use. CMS's determination to cover off-label use is influential in coverage decisions by other insurance plans.
- Currently, Medicare/Medicaid does not pay for treatment in the absence of a disability determination - a concern under study by the early access to treatment legislation now under review.
- The FDA rarely approves infectious disease prevention indications for otherwise entirely healthy individuals, but has done so for prevention of mother to child transmission (PMTCT) using AZT and for herpes prevention.
- Questions about risk compensation—or the possibility that PrEP use will lead to—even encourage- more high-risk behavior due to PrEP users feeling more protected—will undoubtedly be raised as an objection to reimbursement. FDA review of a PrEP application will be subject to intense public, scientific and perhaps Congressional scrutiny, which may extend FDA review time.
- The CDC's Public Health Service Guidelines could recommend off-label or "unapproved use" (such as it did for PEP), introducing a whole new level of legitimacy, and possibly mitigating the FDA's unwillingness to approve antiretrovirals for PrEP.

PrEP financing models using existing—public and private—funding mechanisms in the US

Preliminary CDC modeling suggests that there are 15-20 million potential PrEP users in the US, although that figure is many times the number likely to be the target of initial implementation. Questions remain as to how to integrate PrEP within a comprehensive national and local prevention strategy, maximize equitable access and monitor PrEP's effectiveness, safety and cost. Existing funding systems are unlikely to absorb PrEP costs. Indeed, two thirds of states are already facing budget shortfalls in 2009. ¹

- Government programs pose a demographic mismatch for PrEP coverage. Those at highest risk for HIV in the US are often individuals who are young to middle-aged, black, and/or male. Medicare eligibility is limited to seniors and the disabled, most of who are over 65-years old, female and white. Medicaid covers a population made up largely of pregnant women, children or the disabled. Ryan White Care Act clients are HIV-positive or in some cases the families of HIV-positive people. Many clients (i.e. veterans) of the US Department of Veterans Affairs share demographic characteristics with those who might benefit from PrEP coverage. However, implementing PrEP coverage in the VA system, without specific recommendations from the CDC and other professional bodies, would likely entail significant controversy. Medicaid, while not precluding off-label use, requires that such use be supported by one or more compendia references. Most states today are looking to reduce the items they will include in their programs.
- For private insurance coverage, there's a discrepancy between PrEP costs (~\$900/month wholesale price for TDF in the US; government programs may pay somewhat lower but still expensive prices) and average insurance individual premiums (\$4,700). If covered, PrEP use is likely to be deemed a specialty or "lifestyle" drug subject to much higher co-pay or coinsurance requirements. Since daily use for an undetermined length of time may be the prescribing mode, costs could escalate quickly.
- Ultimately, large employers can decide what coverage is available and so may negotiate with private insurers for PrEP reimbursement, but smaller employers will have little choice since they must join existing health plans. Even large employers now however are reducing insurance benefits. Disincentives to using private insurance reimbursement for PrEP based upon risk include stigma, risks of disclosure, and difficulty securing future coverage if perceived as high risk and seroconversion requiring treatment occurs. Although health plans reimburse for HIV testing, people are not accessing HIV testing through their private insurance companies for these very reasons.
- A new federal program to fund PrEP rollout is an option although obviously very difficult in the current economic environment. Potential sources for PrEP funding under legislation include the National AIDS Strategy, health care reform, domestic PEPFAR, congressional earmarks and Medicare Part D- if Medicare were extended to other users.
- The implementation of and payment for routine testing may serve as an indicator of what's to come with PrEP. After 25 years of HIV testing, the State of California only recently mandated that private insurance cover the service.

¹ (<http://www.nytimes.com/2009/02/02/us/02calif.html>)

Impact of PrEP access on existing funding mechanisms

To roll-out PrEP, do we need to create a new funding mechanism or can we use existing models modified to fit PrEP and infused with new financing?

Implementation will be partially shaped by PrEP's degree of effectiveness. If it proves to be 60% effective, it may be used in targeted, at-risk populations. If it proves 98% effective, its broader use may be warranted. Regardless of population, safety and resistance issues will have to be considered, along with the level of monitoring to ensure safety, which will demand even more resources.

- Potential PrEP providers include routine clinical HIV test providers, STD and family planning clinics, community and rural health centers, providers serving MSM and IDUs, allied CBOs/ASOs, needle-exchange programs and pharmacies—not all of whom are allies because of stigma attached to MSMs, and IDUs etc.
- High efficacy PrEP would be cost-effective if used by high-risk groups in circumstances where safety monitoring is manageable, and drug resistance is uncommon. Future access will depend upon a number of factors such as research findings, supply, community and provider demand, drug pricing and markets.
- A challenge to using existing public funding programs for HIV prevention is that they have been under- and flat-funded for years. Other challenges to public PrEP funding include HIV fatigue in Congress, and lack of knowledge around PrEP.
- The American College of Physicians now recommends that physicians offer routine HIV screening, and repeated screening on a case-by-case basis depending on risk. This may help doctors identify high-risk patients as possible PrEP users.
- PrEP implementation will incur expense beyond the cost of the drug such as HIV testing, counseling, outreach, monitoring and evaluation and other services. The most feasible implementation of PrEP may be one that would start out with demonstration programs in the highest incidence populations, and then transition to stand-alone PrEP programs with new monies. Or, conversely, there could be a comprehensive clinical package of prevention for Americans at high risk for HIV, instead of going it alone with PrEP.
- The health care system is not configured to optimally deliver clinical preventive services.
- Ryan White Care Act funding could cover preventive strategies but some HIV-positive people are already on waiting lists for treatment. There could be concerns that funding for PrEP may threaten these existing treatment funding streams. To justify PrEP funding to the HIV-positive community, emphasis should be placed on increased funding, not a shift in funding.
- Endemic crises in state budgets will mean that state and local health departments may struggle with or resist PrEP implementation until they see budgets increased for drugs, clinicians, and counselors. Program implementers are invested in their current models of prevention.

Action items for PrEP access

- Meet with Gilead to:
 - Understand the company's current thinking on pursuing a Supplemental NDA for a possible prevention indication for TDF and TDF/FTC.

- Discuss avenues to lower pricing for use of TDF and TDF/FTC for prevention. (Viread and Truvada come off patent in 2018 and 2021, respectively, and are available generically in resource-limited countries for \$29.75/month as compared to \$900/month in the US.)
- Identify entities capable of pursuing, with Gilead's acquiescence, a Section 505 NDA for use of TDF and TDF/FTC for prevention.
- Advocate for the addition of lamivudine (3TC) and/or maraviroc to the PrEP clinical pipeline to encourage a competitive market.
- Gather input and foster discussion about PrEP with potential users of PrEP and HIV prevention providers and health care providers, and convene focus groups, develop constituent surveys, and policy analysis on PrEP acceptability.
- Identify lessons for PrEP from PMTCT and PEP rollout, STD (herpes) prevention, family planning and vaccine delivery systems, HIV care delivery systems, and implementation and translational health research. Learn from the introduction of the HPV vaccine, Gardasil, on how to address cultural and political resistance.
- Develop modeling for delivery options, cost and potential impacts.
- Encourage communities to voice rights to healthy sexuality and funding for PrEP.
- Call for a targeted demonstration program of PrEP in high-risk groups in several cities.
- Work with large employers to educate them about including PrEP in private insurance coverage.
- Develop an advocacy plan to have PrEP included as approved for use by Centers for Medicaid and Medicare Services once it is determined to be safe and effective.
- Understand segments of PrEP user populations in more detail and different markets addressed by different reimbursement schemes.
- Compile list of eligibility criteria to qualify for Medicare, Medicaid, and Ryan White programs to establish amendments that would be required to cover PrEP.
- Convene a medical advisory panel to address how to rapidly implement affordable PrEP for those most at risk for HIV acquisition.
- Call for the development of Public Health Service Guidelines for PrEP.
- Call for national guidelines from CDC and one more normative national agency addressing the how's and why's of PrEP.
- Secure approved indicated use and pricing.

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