For Health Care Providers

What you need to know about HIV PrEP

HIV PrEP stands for HIV Pre-exposure Prophylaxis. It is the use of daily or on-demand (event-driven) oral antiretroviral therapy (ART) by HIV negative individuals to reduce the risk of acquiring HIV. HIV PrEP refers to ongoing use of ART before and after potential exposure to HIV.HIV PrEP involves taking the combination medication:

- Emtricitabine 200 mg/tenofovir DISPROXIL FUMARATE 300 mg (e.g. Truvada®)
- Emtricitabine 200 mg/tenofovir ALAFENAMIDE 25 mg (e.g. Descovy®)

These two drugs are part of the nucleoside reverse transcriptase inhibitor (NRTI) class of drugs, and work by blocking HIV reverse transcription, thereby preventing the construction of new proviral DNA.

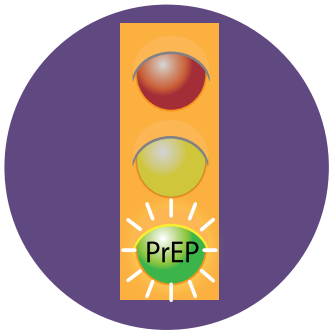
Effectiveness

Reduces risk of HIV by over

90%

When taken as prescribed, PrEP has been shown to reduce the risk of acquiring HIV by over 90%.

Starting HIV PrEP



Time is needed to build up protective levels of PrEP within the body

The time from initiation of daily oral doses of HIV PrEP to maximal protection against HIV acquisition is uncertain.

However, pharmacokinetic data from individuals living with HIV suggest that steady-state levels in the rectal and cervico-vaginal mucosa are reached after 7 days following therapy initiation.

Individuals should be counselled to continue condom use during this period.

Taking HIV PrEP

HIV PrEP tablets can be taken any time of day, with or without food. PrEP is generally taken as one tablet once a day. It does not have to be taken at the same time each day, though those taking PrEP should be counselled to try taking it at roughly the same time every day. This usually helps people remember to take it.

Contraindications and Cautions

Any previously demonstrated hypersensitivity to any components of the medication is a contraindication to its use. For a complete listing, see the DOSAGE FORMS, COMPOSITION AND PACKAGING section of the Product Monograph.

People who already have HIV should not take HIV PrEP; they should be offered antiretroviral therapy.
Do not initiate HIV PrEP if signs or symptoms of acute HIV infection are present, and/or there is clinical suspicion of acute HIV. Speak to an infectious diseases or HIV expert if you are unsure.

Although it is safe to take PrEP with many other medications, it is important to check for drug interactions and/or overlapping toxicities between HIV PrEP and other medications being taken concurrently. Since tenofovir-containing medications are primarily renally eliminated, there is a potential for increased nephrotoxicity with other agents that can affect renal function, including non-steroidal anti-inflammatory drugs (NSAIDS). Consider alternatives to NSAIDS in persons taking HIV PrEP and at risk of renal impairment.

As tenofovir-containing medications have been associated with decreases in bone mineral density in both HIV treatment and HIV PrEP settings, it should be used with caution in persons with a history of osteoporosis or osteomalacia, and fragility fractures.

At present, no specific bone mineral density screening is recommended before or during HIV PrEP use, though individuals on PrEP should be counselled to take bone-protective measures (eg. vitamin D supplementation, weight-bearing exercise).

On-Demand use of HIV-PrEP

The use of daily HIV PrEP is advised for maximal protection if an individual is having ongoing sex over undefined periods of time.

For individuals in whom on-demand (i.e. event-driven) PrEP use is seen as appropriate, the following dosing strategy is recommended:

- Take a loading dose of 2 tablets, 2-24 hrs before anticipated sex, then if sex happens:
  - Take one tablet daily while sexually active
  - Continue taking one tablet daily for two or more days after sexual activity has stopped.

On-demand use of PrEP is not appropriate for individuals co-infected with hepatitis B virus, where continuous daily treatment is required

Missed doses

If an individual misses a dose within 12 hours of the regularly scheduled time, but then remembers it that same day, the missed dose should be taken as soon as possible and resume their normal dosing schedule.

If an individual misses a dose by more than 12 hours and it is almost time for their next dose, they should not take the missed dose and simply resume the usual dosing schedule.

Individuals taking daily PrEP should not take more than 1 dose in a day, and should not take 2 doses at the same time to make up for missing a dose (there is no harm if two tablets are accidentally taken in one day, however).

A minimum of 4 doses per week is required for maximal protection against HIV acquisition, although daily adherence should be encouraged. If more than 3 doses in a given week are missed and an individual has had a high risk exposure event, they may need to be considered for post-exposure prophylaxis.

What if a dose is vomited?

If the tablet is visibly vomited out, suggest that the individual wait an hour for the vomiting to resolve and then take another tablet.

If vomiting occurs an hour or more after taking the tablet, and the tablet is not visible in the vomit, suggest that the individual take the next tablet the next day as usual.

Drugs, medications and hormones

Taking alcohol or using recreational drugs such as heroin and other opioids, cocaine or methamphetamine will not reduce the effectiveness of HIV PrEP.

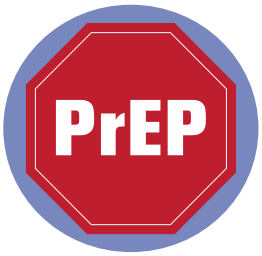
There are no known interactions between HIV PrEP and alcohol or recreational drugs.

HIV PrEP is safe and effective even if taking hormonal contraceptives, sex hormones and many non-prescription medications.

HIV PrEP does not affect the efficacy of oral, injectable or implanted hormonal contraceptives or gender-affirming hormones.

Contraceptives and hormones also do not affect HIV PrEP efficacy. also do not affect HIV PrEP efficacy. HIV PrEP medicines are processed in the kidneys, while contraceptive and gender-affirming hormones are processed in the liver.

Stopping PrEP



When stopping HIV PrEP, the optimal duration of continuation after a recent sexual exposure is unclear. Based on data from the IPERGAY trial, HIV PrEP should be continued for at least 48 hours after a high risk exposure.

However, continued use for as long as 28 days after a high risk exposure is recommended by some groups.
HIV PrEP is not sufficient for the treatment of HIV infection. HIV testing before starting or restarting HIV PrEP is essential to detect infections that require treatment.

Safety

HIV PrEP is safe and well-tolerated

Minor side-effects

About 10% of people who start HIV PrEP will have some short-term, mild side-effects.

Side-effects may include gastrointestinal symptoms (diarrhoea, nausea, decreased appetite, abdominal cramping or flatulence).

Dizziness or headaches have also been reported.

Side-effects are usually mild and resolve without stopping HIV PrEP. Typically, these symptoms start in the first few days or weeks of HIV PrEP use, last a few days and almost always resolve within a month.

Renal side-effects

A very small percentage of individuals will not be able to take HIV PrEP because of kidney problems.

Renal function tests (creatinine and urinalysis or urine albumin-to-creatinine ratio) should be done prior to starting individuals on HIV PrEP and for continued monitoring while on HIV PrEP.

One-time elevations in serum creatinine are seen in approximately one in every 200 HIV PrEP users, but levels usually return to normal on a second test.

If the estimated glomerular filtration rate (eGFR) falls below 60mL/min while on PrEP, or if an individual has an eGFR below 60 mL/min prior to starting PrEP, this does not necessarily mean the individual must either stop (or not start) PrEP. Often, there are possible explanations for this (eg. creatine supplementation, NSAID use, dehydration). Descovy may be an option for individuals with kidney problems (kidney dsyfunction). If this occurs, review some of these issues with the individual. If in doubt or uncertain, consult an infectious diseases or HIV specialist.

Bone mineral density

A slight decrease in bone mineral density (BMD) has been observed in people taking tenofovir-containing medications.

Tenofovir-containing medications for HIV PrEP have been associated with a small decrease in BMD (0.5-1.5%) in the spine and hip in the first six months, but does not progress further. BMD typically returns to normal once PrEP is stopped.

Studies have not demonstrated an increase in bone fractures as a result of these observed decreases in BMD.

Hepatitis B

Acute or chronic hepatitis B virus (HBV) infection is usually indicated by the detection of hepatitis B surface antigen (HBsAg).

In those for whom treatment is indicated, tenofovir-containing medications may be recommended for treatment of HBV. Therefore, oral HIV PrEP containing tenofovir-containing medications can benefit people whose HBV infection warrants treatment. TDF is active against HBV infection at the same dose used for HIV PrEP. Appropriate monitoring for HBV should be performed in accordance with hepatitis B treatment guidelines, and if necessary, in consultation with a qualified practitioner with experience in treating the virus.

When considering HIV PrEP discontinuation, the need for ongoing therapy for HBV should be assessed as a chronic HBV carrier may experience a flare-up of their hepatitis once HIV PrEP is discontinued.

Hepatitis C

There are potential drug interactions between tenofovir-containing medications and some hepatitis C antivirals. A full review should be performed prior to co-administration.

HIV PrEP during pregnancy and breast/chest feeding

HIV PrEP can be used throughout pregnancy and when breast/chest feeding.

There were no differences in pregnancy outcomes, infant birth weight or congenital malformations in HIV PrEP users placebo users among serodiscordant couples in thecompared to Partners PrEP study.

HIV PrEP may be offered or continued during pregnancy if HIV remains a substantial risk for the individual.

Although experience with HIV PrEP during breast/chest feeding is still lacking, there is substantial experience with tenofovir-containing medications during breast/ chest feeding by women with HIV on ART. This demonstrates that although tenofovir-containing medications are secreted in breast milk at very low concentrations, it remains safe to use throughout breast/ chest feeding.

Post Exposure Prophylaxis (PEP)

People who have been exposed to HIV in the preceding 72 hours should be offered PEP if not currently on HIV PrEP or if on HIV PrEP and there are concerns about adherence (eg. more than 3 doses missed in a given week). PEP should be offered as soon as possible after exposure.

After 28 days of PEP, HIV PrEP can be started without a gap if the HIV test remains negative and there is ongoing risk of HIV acquisition. In people with ongoing potential exposure to HIV, there should be no gap between finishing PEP and starting HIV PrEP.

Useful Reading

1. Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, et al. *Preexposure chemoprophylaxis for HIV prevention in men who have sex with men*. The New England Journal of Medicine. 2010; 363(27):2587–99. iPrEx

2. Baeten JM, Donnell D, Ndase P, Mugo NR, Campbell JD, Wangisi J, et al. *Antiretroviral prophylaxis for HIV prevention in heterosexual men and women.* The New England Journal of Medicine. 2012; 367(5):399–410. Partners PrEP

3. Molina JM, Capitant C, Spire B, Pialoux G, Cotte L, Charreau I, et al. *On–Demand Preexposure Prophylaxis in Men at High Risk for HIV–1 Infection*. The New England Journal of Medicine. 2015;373(23):2237–46. 6. ANRS IPERGAY

4. Molina JM, Charreau I, Spire B, Cotte L, Chas J, Capitant C, et al. *Efficacy, safety, and effect on sexual behaviour of on–demand pre–exposure prophylaxis for HIV in men who have sex with men: an observational cohort study.* Lancet HIV 2017; 4: e402 - 10. ANRS IPERGAY

5. McCormack S, Dunn DT, Desai M, Dolling DI, Gafos M, Gilson R, et al. *Pre–exposure prophylaxis to prevent the acquisition of HIV–1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open–label randomised trial*. Lancet. 2016;387(10013):53–60. PROUD

6. Seifert SM GD, Meditz AL, et al. *Dose response for starting and stopping HIV preexposure prophylaxis for men who have sex with men*. Clin Infect Dis. 2015;60 804–10.

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