CDC Updates Post-Exposure Prophylaxis Guidelines

The agency now recommends Biktarvy or a dolutegravir combination to prevent HIV acquisition after non-occupational exposure.

May 7, 2025 By Liz Highleyman

In a long-awaited update, the Centers for Disease Control and Prevention (CDC) issued new guidelines for HIV post-exposure prophylaxis (PEP) on May 6. The new guidance—the first revision since 2016—now includes more modern antiretrovirals taken for a month after non-occupational exposure, such as sex or injection drug use.

Unlike pre-exposure prophylaxis (PrEP), which involves taking antiretroviral pills every day or injections every other month prior to HIV exposure, post-exposure prophylaxis is a month-long course of antiretrovirals started as soon as possible after sex or another type of exposure that presents substantial risk.

Non-occupational PEP should be started within 72 hours after exposure, but the sooner the better. In the new guidance, the CDC emphasizes the importance of starting PEP within 24 hours, if possible.

This can sometimes be difficult, as potential exposures may occur when it's not easy to access the medications, such as over a weekend or while traveling. PEP is typically provided on an emergency basis after the fact, but giving people pills to keep on hand in case of accidental exposure—an approach know as PEP-in-pocket—can be a good alternative for some people.

While one or two drugs used as PrEP can prevent HIV from taking hold in the body, PEP—which is essentially very early treatment—requires a stronger three-drug regimen.

Until this week, the CDC's recommended PEP regimens were raltegravir (Isentress) or dolutegravir (Tivicay) plus tenofovir disoproxil fumarate/emtricitabine (Truvada or generic equivalents). But some providers were already offering newer antiretrovirals.

The revised guidelines are based on a review of research published since the last update. The CDC authors acknowledge that some of the recommendations are not supported by strong evidence due to limited PEP studies. Historically, non-occupational PEP recommendations have been based on observational data, expert opinion, animal studies and extrapolation of data on HIV treatment,

occupational PEP, prevention of perinatal transmission and PrEP. The Food and Drug Administration has not approved any medications specifically for non-occupational PEP, so they are used off-label.

Recommended Regimens

The CDC now recommends two once-daily options for non-occupational PEP, both taken for 28 days:

- Biktarvy (bictegravir/tenofovir alafenamide/emtricitabine).
- Dolutegravir + either tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF) + either emtricitabine or lamivudine.

Biktarvy, a complete regimen taken as one pill once daily, includes the highly effective next-generation integrase inhibitor bictegravir. It is one of the most frequently used regimens for first-time HIV treatment in the United States.

Dolutegravir, also a newer integrase inhibitor, is one of the most widely used antiretrovirals worldwide. The latter regimen could be taken as Tivicay plus Truvada or Dovato (dolutegravir/lamivudine) plus Viread (stand-alone TDF). Generic versions of TDF/emtricitabine and lamivudine are available in the U.S., and a generic combination pill containing TDF, lamivudine and dolutegravir (known as TLD) is available in some other countries.

TDF is generally safe and well tolerated, but it can cause impaired kidney function and minor bone loss in susceptible people. The newly recommended regimens include TAF, a newer version of tenofovir that is easier on the kidneys and bones. It is a preferred option for people with pre-existing kidney disease or poor kidney function. (Click here to learn more about the differences between TDF and TAF.)

The same two PEP options are recommended for pregnant women and for children ages 2 to 12 years. Raltegravir is still an acceptable option, but it has a higher pill burden. Alternative regimens may be considered in special situations.

Guidance for PEP Use

PEP is recommended after a nonoccupational exposure that "presents a substantial risk for HIV transmission," for example, condomless anal or vaginal sex or sharing drug injection equipment with an HIV-positive "source" person who does not have sustained viral suppression or whose status is unknown. The updated guidelines include detailed information about providing PEP after sexual assault. People who take PrEP consistently do not need PEP in addition. PEP medications should be stopped if it is later determined that the "source" person does not have HIV.

A rapid point-of-care or laboratory-based antigen/antibody HIV test (not an oral fluid test) is recommended before starting PEP. A specific type of test should be done if an exposed person has

used long-acting injectable antiretrovirals. However, PEP initiation should not be delayed while waiting for test results. HIV testing should be repeated at four to six weeks after exposure and again at 12 weeks to ensure that infection has not occurred.

People seeking PEP should also be tested for liver and kidney function, hepatitis B, pregnancy and, in some cases, hepatitis C and other sexually transmitted infections, according to the guidance. Doxycycline post-exposure prophylaxis (doxyPEP)—a single dose of the antibiotic taken within 72 hours after sex to prevent chlamydia, gonorrhea and syphilis—may be appropriate for some gay and bisexual men and transgender women; it is currently not recommended for cisgender women.

Providers are encouraged to counsel recipients about whether they could benefit from PrEP on an ongoing basis after they finish a course of PEP. The update also includes emerging PEP implementation strategies, such as PEP-in-pocket, which could be an option for some people with infrequent, repeated HIV exposures who do not want to use PrEP.

Recommendations are similar for PEP after occupational exposure, for example, a health care provider who sustains a needlestick when caring for an HIV-positive patient.

The National Clinician Consultation Center provides tailored non-occupational PEP consultation for U.S. health care providers (888-448-4911; https://nccc.ucsf.edu/clinician-consultation/pep-post-exposure-prophylaxis). Separate guidelines and consultation services are available for occupational PEP and prevention of perinatal HIV transmission.

The full updated non-occupational PEP recommendations are available online.

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