Long-Acting Injectable PrEP Options Expanded: Introducing Lenacapavir: Frequently Asked Questions (FAQs) for Implementation

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Introduction and Background

On June 18, 2025, the U.S Food and Drug Administration (FDA) approved lenacapavir for PrEP (brand name Yeztugo®), making it the second long-acting injectable treatment option available for the primary prevention of HIV. Yeztugo® is manufactured by Gilead Sciences. Lenacapavir is indicated for adults and adolescents weighing at least 35 kilograms (77 pounds) who are at risk of sexually acquiring HIV. This injectable option provides the longest acting form of any PrEP modality yet and serves as an additional option for people vulnerable to HIV transmission preferring an injectable product requiring infrequent administration. With its high effectiveness and every six-month administration, lenacapavir has the potential to improve PrEP adherence and make a significant impact against the HIV epidemic in the United States.[1]

This resource addresses some frequently asked questions to assist with the successful implementation of lenacapavir for PrEP (LEN for PrEP). For additional implementation resources, visit NASTAD's Long-Acting Injectable PrEP microsite.

What is the effectiveness of LEN for PrEP?

Lenacapavir has demonstrated high efficacy in preventing HIV transmission in two large clinical trials:

- **PURPOSE 1 trial (cisgender women in Africa):** Twice-yearly subcutaneous lenacapavir showed 100% efficacy in preventing HIV infections.
- **PURPOSE 2 trial (cisgender men, transgender women, transgender men, and gender non-binary individuals):** Twice-yearly subcutaneous lenacapavir reduced the risk of HIV acquisition by 96% compared to background HIV incidence and was 89% more effective than once-daily oral Truvada®.

Subcutaneous injection of lenacapavir every 6 months is **strongly recommended** by the U.S. Centers for Disease Control and Prevention (CDC) as a PrEP option for persons weighing ≥ 77

[1] https://www.cdc.gov/mmwr/volumes/74/wr/mm7435a1.htm

lbs (≥ 35 kg) who would benefit from HIV prevention. This recommendation is based on a **high certainty of evidence** for efficacy and safety from the PURPOSE 1 and PURPOSE 2 trials. [1]

How is LEN for PrEP administered?

Lenacapavir is provided as two subcutaneous injections (1.5 mL) in the abdomen or anterior thigh once every six months along with two 300mg oral lead in doses (600mg) (lead in doses at day of injection and the following day).[2]

Day 1 - 927 mg (3 mL) LEN by subcutaneous injection (two 1.5-mL injections at least 4 inches apart) and 600 mg orally (two 300-mg tablets)

Day 2 - 600 mg LEN orally (two 300-mg tablets)

Lenacapavir for PrEP Continuation or Maintenance Dose

Every six months (26 weeks) ± two weeks

- 927 mg (3 mL) LEN by subcutaneous injection (two 1.5-mL injections at least 4 inches apart)
- Screening Tests
    - HIV antigen/antibody testing
    - STI Testing (vaginal, oral, rectal, urine, or blood as needed) per PrEP protocols

Provide oral lenacapavir if the continuation visit is more than 28 weeks from the previous injection, more on "oral-bridging" below.

What are the labs required for LEN for PrEP?

According to the FDA- approved package insert, individuals must be tested for HIV-1 infection prior to initiating lenacapavir, and with each subsequent injection of lenacapavir. **However, comprehensive CDC[1] and state clinical guidelines[3] for PrEP also recommend a complete panel of baseline and follow-up tests. Providers should follow these protocols, which typically include:**

- HIV testing (as required)
- Hepatitis B and C screening
- Comprehensive STI testing (e.g., gonorrhea, chlamydia, syphilis) at all relevant anatomic sites
    - Depending on the individual, STI screening follow-up appointments might be more frequent than LEN injections, such as every three months.

[2] https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/220020s000lbl.pdf
[3] https://www.hivguidelines.org/guideline/hiv-prep/?mytab=tab_6&mycollection=pep-prep

What happens if a dose is missed?

The FDA-approved package insert advises that if the scheduled follow up injection is more than 2 weeks delayed, Lenacapavir oral tablets can be used until injections resume ("oral-bridging").[2] The dosing schedule for delayed injection is one 300mg tablet taken once per week for up to 6 months if needed.

If it's been more than 28 weeks since the last injection and oral tablets were not used, the individual is advised to restart initiation from Day 1 (927 mg by subcutaneous injection (2 x 1.5 mL injections) and 600 mg orally (2 x 300 mg tablets)), if clinically appropriate.

Are there any discontinuation considerations for LEN for PrEP?

There are discontinuation considerations as medication levels in the body decline over time. Providers should inform PrEP users that when LEN is discontinued, medication levels in the body decline over 18 months, starting 6 months after the last injection, and do not offer HIV protection after 6 months.[1] This period of declining medication levels over time is called the tail. Assess ongoing HIV risk and prevention plans and offer other PrEP options. Another consideration of discontinuation is potential drug resistance which could emerge if lenacapavir is initiated during undiagnosed acute infection or if transmission occurs during the tail.[4]

Are there any drug interactions for LEN for PrEP?

Lenacapavir has important drug interactions with certain medications, including strong CYP3A inducers (e.g., carbamazepine, phenytoin, rifampin, St. John's wort), and caution is advised with others like buprenorphine, methadone, fentanyl, and oxycodone. Per the FDA-approved package insert, dosage modifications (supplemental doses) of Lenacapavir are recommended when initiating strong or moderate CYP3A inducers. Dosage modifications start on page 5 of the FDA insert[5].

Are there any side effects or injection site reactions?

A "nodule" may form as a result of the subcutaneous injection, leading to an injection site reaction (ISRs); ISRs can include: pain, swelling, redness, and itching. These reactions are typically mild and resolve within a few days or a week. The incidence of ISRs tends to decrease with subsequent injections. While most ISRs are mild, some severe reactions have been reported, sometimes linked to inappropriate injection technique. Applying an ice pack to the injection site before and after the injection can help with injection site reactions.

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[4] van Zyl, G., Prochazka, M., Schmidt, H. M. A., Orrell, C., Schapiro, J. M., McCluskey, S. M., ... & Shafer, R. W. (2025). Lenacapavir-associated drug resistance: implications for scaling up long-acting HIV preexposure prophylaxis. The Lancet HIV.

[5] 2.5 Dosage Modifications for Co-administration with Strong or Moderate CYP3A Inducers https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/220020s000lbl.pdf

What's the difference between the two LAI injectable options?

There are many differences between the two injectable PrEP options, from injection sites to injection frequency. The table below describes the key differences between the two options.

Feature	Apretude	Yeztugo
Brand Name	Apretude	Yeztugo
Active Ingredient	Cabotegravir	Lenacapavir
Drug Class	Integrase Strand Transfer Inhibitor (INSTI)	Capsid Inhibitor
Manufacturer	ViiV Healthcare	Gilead Sciences
FDA Approval for PrEP	December 2021	June 2025
Administration	Intramuscular (IM) injection (deep into the muscle)	Subcutaneous (SC) injection (just under the skin)
Injection Site	Gluteal muscle (buttocks)	Abdomen (stomach area)
Dosing Frequency	Every 2 months (6 times per year)	Every 6 months (Twice per year)
Role of Oral Dosing	**Optional Oral Lead-in:** A 30mg daily pill (Vocabria) may be taken for 28 days before the first injection. This is optional and is used to assess your body's tolerability to the drug.	**Required Oral Initiation:** The oral pills are required to quickly build up the drug to protective levels. The injection alone takes too long to work.
Initiation Schedule	**With Oral Lead-in:** 28 days of oral pills, then first injection. **Without Oral Lead-in:** First injection, followed by a second injection 1 month later. After either method, you move to one injection every 2 months.	**Required 2-Day Start:** * Day 1: Two injections (927 mg total) + Two oral tablets (600 mg total). * Day 2: Two oral tablets (600 mg total). After this, you move to two injections every 6 months.
Wholesale Acquisition Cost (WAC)	**Injection Kit (per 2-month dose):** $4,126; **Oral Tablets (Vocabria)**: No cost; used for optional lead-in.	**Injection Kit (per 6-month dose):** $14,100; **Oral Tablets (Pack of 4 for initiation):** $2,352
Annual WAC (Injections Only)	~$24,000 (6 injections per year)	~$28,200 (2 injections per year)
Common Side Effects	Injection site reactions (pain, tenderness, swelling) are very common. Others: fever, fatigue, headache, rash.	Injection site reactions (swelling, redness, pain, nodules/bumps under the skin) are the most common. Others: headache, nausea.

Coverage and Implementation:

How much does LEN cost?

The wholesale acquisition cost (WAC) price for Yeztugo® is $14,110 per injection kit containing two single-dose vials, each containing 1.5 mL of lenacapavir. The annual WAC of $28,218 is comparable to those for Descovy® (emtricitabine/tenofovir alafenamide fumarate) and injectable Apretude® (cabotegravir).

How can patients access LEN for PrEP?

As LEN for PrEP is approved for subcutaneous injection use only, it should be administered by a licensed medical provider. Provider administered drugs are not through retail community pharmacies, but rather through a limited distribution system involving either specialty distributors or specialty pharmacies. LEN for PrEP can be procured by health care providers through "buy-and-bill", "white bagging", or "clear bagging" mechanisms. These mechanisms are further described in the table below.

Distribution Mechanisms

Buy-and-Bill	Provider or clinic purchases Yeztugo® from a specialty distributor and maintains an inventory of the drug for use on an as-needed basis. Following administration of the drug to a patient, the provider submits a reimbursement claim to the patient's public or private insurance carrier.
White Bagging	Provider submits prescription for Yeztugo® to a specialty pharmacy within Gilead's specialty pharmacy network. The specialty pharmacy processes the claim and ships the product to the provider. Once the Yeztugo® is received by the provider, it can only be administered to the patient who was prescribed the drug.
Clear Bagging	A health system's internal specialty pharmacy maintains inventory of Yeztugo®, processes the claim when a prescription is received from a health system provider, and then delivers the medication in time for the patient's drug administration appointment.

Yeztugo® is currently available via buy-and-bill from the following **specialty distributors**: McKesson Specialty/McKesson Plasma and Biologics, Cardinal Specialty, Besse Medical, ASD Healthcare, Morris & Dickson Specialty, and CuraScript Specialty Distribution.

Yeztugo® is currently available via white-bag mechanisms from the following **specialty pharmacies**: AcariaHealth, Accredo Specialty, Avita Specialty

Pharmacy, Curant Health, CVS Specialty, Genoa Healthcare/Optum, Walgreens/AllianceRxPrime.

More information on ways to access Yeztugo® can be accessed here.

What are Alternate Sites of Care (ASOC)?

ASOCs handle the purchasing, dispensing, and administration of injections, providing another access point in case a patient's main PrEP provider does not have the resources or capacity to administer LEN for PrEP injections. A list of available ASOCs can be found here.

How will the medication and administration be covered by insurers?

Due to the need for Yeztugo® to be administered in a clinical setting, health insurers are likely to cover it as a medical benefit. Insurers may also cover it as a pharmacy benefit, or as both a medical and pharmacy benefit. Cost-sharing requirements will depend on how Yeztugo® is covered:

- Drugs covered as a medical benefit by private insurance plans often require a flat co-insurance rate (e.g., 20% of the total cost of the medication), typically after the plan deductible requirement has been met.
- State Medicaid programs must cover Yeztugo®, but cost-sharing and utilization management (e.g., prior authorization or step therapy) requirements may vary by state. Cost-sharing is typically nominal.
- For Medicare clients, Yeztugo is covered under Part B as a provider-administered drug. Under Medicare Part B, the beneficiary may be responsible for up to 20% of the medication cost after the deductible requirement has been met; supplemental insurance coverage, Medicaid dual-eligibility, or enrollment in the Qualified Medicare Beneficiary (QMB) program may defray cost sharing requirements.
- NASTAD's Lenacapavir for PrEP: Billing and Coding Supplement provides billing guidance for LEN for PrEP oral and injectable components, as well as provider administration for injectable PrEP.

How do clinics stock and store LEN for PrEP?

According to the prescribing information, LEN for PrEP injection kits must be stored in a refrigerator at 2°C to 8°C (36°F to 46°F). It must be stored in the original carton to protect it from light. Do not freeze. Before preparation, the vials may be removed from the refrigerator and brought to room temperature for up to 30 minutes.

Providers and clinics will need to store Yeztugo® received for specific patients via white bagging from specialty pharmacies separately from their own inventories received from specialty distributors for buy-and-bill purposes.

What are the 340B Drug Pricing Program implications for LEN for PrEP?

Yeztugo® is subject to pricing discounts under the 340B Drug Pricing Program. This allows 340B "covered entities" (CEs), such as federally funded HIV prevention programs and Federally Qualified Health Centers (FQHCs), to purchase the drug at a significantly reduced "ceiling price."

- For clinics using the 'buy-and-bill' model, the CE can purchase Yeztugo® at the 340B price and bill the payer (e.g., Medicaid, private insurance) for the drug and administration. This allows the clinic to use the savings to support patient care.
- CEs must have systems in place to prevent duplicate discounts (i.e., billing Medicaid for a 340B-purchased drug where the state has also received a rebate).
- The 340B savings model is often incompatible with 'white bagging,' as the drug is purchased and dispensed by an external specialty pharmacy that may not be part of the CE's 340B program.

How does the August 2023 updated United States Preventive Services Task Force (USPSTF) Grade A recommendation for PrEP impact LEN's coverage and cost sharing?

This is an evolving coverage issue. The Affordable Care Act (ACA) requires most health plans to cover services with a USPSTF Grade A or B recommendation without any patient cost-sharing.

The challenge is that payers are interpreting the 2023 PrEP recommendation in different ways:

- Broad Interpretation: The USPSTF recommendation gives a Grade A to "preexposure prophylaxis (PrEP) with effective antiretroviral therapy" for at-risk individuals. Many stakeholders interpret this broad language to include all FDA-approved PrEP medications, including newly approved options like Yeztugo®.
- Strict Interpretation: However, the 2023 review was finalized before Yeztugo® was approved. Because the supporting evidence for that review only included TDF/FTC, TAF/FTC, and cabotegravir, many payers and pharmacy benefit managers (PBMs) are taking a stricter interpretation.

As a result, many plans are not yet applying the zero-cost-sharing mandate to Yeztugo® and may require utilization management (like prior authorization) or apply patient cost-sharing (copayments, coinsurance, and deductibles).

To close this gap, several states are enacting their own laws to explicitly require state-regulated plans to cover all FDA-approved PrEP medications without cost-sharing. This does not apply to all health plans (such as self-

funded employer plans), so coverage will vary. Providers should be prepared to verify coverage and out-of-pocket cost estimates for each patient.

For questions about LEN for PrEP, please contact NASTAD's PrEP Access team at PrEP@NASTAD.org.