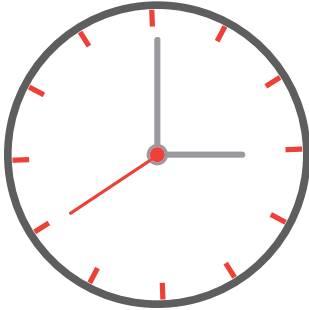




CLINICIAN'S INFORMATION GUIDE

On-Demand (2-1-1) Dosing for HIV PrEP

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ABOUT THIS INFORMATION GUIDE

This information guide is intended for health care professionals involved in care of persons interested in or receiving HIV preexposure prophylaxis (PrEP). The information in this guide pertains to the use of on-demand (2-1-1) dosing for HIV preexposure prophylaxis (PrEP). This guide was created and produced by the University of Washington Infectious Diseases Education & Assessment Program (IDEA) as part of the federally-funded *National HIV PrEP Curriculum* project.

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LAST UPDATED

This educational guide was last updated *October 3, 2025*.

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GENERAL INFORMATION

What is on-demand HIV PrEP?

- On-demand dosing for HIV PrEP involves taking oral HIV PrEP medications timed in relation to a sexual event. This is also referred to as 2-1-1 dosing since two pills are taken 2-24 hours before sex, one pill 24 hours after the first dose, and one pill 48 hours after the first dose.
- On-demand dosing for HIV PrEP was designed as an option when sexual activity occurs relatively infrequently and daily dosing may not be needed or desired.

Who is eligible to receive on-demand dosing?

- On-demand (2-1-1) HIV PrEP is a recommended option only for men who have sex with men who are at risk of acquiring HIV sexually.
- On-demand (2-1-1) HIV PrEP is NOT recommended for heterosexual men, women, people who inject drugs, adolescents, people with hepatitis B, and people with an estimated creatinine clearance <60 mL/min.

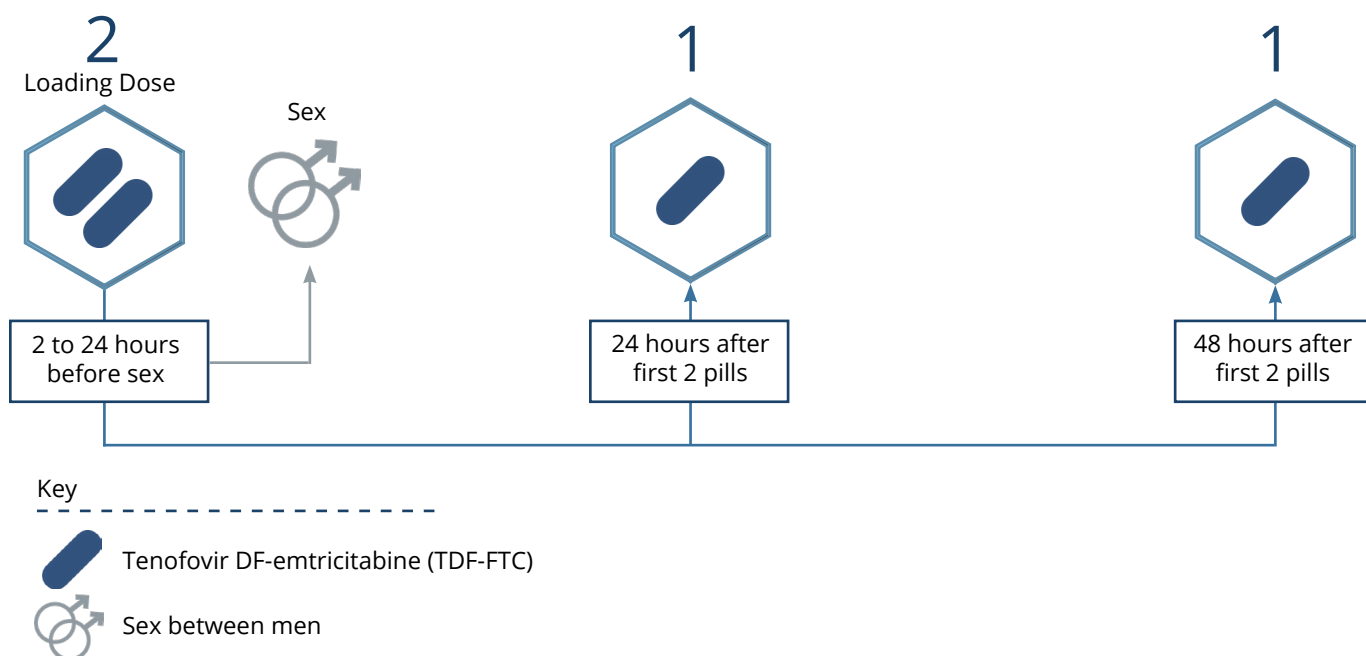
Which medication can be used?

- Tenofovir DF-emtricitabine (TDF-FTC) is the only medication recommended for use as on-demand (2-1-1) dosing for HIV PrEP.
- Tenofovir alafenamide-emtricitabine (TAF-FTC), oral cabotegravir, long-acting injectable cabotegravir (CAB-LA), oral lenacapavir, and injectable lenacapavir (LEN-SQ) are NOT recommended for use as on-demand dosing for HIV PrEP.

ON-DEMAND HIV PREP DOSING: SCENARIO 1

Single sexual encounter

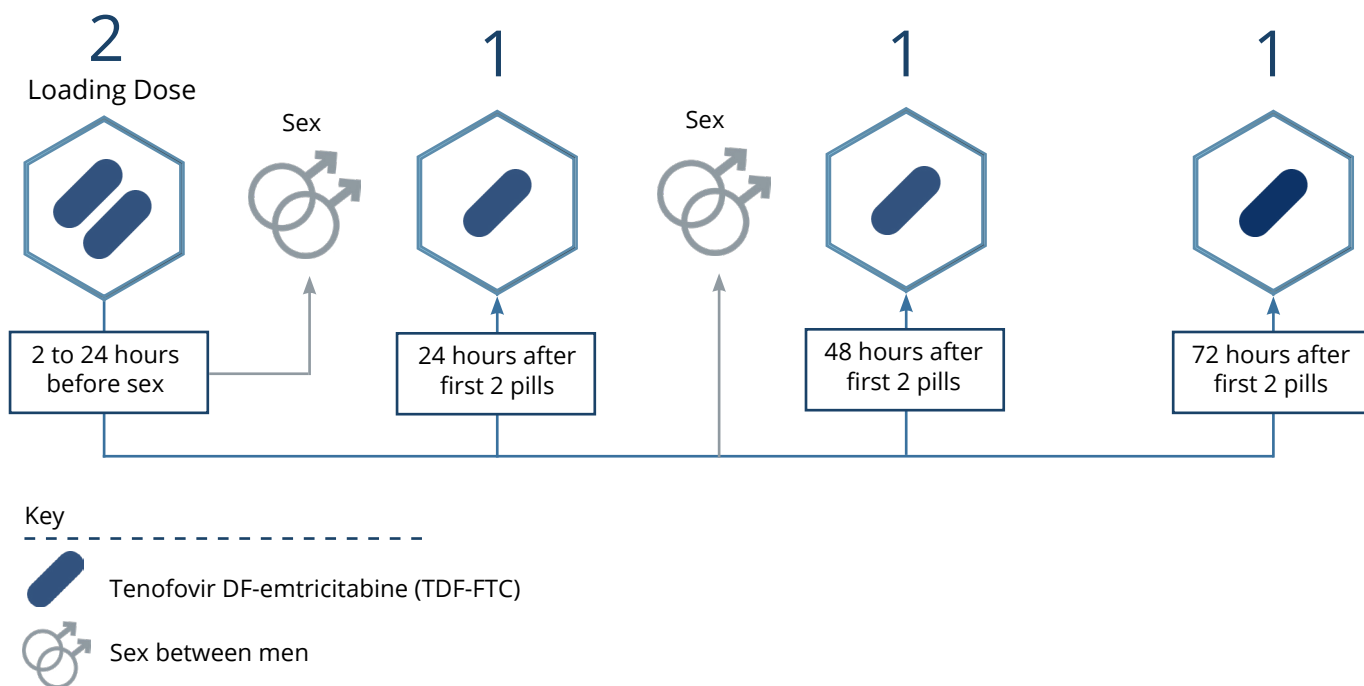
Take a loading dose of two pills 2-24 hours before sex. Then take one additional pill 24 hours after the loading dose and one additional pill 48 hours after loading dose. **Note:** the loading dose is timed around the anticipated sex, whereas all subsequent doses are timed relative to when the loading dose was taken.



ON-DEMAND (2-1-1) HIV PREP DOSING: SCENARIO 2

Sexual encounters on consecutive days

For sex that occurs on consecutive days, take a loading dose of two pills 2-24 hours before the first sexual encounter, then take one additional pill every 24 hours (from the time of the loading dose) until two pills have been taken after the last sexual encounter. **Note:** the loading dose is timed around the anticipated sex, whereas all subsequent doses are timed relative to when the loading dose was taken. The example below shows 2-1-1-1 dosing for sex that occurs on 2 consecutive days. If sex occurs on 3 consecutive days, then dosing should be 2-1-1-1-1.



EDITOR'S NOTE

These dosing instructions are consistent with the design of the IPERGAY study (see page 6) and vary slightly from the guidance provided in the 2021 CDC PrEP Clinical Guidelines.

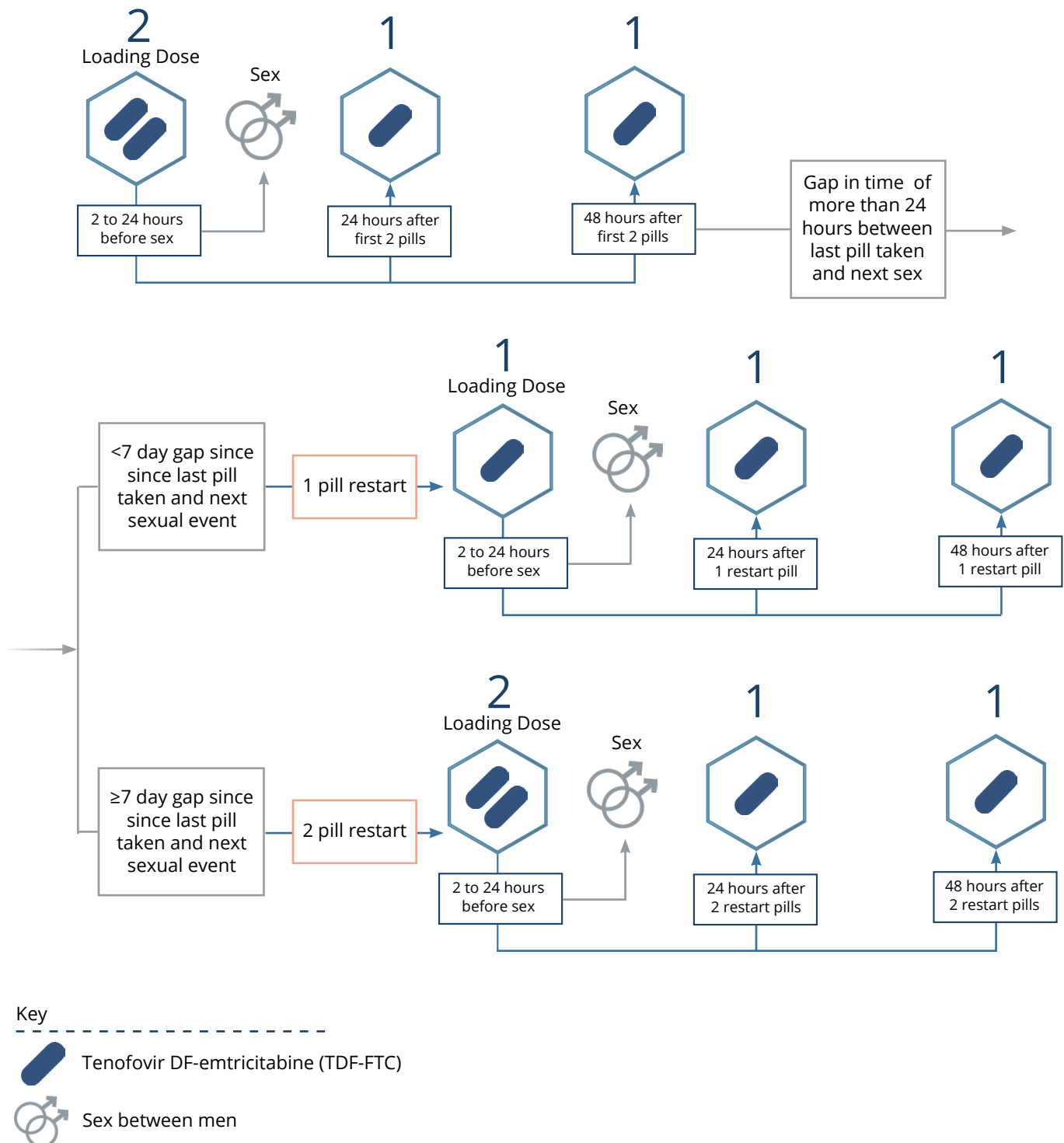
In this scenario, with sex on consecutive days, once a person initiates on-demand HIV PrEP, they should take their subsequent doses at approximately the same time every day as their original 2 pill loading dose, regardless of when sex occurs.

A person utilizing on-demand HIV PrEP dosing should always take two doses (24 hours apart) after their last sexual encounter.

ON-DEMAND (2-1-1) HIV PREP DOSING: SCENARIO 3

Multiple sexual events on non-consecutive days with a gap in pill doses of >24 hours

If on-demand HIV PrEP was very recently administered and new sexual activity occurs after a gap of more than 24 hours since the last dose of TDF-FTC was taken, then on-demand HIV PrEP needs to be restarted. When restarting on-demand HIV PrEP, the schedule will consist of either 1-1-1 dosing (if the gap in time was less than 7 days from when the last pill was taken), or 2-1-1 dosing (if the gap in time was greater than 7 days from the last dose).





The National Clinician Consultation Center (NCCC) provides free expert consultation and guidance for clinicians on providing HIV PrEP, including:

- Medication Initiation
- On-demand (2-1-1) dosing for HIV PrEP
- Ongoing follow-up in persons receiving HIV PrEP
- Diagnosing HIV in persons receiving HIV PrEP
- Initiation of antiretroviral therapy for persons receiving HIV PrEP who are diagnosed with HIV

Call for a PHONE CONSULTATION

(855) 448-7737 or (855) HIV-PrEP
Monday – Friday, 9 a.m. – 8 p.m. ET

To Submit Your Case Online

Go to the NCCC Web Site (<https://nccc.ucsf.edu/clinician-consultation/prep-pre-exposure-prophylaxis/>) or scan the QR code above

Note: The National HIV PrEP Curriculum does not provide clinical consultation or medical advice.

IPIRGAY

On-Demand TDF-FTC as HIV PrEP for MSM

Summary

On-demand (2-1-1) tenofovir DF-emtricitabine (TDF-FTC) was highly effective at preventing HIV infection for MSM

Study Design

Randomized, phase 3, double-blind, placebo-controlled trial conducted in France and Canada

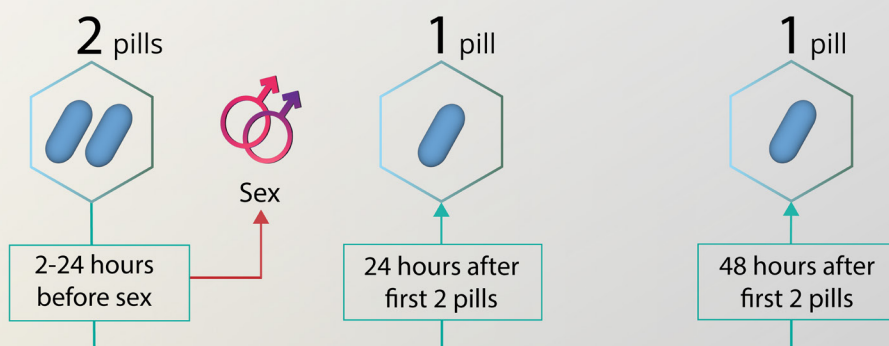
Participants

400

Adult HIV-seronegative
MSM

- Condomless rectal sex in prior 6 months
- No hepatitis B
- Normal renal function

On-demand (2-1-1) TDF-FTC Dosing Example



Interventions

Placebo

On-demand
(2-1-1) dosing

n = 201



TDF-FTC

On-demand
(2-1-1) dosing

n = 199



Results

New HIV
Infections

14

2

Incident HIV
Infections
(per 100 person-years)

6.60

0.91

HIV Risk
Reduction

86% relative risk reduction in HIV incidence
(95% CI 40 to 98; p=0.002)

Source: Molina JM, Capitant C, Spire B, et al. N Engl J Med. 2015;373:2237-46. [[PMID: 26624850](https://pubmed.ncbi.nlm.nih.gov/26624850/)]

PREVENIR

On-Demand TDF-FTC vs. Daily TDF-FTC for HIV PrEP

Summary

On-demand (2-1-1) and daily dosing of tenofovir DF-emtricitabine (TDF-FTC) were equally effective at preventing HIV acquisition in a trial of mainly men who have sex with men (MSM)

Study Design

Prospective, observational cohort study conducted at 26 sites in the Paris region of France (participants could choose daily vs. on-demand dosing).

Participants

3,056

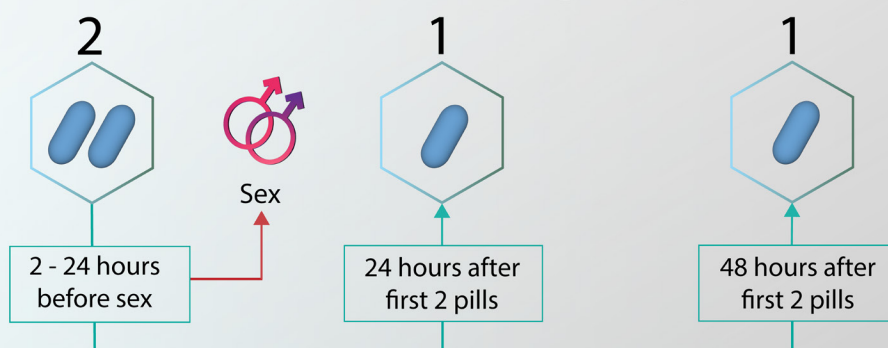
Adults

98.7% MSM



44.0% HIV PrEP naive

On-demand (2-1-1) Dosing Example

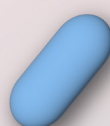


Interventions

TDF-FTC

Daily

n = 1,540



TDF-FTC

On-demand
(2-1-1) dosing

n = 1,509



Results

New HIV
Infections

3

3

Incident HIV
Infections
(per 100 person-years)

0.195

0.199

HIV Risk
Reduction

No statistically significant difference
(95% CI 0.13 to 7.49; p=0.99)

Source: Molina JM, Ghosn J, Assoumou L, et al. Lancet HIV. 2022;9:e554-e562. [\[PMID: 35772417\]](https://pubmed.ncbi.nlm.nih.gov/35772417/)

FREQUENTLY ASKED QUESTIONS

1. Who is a good candidate for on-demand HIV PrEP?

The CDC HIV PrEP Guidelines recommend on-demand dosing with tenofovir DF-emtricitabine (TDF-FTC) for HIV PrEP as an off-label option only for adult men who have sex with men (MSM). Per the CDC Guidelines, clinicians may consider prescribing TDF-FTC on-demand dosing for adult MSM who have sex relatively infrequently (less than once per week), tend to anticipate sex (so they can take the pills at least 2 hours before sex each time), are able to adhere to the complex dosing pattern, have normal renal function, and do not have hepatitis B virus (HBV) infection. Some MSM who meet these criteria may prefer the on-demand TDF-FTC dosing option, while others may prefer oral TDF-FTC or TAF-FTC daily dosing, CAB-LA, or LEN-SQ. At this time, due to inadequate data, the CDC does not recommend prescribing on-demand HIV PrEP for women or adolescents.

2. Is on-demand HIV PrEP as effective as daily HIV PrEP?

Yes, if taken correctly. A randomized controlled trial (IPERGAY) of on-demand TDF-FTC for HIV PrEP in adult MSM found the option of on-demand TDF-FTC dosing to be more effective than placebo (86% estimated HIV risk reduction). In this trial, however, participants took three to four TDF-FTC pills per week on average, so it is debatable whether the trial adequately assessed efficacy for MSM who have sex infrequently. In addition, a prospective, observational study (PREVENIR) compared daily TDF-FTC to on-demand TDF-FTC for HIV PrEP and found comparable efficacy between the two options. Therefore, on-demand HIV PrEP is probably as effective as daily HIV PrEP for MSM who are good candidates and who adhere well to the dosing, though efficacy data for on-demand HIV PrEP are not as robust as efficacy data for daily HIV PrEP. Further, some studies have found coverage of sex acts to be lower with on-demand HIV PrEP than with daily HIV PrEP, so encouraging proper adherence to on-demand dosing is critical to ensuring effectiveness.

3. Is it okay to switch between daily HIV PrEP and on-demand HIV PrEP?

Yes. For MSM who initiate daily HIV PrEP but then wish to switch to on-demand HIV PrEP because sex becomes less frequent (and they are good candidates for the on-demand HIV PrEP option), it is reasonable to switch, as long as TDF-FTC is the medication used for on-demand HIV PrEP. Similarly, if an individual starts on-demand HIV PrEP and sex becomes more frequent, such as more than once per week, it is recommended they switch to oral TDF-FTC or TAF-FTC daily dosing, CAB-LA, or LEN-SQ.

4. Can tenofovir alafenamide-emtricitabine (TAF-FTC) be used for on-demand dosing?

No. TAF-FTC has not been studied for on-demand HIV PrEP and therefore it is not recommended for on-demand dosing.

5. Can you use on-demand HIV PrEP if a person has a baseline creatinine clearance of less than 60 mL/min?

No. There are no data for the safety or efficacy of on-demand HIV PrEP for individuals with creatinine clearance below 60 mL/min. Because the only option for on-demand HIV PrEP is TDF-FTC and this medication is not recommended for HIV PrEP in persons who have a creatinine clearance less than 60 mL/min, on-demand HIV PrEP should not be used for anyone with a creatinine clearance less than 60 mL/min.

FREQUENTLY ASKED QUESTIONS

6. What supply of medications should you give someone prescribed on-demand HIV PrEP?

For off-label, on-demand HIV PrEP, CDC recommends prescribing no more than 30 TDF-FTC pills at one time, without automated refills. This quantity is sufficient for approximately 7 sexual encounters. For daily oral HIV PrEP dosing, clinicians typically prescribe a quantity of 90 tablets, but this quantity is not usually given for on-demand HIV PrEP since the patient may not return for repeat HIV and sexually transmitted infection (STI) screening in a timely manner (e.g., 90 tablets for an individual taking on-demand dosing and having sex less than once per week would last for at least 6 months, which is longer than the recommended every 3-month HIV and STI screening for MSM receiving HIV PrEP). If an individual is having sex more frequently than initially anticipated and runs out of the 30-day TDF-FTC supply before 3 months, then a refill can be provided, as long as HIV and STI testing occurs every 3 months; for individuals with frequent (more than once per week) use of on-demand dosing, it is important to regularly discuss the option of switching to daily oral HIV PrEP, CAB-LA, or LEN-SQ.

7. How often should a person taking on-demand HIV PrEP have medical provider visits and laboratory studies ordered?

Persons taking on-demand TDF-FTC HIV PrEP should typically have repeat visits with a medical provider every 3 to 6 months; these visits can occur either in person or via telemedicine. Repeat HIV and STI testing should be performed every 3 months. Serum creatinine should be repeated every 6 to 12 months, depending on age and baseline estimated creatinine clearance (every 6 months for persons ≥ 50 years of age or who have an estimated creatinine clearance less than 90 mL/min). If the individual has not had any sexual encounters during the 3-month time period, laboratory testing can be deferred until sexual activity resumes.

8. Is there a greater risk of developing HIV drug-resistance for those using on-demand HIV PrEP than with daily HIV PrEP?

Probably not. There are no data that suggest HIV drug resistance is more likely with on-demand HIV PrEP than with daily HIV PrEP, though few studies have examined this question. In the IPERGAY trial, HIV drug resistance was not detected for participants who acquired HIV in the on-demand HIV PrEP arm, though the number of HIV acquisitions was small. More data are needed to compare the risks of developing HIV drug resistance with HIV acquisition for persons prescribed on-demand versus daily HIV PrEP.

9. Can you transition from non-occupational HIV postexposure prophylaxis (nPEP) directly to on-demand HIV PrEP?

Yes, if an individual is a good candidate for on-demand HIV PrEP, they can transition immediately from non-occupational HIV postexposure prophylaxis (nPEP) to on-demand HIV PrEP with TDF-FTC. It is important to order recommended baseline laboratory studies, including repeat HIV testing, prior to starting HIV PrEP, but there is no need to delay HIV PrEP while awaiting the additional HIV test results.

FREQUENTLY ASKED QUESTIONS

10. Why is on-demand HIV PrEP NOT recommended for people who have chronic active HBV infection?

On-demand HIV PrEP should not be used in people who have chronic hepatitis B virus (HBV) infection. The rationale for this recommendation is that both tenofovir DF (TDF) and emtricitabine (FTC) have activity against HBV, so use of on-demand HIV PrEP would be providing intermittent HBV treatment, which is not recommended due to the risk of HBV-related hepatic flares and HBV drug resistance. Therefore, a negative hepatitis B surface antigen (HBsAg) test should be confirmed and documented prior to initiating on-demand HIV PrEP. Persons who test negative for HBsAg and are not immune to HBV should receive hepatitis B immunization.

11. How do medication side effects compare with on-demand HIV PrEP dosing versus daily HIV PrEP dosing, CAB-LA, or LEN-SQ?

Overall, both on-demand and daily TDF-FTC HIV PrEP tend to be well tolerated, but “start-up syndrome” symptoms (nausea, diarrhea, abdominal discomfort, headache, fatigue, and other generalized side effects) may be more likely with on-demand dosing because the individual stops and starts the medication and thereby experiences this “start-up syndrome” repeatedly. In the PREVENIR trial, on-demand HIV PrEP had a smaller impact on renal function (based on estimated glomerular filtration rate) than daily HIV PrEP, but the difference was not statistically significant. It is possible that on-demand TDF-FTC dosing has less long-term effects on renal function and on bone-mineral density than daily dosing, but this has not been confirmed. Tolerability of on-demand TDF-FTC has not been compared head-to-head versus daily dosing of TAF-FTC, CAB-LA, or LEN-SQ.

12. Does on-demand dosing need to be changed if a person has sex multiple times on the same day/night?

No. For example, a person planning to have sex on a Friday night takes the 2-pill loading dose Friday morning, and has sex multiple times on Friday night. No change in the dosing needs to occur and they should complete the on-demand dosing—take 1 pill Saturday morning and 1 pill Sunday morning. If another sexual encounter occurs more than 24 hours after the 2-pill loading dose, they would need to extend the on-demand dosing for an additional day. If a person is anticipating having sex multiple times on the same day/night it is very important they time taking the 2-pill loading dose 2-24 hours based on when the first episode of sex is anticipated to occur.

13. If a person forgets to take the 2 pills prior to sex or they forget to take one or more post-sex doses, what should they do?

There are no formal recommendations for guiding persons who miss one or more pre-sex or post-sex on-demand HIV PrEP doses. Most experts would advise individuals who are prescribed on-demand HIV PrEP and forget their pre-sex dose to seek care to discuss possible non-occupational HIV postexposure prophylaxis (PEP). For persons missing one post-sex dose, most experts would not recommend initiating nonoccupational PEP. The approach to missing multiple post-sex doses should be individualized, but regardless of the recommendation, counseling should include consideration for switching to daily oral HIV PrEP, CAB-LA, or LEN-SQ.

FREQUENTLY ASKED QUESTIONS

14. Does on-demand HIV PrEP protect against STIs?

No. Persons receiving TDF-FTC, or any HIV PrEP, should receive counseling that HIV PrEP does not prevent bacterial sexually transmitted infections (STIs). Therefore, persons taking HIV PrEP who are having condomless sex should have regular testing for bacterial STIs. In addition, TDF-FTC HIV PrEP is not recommended as a strategy to prevent the sexual transmission of viruses other than HIV. Individuals should receive counseling on methods to prevent acquisition of these viruses, including condom use and immunizations for human papillomavirus, mpox, and hepatitis B.

15. Is on-demand HIV PrEP covered by insurance?

On-demand HIV PrEP is considered off-label by the CDC, so it is not guaranteed to be covered by insurance plans. That said, when prescribed for appropriate HIV PrEP candidates, it is usually covered by insurance plans that cover daily HIV PrEP.

16. If a person prescribed on-demand HIV PrEP acquires HIV infection, which antiretroviral therapy regimen should be prescribed?

For a person who acquires HIV while taking TDF-FTC for HIV PrEP, including persons taking on-demand dosing, blood should be drawn for an HIV drug-resistance genotype assay. While awaiting the genotype results, most experts recommend starting standard three-drug antiretroviral therapy with (1) bictegravir-tenofovir alafenamide-emtricitabine or (2) dolutegravir plus either TAF-FTC or TDF-FTC. This approach is the same as when a person acquires HIV while taking daily oral HIV PrEP.

REFERENCES

- Antoni G, Tremblay C, Delaunay C, et al. On-demand pre-exposure prophylaxis with tenofovir disoproxil fumarate plus emtricitabine among men who have sex with men with less frequent sexual intercourse: a post-hoc analysis of the ANRS IPERGAY trial. *Lancet HIV*. 2020;7:e113-e120. [PMID: 31784343]
- Bauer R, Netzer E, Pintado C, et al. Coverage of Sex Acts by Event-Driven Pre-exposure Prophylaxis: A Sub-Study of the ANRS IPERGAY Trial. *AIDS Behav*. 2020;24:3244-51. [PMID: 32350771]
- Delaunay C, Rodriguez C, Capitain C, et al. Drug resistance among patients who acquired HIV infection in a pre-exposure prophylaxis trial. *AIDS*. 2018;32:2353-61. [PMID: 30096070]
- Dimitrov D, Moore JR, Wood D, et al. Predicted Effectiveness of Daily and Nondaily Preexposure Prophylaxis for Men Who Have Sex With Men Based on Sex and Pill-taking Patterns From the Human Immuno Virus Prevention Trials Network 067/ADAPT Study. *Clin Infect Dis*. 2020;71:249-55. [PMID: 31437276]
- Durand-Zaleski I, Mutuon P, Charreau I, et al. Costs and benefits of on-demand HIV preexposure prophylaxis in MSM. *AIDS*. 2018;32:95-102. [PMID: 29210777]
- Goldwirth L, Bauer R, Liegeon G, et al. Estimated pill intake with on-demand PrEP with oral TDF/FTC using TFV-DP concentration in dried blood spots in the ANRS IPERGAY trial. *J Antimicrob Chemother*. 2021;76:2675-80. [PMID: 34278433]
- Liegeon G, Assoumou L, Ghosn J, et al. Impact on renal function of daily and on-demand HIV pre-exposure prophylaxis in the ANRS-PREVENIR study. *J Antimicrob Chemother*. 2022;77:3427-35. [PMID: 36205009]
- Molina JM, Capitain C, Spire B, et al. On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection. *N Engl J Med*. 2015;373:2237-46. [PMID: 26624850]
- Molina JM, Ghosn J, Assoumou L, et al. Daily and on-demand HIV pre-exposure prophylaxis with emtricitabine and tenofovir disoproxil (ANRS PREVENIR): a prospective observational cohort study. *Lancet HIV*. 2022;9:e554-e562. [PMID: 35772417]
- Saberi P, Scott HM. On-Demand Oral Pre-exposure Prophylaxis with Tenofovir/Emtricitabine: What Every Clinician Needs to Know. *J Gen Intern Med*. 2020;35:1285-8. [PMID: 31965523]

DISCLOSURES

Dr. Spach, Dr. Wood, Dr. Bacon, and Dr. Stekler have no disclosures

APPRECIATION

The authors would like to thank Peter Harrison, MPH and Carol Kono-Noble for their design and production work.

ACKNOWLEDGEMENT

The Health Resources and Services Administration (HRSA), Department of Health and Human Services (HHS) and Centers for Disease Control and Prevention (CDC) provided financial support for the National HIV PrEP Curriculum. The award provided 100% of total costs and totaled \$299,994 from HRSA and \$603,203 from CDC. The contents are those of the author. They may not reflect the policies of HRSA, HHS, CDC, or the U.S. Government.

