



Lenacapavir PrEP Does Not Interfere With Hormone Therapy for Trans People

Levels of feminizing and masculinizing hormones remained generally comparable before and after lenacapavir administration.

December 16, 2025 By [Liz Highleyman](#)

Twice-yearly lenacapavir (Yeztugo) injections for pre-exposure prophylaxis (PrEP) do not have clinically meaningful interactions with gender-affirming hormone therapy for transgender women, trans men or other gender-diverse people, according to study results presented at [IDWeek 2025](#).

“In the most gender-diverse Phase III PrEP trial conducted to date, lenacapavir had no clinically significant impact on feminizing or masculinizing gender-affirming therapy concentrations,” the researchers concluded.

Transgender, gender-nonconforming and nonbinary people are at greater risk for HIV acquisition and are more likely to be living with the virus compared with the population at large. Though they make up perhaps 1% of the U.S. population, trans people accounted for 2% of new HIV diagnoses in 2019, according to the Centers for Disease Control and Prevention. This is largely based on trans women, as HIV data for trans men and nonbinary people remain scarce.

Prior studies have found that some trans people are hesitant to take antiretrovirals for PrEP or HIV treatment due to concerns about their impact on hormone therapy. Estimates suggest that around 20% of gender-diverse people have used PrEP, and adherence can be as low as 30%.

The Food and Drug Administration [approved lenacapavir PrEP in June](#), making it the longest-acting HIV prevention option. The approval is supported by two large studies showing that the biannual injections dramatically reduced HIV acquisition. The Phase III [PURPOSE 1 trial](#) found that twice-yearly lenacapavir PrEP was 100% effective for young cisgender women in Africa. [PURPOSE 2](#) showed that lenacapavir injections reduced the risk of HIV acquisition by 96% relative to background incidence for gay and bisexual men and gender-diverse people in the United States and six other countries. In both trials, lenacapavir injections were safe and well tolerated.

Jill Blumenthal, MD, of the University of California San Diego, and colleagues looked at interactions between lenacapavir and gender-affirming hormone therapy, including estradiol (a form of

estrogen) and testosterone. These hormones are metabolized by enzymes such as CYP3A4. Lenacapavir is a moderate CYP3A inhibitor, so it could potentially affect hormone levels. An earlier study found that blood levels of lenacapavir did not change when administered with gender-affirming hormone therapy.

In this study, the researchers conducted a pharmacokinetic analysis using blood samples from a subset of PURPOSE 2 participants using gender-affirming hormones, measuring plasma levels of estradiol, testosterone and dihydrotestosterone (an active metabolite) through 52 weeks. Among the more than 2,000 study participants, 14% identified as trans women, 1% as trans men and 6% as nonbinary (mostly assigned female at birth). Of these, a total of 253 people reported using gender-affirming hormones.

Among 115 people taking estradiol, concentrations of the hormone were generally comparable before and after lenacapavir administration. Likewise, testosterone and dihydrotestosterone levels generally did not change in 25 people using masculinizing hormones.

“Taken together with our prior findings that gender-affirming hormone therapy had no significant effect on lenacapavir pharmacokinetics, these data support the concurrent use of twice-yearly lenacapavir PrEP and feminizing or masculinizing gender-affirming hormone therapy without dose adjustment in gender-diverse individuals, addressing a key barrier to PrEP uptake and adherence in a population that is disproportionately vulnerable to HIV acquisition,” the researchers concluded.

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