Yeztugo® (lenacapavir) – New drug approval

- On June 18, 2025, Gilead announced the FDA approval of Yeztugo (lenacapavir), for **pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults and adolescents weighing at least 35 kg who are at risk for HIV-1 acquisition**.
    - Individuals must have a negative HIV-1 test prior to initiating Yeztugo.
- Lenacapavir is also available under the brand name Sunlenca®, in combination with other antiretroviral(s), for the treatment of HIV-1 infection in heavily treatment-experienced adults with multidrug resistant HIV-1 whose current antiretroviral regimen is failing due to resistance, intolerance, or safety considerations.
- Yeztugo is the first twice yearly injection for HIV PrEP.
    - Other treatment options currently approved for HIV PrEP include daily oral medications, Truvada® (emtricitabine/tenofovir disoproxil fumarate) and Descovy® (emtricitabine/tenofovir alafenamide fumarate), and ViiV's bimonthly intramuscular drug, Apretude (cabotegravir).
    - Truvada is also available generically.
- The efficacy of Yeztugo was established in two randomized, double-blind, active-controlled studies (PURPOSE 1 and PURPOSE 2).
- PURPOSE 1 was in 5,338 cisgender adolescent girls and young women between 16 and 25 years of age who had unknown HIV-1 status at screening and who were at risk of acquiring HIV-1 based on sexual activity with male partners. Participants were randomized to Yeztugo, Descovy, or Truvada. The efficacy endpoint was the rate of incident HIV-1 infections per 100 person-years in participants randomized to Yeztugo compared with the rate of incident HIV-1 infections per 100 person-years in participants randomized to Truvada.
    - **Yeztugo demonstrated superiority with a 100% reduction in the risk of incident HIV-1 infection over Truvada**. The incidence rate per 100 person-years was 0.00 with Yeztugo and 1.69 with Truvada (rate ratio 0.000, 95% CI: 0.000, 0.101; $p < 0.0001$).
- PURPOSE 2 was in 3,265 cisgender men, transgender women, transgender men, and gender nonbinary individuals 16 years of age and older who had unknown HIV-1 status at screening and who were at risk of acquiring HIV-1 based on sexual activity with male partners. Participants were randomized to Yeztugo or Truvada. The efficacy endpoint was the rate of incident HIV-1 infections per 100 person-years in participants randomized to Yeztugo compared with the rate of incident HIV-1 infections per 100 person-years in participants randomized to Truvada.
    - **Yeztugo demonstrated superiority with an 89% reduction in the risk of incident HIV-1 infection over Truvada**. The incidence rate per 100 person-years was 0.1 with Yeztugo and 0.93 with Truvada (rate ratio 0.111, 95% CI: 0.024, 0.513; $p = 0.00245$).
- Yeztugo carries a boxed warning for risk of drug resistance with use of Yeztugo for HIV-1 PrEP in undiagnosed HIV-1 infection.
- Yeztugo is contraindicated in individuals with unknown or positive HIV-1 status.

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- Additional warnings and precautions for Yeztugo include comprehensive management to reduce the risk of HIV-1 infection and other sexually acquired infections; long-acting properties and potential associated risks with Yeztugo; and serious injection site reactions with improper administration.

- The most common adverse reactions (≥ 5%) with Yeztugo use were injection site reactions, headache, and nausea.

- The Yeztugo dosing schedule consists of a required initiation dosing (subcutaneous injections and oral tablets) followed by once every 6-months continuation dosing (subcutaneous injections).

    — Initiation: On day 1, the dosage is 927 mg by subcutaneous injection (2 x 1.5 mL injections) and 600 mg orally (2 x 300 mg tablets). On day 2, the dosage is 600 mg orally (2 x 300 mg tablets).
    — Continuation of therapy: 927 mg by subcutaneous injection (2 x 1.5 mL injections) every 6 months.

- Yeztugo injection is only for subcutaneous administration into the abdomen by a healthcare provider.

- The annual list price for Yeztugo is $28,218.

- Gilead's launch plans for Yeztugo are pending. Yeztugo will be available as a 300 mg tablet and 463.5 mg/1.5 mL single-dose vials.

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