Lenacapavir PrEP Still Effective With Longer Follow-Up

Only one person acquired HIV during an open-label extension of the PURPOSE 1 and PURPOSE 2 trials.

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Twice-yearly lenacapavir pre-exposure prophylaxis (PrEP) continues to provide highly effective protection against HIV after an additional year of follow-up, according to study findings presented at the 26th International AIDS Conference (AIDS 2026) in Rio de Janeiro.

No new cases of HIV acquisition occurred during the first 52 weeks of an open-label extension of the PURPOSE 1 trial, which enrolled more than 5,300 women in Africa, while a single case was reported in an extension of PURPOSE 2, which enrolled over 3,200 gay and bisexual men and gender-diverse people in seven countries.

But as the evidence for the effectiveness of long-acting PrEP grows, so, too, do calls for broader access. Lenacapavir could help end the HIV epidemic, health experts and advocates say, but only if it is available to everyone who could benefit worldwide.

Lenacapavir, the first HIV capsid inhibitor, is an antiretroviral drug that blocks viral replication, but its efficacy and long duration mean it acts almost like a vaccine. Lenacapavir was initially approved in 2022 under the brand name Sunlenca as part of combination therapy for treatment-experienced people with multidrug-resistant HIV. Lenacapavir alone, branded as Yeztugo, was approved for PrEP in June 2025.

The PrEP approval was supported by two pivotal Phase III studies showing that lenacapavir injections every six months dramatically reduced HIV acquisition in groups at high risk.

Results from PURPOSE 1, first presented at the 2024 International AIDS Conference and published in The New England Journal of Medicine, showed that twice-yearly lenacapavir PrEP was 100% effective for young cisgender women in South Africa and Uganda. The injections significantly reduced HIV incidence compared with the background rate and were superior to daily tenofovir disoproxil fumarate/emtricitabine pills (TDF/FTC; Truvada or generic equivalents).

Results from PURPOSE 2, presented at the 2024 HIV Research for Prevention Conference last October and also published in The New England Journal of Medicine, showed that lenacapavir

injections every six months reduced the risk of HIV acquisition by 96% relative to background incidence and by 89% compared to daily TDF/FTC for men who have sex with men and transgender and gender-diverse people in the United States, Argentina, Brazil, Mexico, Peru, South Africa and Thailand. In both trials, lenacapavir was safe and generally well tolerated.

The randomized, double-blind portion of the trials was followed by an open-label extension in which participants initially assigned to lenacapavir could choose to continue using it, while those originally assigned to daily oral PrEP could switch to lenacapavir injections. In both trials, 95% of participants opted to use lenacapavir during the extension phase.

In PURPOSE 1, there were zero new HIV acquisitions during the first 52 weeks of the open-label extension phase among the 4,632 participants who either stayed on lenacapavir or switched to it from daily PrEP. Cumulatively, from the start of the trial, one participant acquired HIV while receiving blinded lenacapavir, and another did so after switching from lenacapavir to open-label TDF/FTC, yielding an incidence rate of 0.03 cases per 100 person-years.

In PURPOSE 2, one of the 2,179 participants who stayed on lenacapavir during the open-label extension acquired HIV, in addition to three previously reported new cases during the randomized phase. There were no new HIV diagnoses among the 825 people who switched to lenacapavir from daily oral PrEP. Altogether, the incidence rate was 0.07 cases per 100 person-years.

The participant who acquired HIV during the extension phase received all injections on time, and lenacapavir drug levels were generally within the expected range. This person, described as gender-diverse, was diagnosed with HIV at week 39 of the extension, at which point drug resistance testing revealed a Q67H capsid mutation. The person was also diagnosed with chlamydia, gonorrhea and syphilis during the trial.

Adherence to lenacapavir was high in both studies, reaching 97% for the third extension phase injection in PURPOSE 1 and 92% in PURPOSE 2. No new safety or tolerability concerns were identified, and less than 1% of participants discontinued lenacapavir due to injection-site reactions.

Access Is Key

To have a real impact on the HIV epidemic, long-acting PrEP must be widely available and affordable to those who need it worldwide, but the high cost of lenacapavir could keep it out of reach.

Drugmaker Gilead Sciences has to allow manufacturers to supply generic versions of lenacapavir in more than 100 primarily low-income countries, but the deal leaves out some middle-income countries with a high burden of HIV, such as Brazil.

“If we deliver it where it is needed most, lenacapavir for HIV prevention has the potential to help curb the global pandemic,” outgoing International AIDS Society president and AIDS 2026 cochair

Beatriz Grinsztejn, a member of the PURPOSE 2 study team, said at an advance media briefing.

Policy changes and funding cuts that threaten the global HIV response were a key theme of the conference. According to a new report from amfAR, cuts to PEPFAR, the President's Emergency Plan for AIDS Relief, have led to severe disruptions in HIV services in countries that bear the brunt of the epidemic. Prevention services, including PrEP, have been most severely impacted.

While twice-yearly PrEP has been hailed as a major breakthrough, "progress is not the same as victory," UNAIDS executive director Winnie Byanyima said at the AIDS 2026 opening press conference. "Scientific breakthroughs alone will not end AIDS.…Science has done its job. Now politics must do its job."

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