



Twice-Yearly Injectable PrEP for Transgender People and Substance Users

Lenacapavir pre-exposure prophylaxis (PrEP) may be a good option for transgender people and people who use drugs and alcohol.

February 16, 2026 By [Liz Highleyman](#)

Lenacapavir pre-exposure prophylaxis (PrEP) may be a good option for transgender people and people who use drugs and alcohol, according to two studies presented at IDWeek. Lenacapavir PrEP (brand name Yeztugo) was approved in June 2025 after two large clinical trials showed that injections every six months dramatically lowered the risk of HIV for young cisgender women in Africa (PURPOSE 1) and for gay and bisexual men and gender-diverse people in the United States and six other countries (PURPOSE 2).

Transgender people are at greater risk for HIV, but previous studies have found that some are hesitant to take antiretrovirals for prevention or treatment due to concerns about their impact on gender-affirming hormone therapy.

In the first study, researchers looked at interactions between hormones and lenacapavir—a moderate inhibitor of CYP3A, an enzyme that metabolizes many drugs and hormones—in PURPOSE 2. Among 115 people taking estradiol (a form of estrogen), concentrations were comparable before and after lenacapavir administration. Similarly, testosterone and dihydro-testosterone levels generally did not change in 25 people using masculinizing hormones. These reassuring data address “a key barrier to PrEP uptake and adherence in a population that is disproportionately vulnerable to HIV acquisition,” the researchers concluded.

Many people who use substances are also at elevated risk for HIV, but social and individual barriers can make taking daily PrEP pills a challenge. The second study looked at lenacapavir PrEP adherence and safety among people who used drugs or engaged in binge drinking in PURPOSE 2. Among the more than 2,000 total participants, more than a third reported recent drug use (excluding cannabis), and 41% reported at least monthly binge drinking.

Adherence exceeded 90% and was comparable between people who did and did not use drugs or binge drink as well as across different types of substance use. The frequency of adverse events was also similar regardless of substance use. No clinically meaningful interactions between lenacapavir and fentanyl were noted. To learn more, the ongoing PURPOSE 4 trial is studying lenacapavir and daily oral PrEP specifically for people who inject drugs.

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