INDIAN HEALTH SERVICE
National Pharmacy and Therapeutics Committee
Formulary Brief: ***Lenacapavir for HIV PrEP***

-November 2025-

Background:

The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) reviewed the injectable medications for pre-exposure prophylaxis (PrEP) of human immunodeficiency virus (HIV) at the Fall Meeting in November 2025. Currently, oral tenofovir disoproxil fumarate/emtricitabine is listed on the National Core Formulary (NCF) relevant to HIV PrEP.[1] In June 2025, the U.S. Food and Drug Administration approved lenacapavir, a long-acting HIV capsid inhibitor given subcutaneously every 6 months (along with an initial 2-day oral loading dose), for use as PrEP for HIV exposure in adults and adolescents weighing ≥35 kilograms (kg).[2] Other existing PrEP options include daily oral tenofovir/emtricitabine regimens and the longer-acting injectable, cabotegravir. Following review, including both clinical and pharmacoeconomic considerations, the NPTC made **no modifications** to the NCF.

Discussion:

Lenacapavir is a novel long-acting agent in the capsid inhibitor class, targeting multiple stages of the HIV-1 lifecycle and offering a dosing interval of every 6 months (twice yearly) for HIV PrEP. [2,5] Lenacapavir is administered subcutaneously by a healthcare provider.

Studies: Two randomized controlled clinical trials (RCTs) offer strong evidence for the use of lenacapavir every 6 months for HIV prevention. In the PURPOSE 1 study of 5,338 cisgender adult and adolescent females aged 16 years and older in South Africa and Uganda, lenacapavir was superior to daily oral tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) and tenofovir alafenamide/emtricitabine (TAF/FTC) for HIV prevention, with 100% efficacy.[3] The PURPOSE 2 study also found lenacapavir to be superior to TDF/FTC for HIV prevention among at-risk individuals with 96% efficacy.[4] Superiority of lenacapavir was attributable to decreased adherence to oral PrEP regimens.[1,4]

Safety and Tolerability: Both PURPOSE 1 and PURPOSE 2 found lenacapavir to be safe and well tolerated, with injection site reactions reported as the main adverse effect(s). This led to treatment discontinuation in 0.2% of participants in the PURPOSE 1 study and 1.2% in the PURPOSE 2 study.[1,4] Lenacapavir was highly effective at reducing HIV infections among trial participants in Phase 3; 99.9% of participants did not acquire HIV in the lenacapavir group, with two incident cases among 2,179 participants (0.10/100 person-years, 95% CI: 0.01-0.37), despite reported high levels of sexual behavior, engaging in sexual behavior under the influence of drugs, and sexually transmitted infections (STI) observed among PURPOSE 2 participants.[1,4]

Results: The results demonstrated superiority of twice-yearly lenacapavir over background HIV regimens (2.37/100 person-years, 95% CI: 1.65-3.42; primary endpoint), with 96% relative risk reduction (IRR 0.04, 95% CI: 0.01-0.18; $p<0.0001$). Additionally, twice-yearly lenacapavir was 89% more effective at reducing HIV infections than once-daily TDF/FTC (IRR 0.11, 95% CI: 0.02-0.51; $p=0.00245$). There were 2 breakthrough HIV infections in PURPOSE 2, with lenacapavir resistance and high viral loads, with the potential for HIV transmission to sex partners. [1,4]

Ongoing Studies: The PURPOSE 3 (among women in the U.S.), PURPOSE 4 (among people who inject drugs in the U.S.), and PURPOSE 5 (among individuals not yet on PrEP therapy in the United Kingdom and France) trials are in progress and expected to complete in 2027, 2028, and 2029 respectively.[3]

Lenacapavir Administration (PrEP)

Initiation / maintenance:

- Day 1: 927mg lenacapavir subcutaneous and 600mg lenacapavir orally
- Day 2: 600mg lenacapavir orally, followed by subcutaneous injection every 6 months (twice yearly)

Notably, clinical trials used fixed-dose lenacapavir without oral lead-in. [2,3]

Baseline Assessment: Confirm HIV-negative status with antigen/antibody and HIV RNA to reduce risk of dosing during acute infection. Assess renal function, pregnancy status, STI screening, and Hepatitis B and C where indicated.[2]

Ongoing Monitoring: Clinicians should order HIV testing at or before each injection (antigen/antibody ± RNA) along with interval STI screening per risk and guideline recommendations.[2,6,7] This regimen would require 2 visits per year provided no additional monitoring visits are required.[2]

Special Populations and Considerations: Weight: Approved down to 35 kg for HIV PrEP indication in US.[2] Indication includes adolescents ≥35 kg. Drug interactions include monitoring for CYP3A/P-glycoprotein modulators.[2]

Findings:

HIV infection is common throughout the IHS including in tribal communities. However, effective HIV prevention strategies are available for individuals who have risk factors for HIV acquisition. The clinical support and resources necessary to prevent HIV infection are readily available. With HIV prevention available on the NCF alongside robust guidelines and simple dosing strategies, IHS clinicians can ensure all patients in the service population have access to HIV PrEP medications.

With continued routine screening and risk-based testing, rapid delivery of therapy to those with infection, widespread use of prevention tools including PrEP and a rapid response to clusters of new infection, HIV elimination by 2030 is possible. The twice-yearly dosing has the potential to reduce clinic visits, improve adherence, and expand access for those who struggle with daily dosing. While efficacy is excellent, long-term real-world data on effectiveness, adherence, and service delivery in diverse settings are still emerging.[7] Infrastructure and programmatic capacity to deliver twice-yearly subcutaneous lenacapavir injections and manage the long tail (or wearing off) period may vary by site. Resistance risk remains if HIV acquisition occurs during the tail period; necessitating the need for robust monitoring and bridging strategies. [2,6,7]

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov . For more information about the NPTC, please visit the NPTC website.

References:

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