POPULATION HEALTH DIVISION
SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH

Important HIV Prevention and Treatment Updates for San Francisco Providers

February 12, 2019

Dear Colleague,

We're writing to share with you recommendations on how to incorporate new developments in HIV prevention and care into your practice. If you are receiving this update on paper, an electronic version with embedded hyperlinks to outside resources is available on the SFDPH Disease Prevention and Control website, at https://www.sfcdcp.org/ .

The San Francisco Department of Public Health recommends that you:

- **Screen all sexually active MSM, trans women, and trans men who have sex with men for STDs, using urine, pharyngeal, and rectal NAAT testing, and a serum RPR for syphilis, every 3 months, regardless of HIV serostatus.**
  Updated CDC recommendations on which HIV tests to use when prescribing daily PrEP, and how often to screen for bacterial STIs: CDC now recommends antigen/antibody testing over antibody-only testing; they also provide guidance on interpretation of HIV RNA testing used for PrEP. See details below. Furthermore, CDC now recommends that MSM "at high risk for recurrent STIs" undergo screening every three months.

- **Offer daily PrEP for persons <18 years old who are at-risk for HIV.**
  Emtricitabine/tenofovir disoproxil fumarate (Truvada®) is now approved for persons < 18 years of age (weighing >35 kg) by the FDA. See details below.

- **Consider a "2-1-1" dosing regimen for men who have sex with men (MSM) who are ambivalent about daily pre-exposure prophylaxis for HIV (PrEP).**
  There is a non-daily dosing strategy for PrEP that was studied in MSM in France and Canada, and is being used in some clinics in Europe and Canada. This non-daily strategy, also known as "Intermittent", "Event-Driven," "Sex-Driven," "On Demand," or "2-1-1" PrEP, may be appropriate for some MSM. SFDPH has released guidance on this dosing strategy (see below) for MSM who do not want to use daily emtricitabine/tenofovir disoproxil fumarate (also known as FTC/TDF or Truvada®), which is currently the only FDA-approved dosing strategy for PrEP in the United States.

- **Inform patients living with HIV that maintaining an undetectable viral load eliminates the risk of transmitting HIV to sexual partners.**

Here is a link to the UCSF HIVInSite article supporting the Undetectable = Untransmittable ("U=U") message.

- **Discuss the risks of dolutegravir use with women of child-bearing age, and discontinue use if women are considering pregnancy.**
  Recent data suggest a possible association between use of the antiretroviral drug dolutegravir by women around the time of conception, and subsequent neural tube defects in their infants. The U.S. Public Health Service has issued recommendations regarding the use of dolutegravir (Tivicay®) for ongoing antiretroviral therapy (ART) or post-exposure prophylaxis (PEP) by women of childbearing potential (this also applies to co-formulations of dolutegravir such as dolutegravir/abacavir/lamivudine, or Triumeq®, and dolutegravir/rilpivirine, or Juluca®). More details, as well as links to USPHS recommendations can be found below.

NEW GUIDANCE FROM CDC/FDA ON DAILY PrEP

- **FDA has approved daily oral pre-exposure prophylaxis (PrEP) with Truvada® for adolescents and adults who weigh at least 35 kilograms (77 pounds)**
  - On May 15, 2018, the Food and Drug Administration approved an indication for Truvada for pre-exposure prophylaxis (PrEP) in adults and adolescents who weigh at least 35 kg (77 lb).
  - The indications for PrEP, initial and follow-up prescribing and laboratory testing recommendations are the same for adolescents and adults.
  - Insurance coverage for Truvada® for PrEP in adolescents:
    - Medi-Cal: Covered
    - Gilead Advancing Access: Covered. Adolescent patients do not need to document parental consent on the application form; however, the application must be co-signed by an adult advocate (can be a health care provider or patient navigator).
    - Commercial insurance: Most plans cover, with varying copay costs.
    - Youth under 18 covered under their parents' insurance can request to keep their health information private by submitting a confidential communication request.

- **Updated Laboratory Testing Guidance for Daily PrEP** (March 2018 revision to 2017 guidelines)
  - The recommendation for HIV testing was updated to indicate a preference for antigen/antibody testing (rather than antibody-only) whenever possible. If antibody-only tests (rapid or lab-based) are used for PrEP initiation, an antigen/antibody test should also be drawn with baseline labs to detect unrecognized acute infection.
  - The guidance for follow-up STI testing was revised for MSM "at high risk for recurrent STIs (e.g., those with recent STIs or multiple sex partners)" to recommend STI testing every three months, consistent with the 2015 STD guidelines.

SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH (SFDPH) STATEMENT on NON-DAILY (2-1-1) EMTRICITABINE/TENOFOVIR DOSING for PrEP

- **SFDPH strongly recommends HIV pre-exposure prophylaxis (PrEP)** with emtricitabine/tenofovir disoproxil fumarate (FTC/TDF, Truvada®) as a highly effective strategy for the prevention of sexual HIV acquisition. While not 100% effective (as breakthrough cases have occurred, predominantly with drug-resistant virus), levels of efficacy are very high with daily dosing.

- **The best-studied way to take PrEP is to take one pill daily of Truvada®, and this is the first-line regimen recommended by SFDPH.** There are many advantages to daily PrEP, including that it has been shown in multiple studies worldwide to be effective at preventing HIV infection during anal and vaginal sex, and in persons who inject drugs or anticipate doing so. Daily PrEP is a simple dosing regimen that is independent of sexual activity – planning or anticipating sex is not required. As of September 2018, daily Truvada® is the only PrEP regimen approved by the US Food and Drug Administration (FDA) and recommended by the Centers for Disease Control and Prevention (CDC), although other guideline committees, such as IAS-USA, also endorse on-demand PrEP as an alternative dosing option (see Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults—2018 Recommendations of the International Antiviral Society-USA).

- **Researchers have studied whether non-daily PrEP dosing strategies are also protective.** These dosing strategies have been referred to as “intermittent PrEP,” “event-driven PrEP” and “on-demand PrEP.”

- **The only non-daily dosing strategy for which there are efficacy data is sometimes referred to as “2-1-1.”** In the Ipergay and Prevenir studies, which primarily enrolled men who have sex with men (MSM), participants took 2 Truvada® tablets 2-24 hours before sex (closer to 24 hours before sex was preferred), another pill 24 hours after the first 2 pills, and another pill 24 hours after that. Hence the name “2-1-1.” If they continued to have sex on multiple consecutive days, they continued taking one Truvada® per day until 48 hours after their last sexual intercourse. If patients had a gap of less than 7 days between their last pill and their next intercourse, they were allowed to use a loading dose of one Truvada® tablet rather than two. This approach reduced HIV risk by 86% compared to placebo in IPERGAY. Participants took an average of 4 pills per week (a dosing frequency associated with high levels of protection in studies of daily PrEP). There are fewer data on men having infrequent sex.

- 2-1-1 PrEP is offered at some sexual health clinics in the UK, Amsterdam, France and Montreal and experience in these settings further supports that it is an effective HIV prevention strategy for MSM. However, there are much less data about 2-1-1 PrEP as compared to daily PrEP, and no comprehensive data yet from the US.

- **2-1-1 has not been studied in cis-women, cis-men who have sex with women, trans men, trans women, or people who inject drugs.** Current research suggests that non-daily Truvada® should be effective for insertive and receptive anal sex, but is not likely to reach or remain at high enough levels in the cervix or vagina to provide effective protection against HIV

infection caused by exposure to HIV at these anatomical sites. Therefore, SFDPH does not recommend the use of nondaily PrEP for HIV prevention by cis women who have vaginal sex, trans men who use their front-hole, or vagina, for sex, trans women using their neo-vagina for sex, or people who inject drugs. **2-1-1 dosing is appropriate for rectal protection only**. Based on Ipergay, 2-1-1 dosing appears to be protective for the insertive partner during anal sex.

- While daily PrEP has advantages, including being the only FDA-approved PrEP regimen in the US, we provide guidance regarding "off label" use. The event-driven approach may be appropriate for some people who are exposed to HIV rectally. SFDPH supports nondaily PrEP, using the 2-1-1 dosing strategy, as an alternative to daily dosing for persons who:
    - Are at ongoing risk of HIV infection through anal sex; and
    - Prefer not to take daily PrEP despite counseling about safety and tolerability of daily PrEP; and
    - Anticipate being able to plan their sexual intercourse and
        - Take their pre-sex dose of 2 Truvada® tablets at least 2 hours (and preferably closer to 24 hours) before sexual activity, or
        - delay sexual activity for at least 2 hours (and preferably 24 hours) after taking their "pre-sex" dose of 2 Truvada® tablets; and
    - Are able to take daily doses of Truvada® for 48 hours after their last sexual intercourse.

- It is important that patients and providers consider the following when deciding whether or not to take or prescribe 2-1-1 PrEP vs daily PrEP:
    - 2-1-1 PrEP has a similar toxicity and side effect profile to daily PrEP. Therefore individuals should not choose 2-1-1 PrEP for the purposes of decreasing side effects or toxicity, and should not expect that they will have fewer side effects on 2-1-1 PrEP
    - Individuals opting to use 2-1-1 PrEP should ensure that every sexual episode is covered by condoms, PrEP, or both. **A recent analysis of 2-1-1 PrEP dosing, showing that it was effective, focused on MSM who had infrequent sex (approximately 10 pills or 2-3 sex acts/month) AND used their PrEP "systematically or often" rather than "sometimes," that is, they did not pick and choose when or with whom to use PrEP, but used it with most/all partners.**
    - Using condoms in addition to these strategies reduces risk for other sexually transmitted diseases (e.g. syphilis, gonorrhea and chlamydia).
    - There are patient assistance programs to help cover PrEP for uninsured patients and to cover co-payments for insured patients. Patients should not choose 2-1-1 PrEP simply for cost concerns, without first talking to a PrEP navigator to explore how they can access daily PrEP.
    - Like daily PrEP, 2-1-1 PrEP should be prescribed by a provider, not borrowed from friends or sex partners.
    - Patients taking either daily or 2-1-1 PrEP should be tested for HIV and STDs at least every 3 months.
    - People using the 2-1-1 dosing strategy for PrEP may find that they want to switch to daily PrEP, and vice-versa, when their frequency of sexual intercourse changes. Providers should talk with patients about what PrEP dosing strategy they are using, and

should ensure that patients receive HIV testing prior to re-starting PrEP if they have had a period of sexual activity during which they were not using daily or 2-1-1 PrEP.

- CDC and SFDPH guidelines advise that individuals should take daily PrEP for 7 days to achieve protection for anal sex. However data from Ipergay on 2-1-1 dosing suggests that taking 2 pills 2-24 hours before sex (along with the post-sex doses) is also protective. Providers and persons opting for daily PrEP may ask whether they can simply take a 2-tablet loading dose, rather than wait for 7 daily doses. SFDPH endorses a shared decision-making approach, whereby providers discuss the very high effectiveness of PrEP when studied using both initiation strategies, and helping patients decide what is going to be most effective for them.

WARNING ON DOLUTEGRAVIR USE (INCLUDING FOR POSTEXPOSURE PROPHYLAXIS, OR PEP) IN WOMEN OF CHILDBEARING AGE

- The Department of Health and Human Services (DHHS) Antiretroviral Guidelines Panels have issued recommendations regarding the use of antiretroviral therapy containing dolutegravir (including the branded medications Tivicay®, Triumeq®, and Juluca ®) in women of childbearing potential, after a report of neural tube defects in four infants born during a study of 596 women who initiated ART including dolutegravir prior to pregnancy and were receiving it at the time of conception. These recommendations are detailed and address highly relevant clinical scenarios such as whether or not to use (or discontinue if already using) dolutegravir, based on use of contraception or stage of pregnancy, as well as alternatives to dolutegravir in adults and adolescents with HIV who are pregnant or of childbearing potential. They are summarized in an on-line DHHS document entitled Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States. In brief, DHHS recommends that dolutegravir not be used in pregnant women during the first trimester, or in nonpregnant women who are trying to conceive, but that dolutegravir is a preferred integrase inhibitor for use during pregnancy after the first trimester.

- In addition, CDC recommends alternatives to dolutegravir for post-exposure prophylaxis (PEP) in non-pregnant women of childbearing potential who are sexually active or have been sexually assaulted and are not using an effective birth control method, and pregnant women early in pregnancy (first 28 days). The preferred PEP regimen in these scenarios consists of raltegravir (Isentress®) 400mg twice daily, plus emtricitabine/tenofovir disoproxil fumarate(Truvada®) once daily. Additional alternatives for PEP are available in the CDC PEP guidelines, should raltegravir be unavailable. Although raltegravir and dolutegravir are both integrase strand transfer inhibitors there is no evidence yet that neural tube defects are associated with raltegravir.

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