

MAGNET CLINICAL PROTOCOLS	Page 1 of
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PrEP 211 Dosing Strategy	

Background:

Oral FTC/TDF pre-exposure prophylaxis is safe and effective for HIV prevention (reviewed in [1]. While most clinical trials evaluated a recommendation for daily dosing [2-10], dosing before and after sex has also been effective in animal studies [11] and a large clinical trial in men who have sex with men (MSM), called Ipergay [12]. The trial evaluated a recommendation for 2 tablets to be taken 2 to 24 hours before sex, a third tablet to be taken the day after sex, and a fourth tablet to be taken 2 days after sex. This regimen was called “On-Demand Dosing” in the original manuscript, although we will refer to it as 211 dosing for clarity. Such 211 dosing was associated with a 86% reduction in HIV incidence relative to placebo on an intention to treat basis; no one become infected while attempting such PrEP use [12]. Additional closely monitored clinical experience has identified more than 1800 MSM who received FTC/TDF PrEP with 211 dosing recommendation in France, Canada, and the Netherlands, and none have become HIV infected [13]. Clinical experience indicates that 22% to 57% of men will select this dosing strategy if it is offered [14, 15]. Such 211 dosing is recommended as an alternative regimen for MSM by the European AIDS Clinical Society and by the French Department of Health. The World Health Organization highlights that PrEP used with 211 dosing recommendations is safe and effective for MSM. San Francisco has established PrEP has a pillar for HIV prevention and PrEP use has increased to 12,500 people by 2016, yet there continue to be substantial disparities in PrEP uptake and 30 to 50% of MSM in San Francisco at imminent risk for acquiring HIV are not using PrEP. This SOP for 211 dosing recommendations is designed to be implemented for MSM and transgender women at sexual health services at the San Francisco AIDS Foundation. Given the lack of information, 211 dosing is not be offered to cis-gender women.

Recommendations for 211 dosing

Eligible Clients: A shared decision-making approach for consideration of daily and 211 dosing for PrEP among MSM. In this model, the health care provider provides information about highly effective alternative choices, encourages the client to consider these choices in their own context, and then make a decision. The advantages and disadvantages of daily versus 211 dosing are reviewed in the initial PrEP counseling and the client will determine the appropriate strategy for their sexual health plan with the support of the clinician. While not exclusive, the following clients may benefit from 211 dosing:

1. Clients who have infrequent anal sex (ie, three times per month or less)
2. Clients who have dose limiting creatinine elevations on daily emtricitabine/tenofovir
3. Clients whose timing of sexual encounters is predictable

Ineligible Clients: The following clients should not be encouraged to use 211 dosing:

1. Clients who have vaginal/front hole HIV exposures
2. Clients who are not able to reliably predict when they will have sex
3. Clients with a history of difficulties adhering to 211 dosing requiring nPEP
4. Clients with active Hepatitis B (HBsAg+)

Use Cautiously: The following clients may use 211 dosing but there is insufficient evidence to fully recommend the strategy:

1. Transfemme clients
2. Transmasculine clients who only have anal sex exposures to HIV
3. Cis women who only have anal sex exposures to HIV
4. Younger clients
5. Use of Estradiol or Testosterone

Hormones:

There are 2 small studies showing the use of estradiol may decreased tenofovir levels 17-44% [16,17]. This decrease is not significant enough to decrease the efficacy of daily PrEP but may impact the use of PrEP 211. For people on estradiol, daily PrEP is the preferred dosing strategy and PrEP 211 may be used as a harm reduction strategy if daily PrEP is not otherwise an option. There is unpublished data showing testosterone may also have a similar impact. Until more research is completed, for people on testosterone, daily PrEP is the preferred dosing strategy and PrEP 211 may be used as a harm reduction strategy if daily PrEP is not otherwise an option.

Initiating PrEP 211 dosing

Clients may change between daily and 211 dosing as needed. Clients who elect 211 dosing must have PrEP 211 counseling and sign an acknowledgment.

PrEP 211 Counseling:

211 Counseling includes:

1. Review of the evidence
2. Clients who may benefit from 211 dosing
3. 211 dosing guidelines
4. Missed dose guidelines including when to access nPEP

Review of the evidence

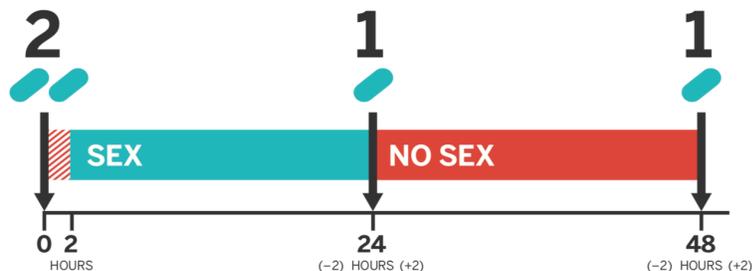
The main studies for PrEP 211 dosing are to be briefly reviewed. Clients should be informed that this dosing strategy has not been reviewed by the FDA, nor recommended by the CDC, but there are clinical studies and clinical data to support this dosing strategy for certain clients and the San Francisco Department of Public Health and the International AIDS Society in the USA (professional medical society) endorse the PrEP 211 strategy.

PrEP 211 dosing guidelines

One day:

For a single day, clients will be instructed to take 2 emtricitabine/tenofovir tablets 2-24 hours before sex, then 1 pill 24 hours after the initial dose, and a second pill 48 hours after the initial dose.

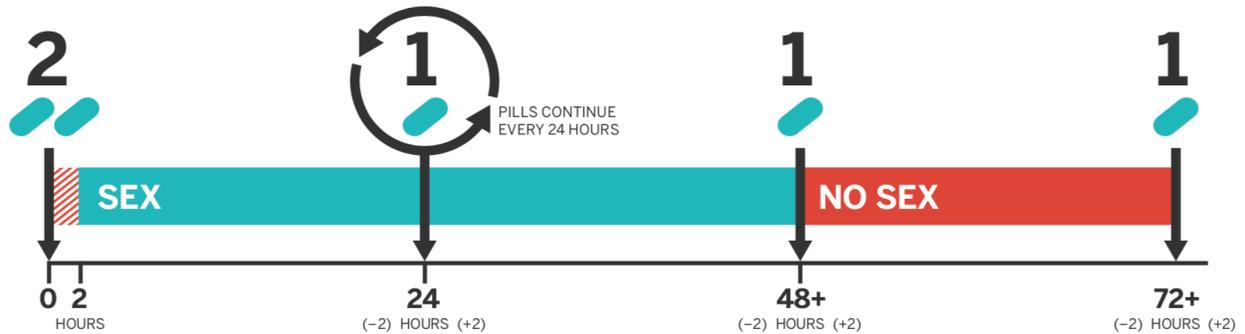
SEX WITHIN 24 HOURS OF THE FIRST DOSE



Multiple days:

For multiple days, the client will be instructed to take 2 emtricitabine/tenofovir tablets 2-24 hours before the first sex occurrence, and then 1 pill daily until 2 days have gone by without sexual activity.

SEX BEYOND 24 HOURS AFTER THE FIRST DOSE



For any new sexual encounter while off emtricitabine/tenofovir, the client should restart with 2 doses and continue with daily dosing until 2 days have gone by without sexual activity regardless of any prior doses that were taken.

Missed dose guidelines:

Clients may find that they made a dosing error by missing a dose or taking pills at the wrong time. Clients should be instructed to call the clinic to assess the missed dose situation.

In general, failure to use 211 dosing as recommended should lead to an assessment of whether the exposure involved a substantial known or potential exposure to HIV-infected fluids. If there was a substantial exposure to HIV-1 infected fluids in the past 72 hours that was not covered by pre- and post exposure dosing according to 211 guidelines, the client should be offered 28 days of post-exposure prophylaxis (PEP).

Specific examples are given below regarding how CDC recommendations for PEP could be applied to situations where PrEP was attempted (in either a daily or 211 dosing schedule) but full adherence was not achieved.

a. Sex is considered to have been protected among MSM if four or more oral FTC/TDF tablets were taken in the 7 days before sex.

b. Sex is not considered to be protected if there was less than 4 tablets taken in the previous 7 days, and any of the following occurred: the pre-sex dose was not taken or was taken less than 2 hours before sex, the first post-sex dose was taken more than 26 hours after the prior dose, or the second post-sex dose was taken more than 26 hours after the first post-sex dose. In any of these circumstances, the risk of the sexual exposure should be assessed and nPEP should be offered if there was substantial exposure to fluids that were HIV-infected or potentially HIV-infected.

nPEP rescue protocol: If the client chooses to take nPEP for an unprotected sex event, the following is recommended:

- 1) Client should take 2 doses of emtricitabine/tenofovir from the existing supply immediately.
- 2) The client should continue on daily oral emtricitabine/tenofovir for 28 days, after which they should consider remaining on daily PrEP.
- 3) As soon as possible, and ideally within 72 hours of starting nPEP, the client should contact the clinic to add dolutegravir to be taken with FTC/TDF for a total of 28 days of nPEP. The client does not need to come in for a visit and may have the prescription eprescribed to their closest pharmacy.

211 dosing prescription

The prescription is to be written for daily emtricitabine/tenofovir 200mg/300mg take 1 pill by mouth daily #30.

Clinical Follow up

All clients who are on daily or 211 dosing will follow the same clinical follow up in the PrEP Health Program protocol. Gonorrhea and Chlamydia testing may be declined if the client has not had sex since their last visit. HIV antibody and Syphilis tests are required.

Follow up Assessments:

The RN follow up orders are the same as the daily dosing the PrEP Health Program protocol.

HIV infections while on PrEP follow the PrEP HIV Seroconversion protocol.

QA Monitoring

As a new strategy, PrEP 211 will undergo monthly quality assurance to ensure a proper roll out.

Every month, the clinic will assess:

1. Number of clients electing to start PrEP 211 dosing versus Daily PrEP
2. Number of clients self-reporting the use of PrEP 211 versus daily PrEP
3. Number of clients who change strategies
4. Number of people with unprotected last sexual encounter
5. New HIV infections
 - a. Reported immediately to CMO and Medical Director.

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Kiosk Questions

Are you still taking Truvada for PrEP as part of your sexual health plan?

- Yes
- No

[Trigger No]

What is the reason you are no longer using Truvada for PrEP?

- Too costly
- Other insurance issue
- Ran out of meds (not due to cost or insurance)
- I am using condoms all the time
- I do not feel I am at risk of getting HIV
- I was having side effects
- Other

[Trigger Yes]

In the last 30 days, how many PrEP pills did you take?

Numeric response

In the last 90 days, how did you take your Truvada for PrEP?

- Daily PrEP - I took a pill everyday
- PrEP 211 - I only took pills when I had sex
- Both strategies - I used both Daily PrEP and PrEP 211

In the last 90 days, did you have anal or vaginal/front hole sex?

- Yes
- No
- Not sure/Do not remember

[No or Not Sure-end questions]

[Trigger yes]

Thinking of the last time you had anal or vaginal/front hole sex, did you take Truvada for PrEP between 2 and 24 hours BEFORE sex?

- Yes-I took 1 pill on that day
- Yes-I took 2 pills at one time on that day
- No
- Not sure/Do not remember

Thinking of this last time you had anal or vaginal/front hole sex, did you take another pill of Truvada for PrEP in the 24 hours (1 day) AFTER sex?

- Yes
- No
- Not yet I had sex less than 24 hours ago
- Not sure/Do not remember

Thinking of this last time you had anal or vaginal/front hole sex, did you **also take another pill of Truvada for PrEP 48 hours (2 Days) AFTER sex?**

- Yes
- No
- Not yet I had sex less than 48 hours ago
- Not sure/Do not remember

Thinking of this last time you had anal or vaginal/front hole sex, select any additional ways you protected yourself.

- Used a condom
- Partner told me they had an undetectable HIV Viral Load - U=U
- Partner told me they were on PrEP
- I only topped
- Other
- None of the above applies