FDAs new approval: yeztugo (lenacapavir): A longer lasting avenue against HIV

Maryam Tanveer[1], Ahsan Kamal[2]

Dear Editor, The human immunodeficiency virus is an RNA retrovirus transmitted through bodily fluids: blood, semen, pre-seminal fluid, rectal fluids, vaginal fluids, and breast milk. HIV targets the T-helper cell, weakening the body's immune system, which can progress to acquired Immune Deficiency Syndrome (AIDS), where opportunistic infections become fatal. There is no cure for HIV; treatment involves the administration of antiretroviral (ARV) drugs, which stop the viral replication.[1] According to the WHO, HIV has claimed an estimated 44.1 million lives to date, with an estimated 40.8 million people living withthe virus. According to the National AIDS Control Programme (NACP) (Government of Pakistan), an estimated 0.33 million people are living with AIDS in Pakistan, while only around 76000 are registered with NACP, and only around 54000 are receiving ARV.

On June 18, 2025, Yeztugo (Lencapavir) was approved by the U.S. Food and Drug Administration (FDA) for the prevention of HIV. Lenacapavir, a PrEP (Pre-Exposure Prophylaxis), is to be administered subcutaneously once every six months. It prevents HIV by interfering with two steps of viral replication. It binds a hydrophobic pocket between two capsid subunits, interfering with uncoating and capsid-mediated pre-integration complex uptake by the nucleus. In addition, it interferes in the capsid assembly after viral genome replication, providing dual-step interference in the viral replication cycle.[2]

PrEP for HIV that existed before Lenacapavir, either had to be administered every day orally (Tenofovir Disoproxil/Emtricitabine) or injected every two months (Cabotegravir long-acting). Multiple studies have shown the oral PrEP to be highly effective, but people have difficulty in adherence, resulting in lower real-life efficacy.[3] The introduction of CAB-LA offered superior protection by mitigating daily pill adherence challenges, and Lenacapvir has the potential to provide longer protection, reducing adherence challenges further.

The FDA advises against starting Lenacapavir without screening for HIV-1 and only be started in patients who test negative. Administration in HIV-1-positive individuals may result in resistance development in the virus. Adverse effects of the drug include injection site reactions in 62% patients, nausea in 13%, diarrhoea in 11% and constipation in 11%. Since none of these are long-term effects, lenacapavir shows promise in preventing HIV.[4]

Yeztugo (lenacapavir) is a drug that has the potential to prevent HIV and could help Pakistan in its fight against HIV, which is prevalent in country's key populations. However, the safety of its use in pregnant women remains in question. Further clinical trials may be necessary to establish confidence in its efficacy and safety.

Disclaimer: None.

Conflict of interest: None.

Funding disclosure: None.

DOI: https://doi.org/10.47391/JPMA.33073

References

1. van Heuvel Y, Schatz S, Rosengarten JF, Stitz J. Infectious RNA: Human Immunodeficiency Virus (HIV) Biology, Therapeutic Intervention, and the Quest for a Vaccine. Toxins (Basel) 2022;14:138. doi: 10.3390/toxins14020138.
2. Dvory-Sobol H, Shaik N, Callebaut C, Rhee MS. Lenacapavir: a first-in-class HIV-1 capsid inhibitor. Curr Opin HIV AIDS 2022;17:15-21. doi: 10.1097/COH.0000000000000713.
3. World Health Organization (WHO). Guidelines on long-acting injectable cabotegravir for HIV prevention. [Online] 2022 [Cited 2026 June 26]. Available from URL: https://www.who.int/publications/i/item/9789240054097
4. Lenacapavir for multidrug-resistant HIV-1 infection. Aust Prescr 2025;48:63-4. doi: 10.18773/austprescr.2025.012.

[1]2nd year MBBS Student, Bahria University Medical and Dental College, Karachi, Pakistan; [2]2nd Year MBBS Student, CMH Lahore Medical College and Institute of Dentistry, Lahore, Pakistan
Correspondence: Maryam Tanveer. e-mail: tanveermaryam2005@gmail.com
ORCID ID: 0009-0004-5214-9621

Submission completed: 13-10-2025 **1st Revision received:** 11-04-2026
Acceptance: 25-04-2026 **2nd Revision received:** 24-04-2026

Author Contribution:
MT & AK: Concept, design, data acquisition, analysis, interpretation, drafting, revision, final approval and agreement to be accountable for all aspects of the work.