“On-Demand” Dosing for PrEP: Guidance for Medical Providers

Daily dosing is the only Food and Drug Administration (FDA)-approved schedule for taking pre-exposure prophylaxis (PrEP) to prevent HIV. Robust data support the intermittent or “on-demand” use of PrEP before and after sexual activity by cisgender gay, bisexual and other men who have sex with men. We provide guidance on the off-label but evidence-based use of on-demand PrEP.

Recommended dosing for on-demand PrEP

The International Antiviral Society-USA supports the use of on-demand PrEP for gay, bisexual and other men who have sex with men, using a “2-1-1” schedule in which individuals take two tablets two to 24 hours before sex, one tablet 24 hours after the first dose, and another tablet 24 hours later. If they have sex again before the end of this 48-hour period, they should continue to take PrEP once every 24 hours until 48 hours after their last sexual episode. The next time they anticipate having sex, they should take a new pre-exposure dose of two pills — unless they last took PrEP at some point in the prior seven days, in which case they can initiate on-demand PrEP with a one-pill loading dose. (The San Francisco Department of Public Health also provides guidance on PrEP on demand.)

Evidence of the efficacy of on-demand PrEP

The IPERGAY trial found that taking PrEP on a 2-1-1 schedule reduced risk of HIV infection by 86% in men who have sex with men. A sub-study confirmed high efficacy among men with less-active sex lives who took doses of PrEP on demand fewer than three times per week on average.

A subsequent study, mainly among men who have sex with men, Prévenir, documented zero HIV infections over 361 person-years of follow-up. In addition, pharmacological studies have demonstrated that individuals achieve target levels of PrEP medicines in colorectal tissue 98% of the time 24 hours after an initial two-pill dose, and 81% of the time two hours after taking a two-pill dose.

Though we lack pharmacological evidence on drug concentrations in penile tissue, the IPERGAY study that showed the effectiveness of intermittent dosing in men who were the insertive partner when engaged in anal sex. This evidence suggests that PrEP on a 2-1-1 dosing schedule provides effective protection during receptive and insertive anal sex.
Who can benefit from on-demand PrEP?

While taking PrEP on demand has only been studied and recommended for cisgender men who have sex with men, on-demand PrEP may be recommended for men who:

- Experience periods of sexual inactivity
- Have impaired kidney function
- Use condoms during sex in many but not in all situations
- Cannot afford daily PrEP
- Or otherwise do not want to commit to continuous daily therapy

Non-daily dosing can expand PrEP access and help reduce barriers to highly effective HIV prevention. In a New York City study that explored different dosing strategies, some men who have sex with men said it appealed to them to take PrEP only around periods of sexual activity.

Evidence for other patient groups

Few data are available on whether taking PrEP on a 2-1-1 schedule would be effective for people who inject drugs intermittently; heterosexual cisgender women and men; and transgender persons. While there are limited data on the efficacy of on-demand PrEP for transgender persons having anal sex, PrEP and gender-affirming hormones have no known drug interactions. Intermittent dosing may be less protective for people having receptive vaginal sex, as a study found that it takes more days of PrEP dosing to achieve protective levels in cervical or vaginal tissue than in rectal tissue.

Counseling around daily versus on-demand PrEP

Counsel men who have sex with men about the effectiveness and safety of daily PrEP, and about availability of financial assistance. Tell patients who are considering taking PrEP on demand:

- Taking daily PrEP is preferred, but on-demand PrEP may be an option if you are unable or unwilling to take PrEP every day.
- On-demand PrEP works best when you can anticipate when you will have sex. If you think you might have sex, take two pills beforehand. You can stop taking PrEP if you do not have sex.
- Taking two PrEP pills 24 hours before sex provides the best protection, but taking the initial dose as little as two hours before sex also helps protect against HIV.
- While highly effective, PrEP does not provide 100% protection. Rare cases of HIV transmission, despite the individuals taking PrEP daily or on demand correctly, have occurred.
- Condoms provide additional protection against HIV and other sexually transmitted infections (STIs). Make sure you use condoms or another prevention method when not taking PrEP.
- If you forget to take PrEP, emergency PEP (post-exposure prophylaxis) can prevent HIV if started within 72 hours of a possible exposure to HIV.
- Taking PrEP under a doctor or nurse’s care helps ensure that the medicine is working correctly.
- You may need to refill your prescription less often if you use PrEP on demand, but you should still come in every three months for testing to make sure you do not have undiagnosed HIV or other STIs.

More information

PrEP and PEP: Information for Medical Providers
PrEP and PEP Action Kit
HIV Information for Providers