This non-promotional infographic is intended to be used as an educational resource only. It is not intended to provide medical advice.

Lenacapavir for PrEP Injections and Injection-site Reaction (ISR) Care

Highlights of Prescribing Information

LEN for PrEP, a human immunodeficiency virus type 1 (HIV-1) capsid inhibitor, is indicated 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 LEN for PrEP.[1]

BOXED WARNING: RISK OF DRUG RESISTANCE WITH USE OF LEN for PrEP FOR HIV-1 PRE-EXPOSURE PROPHYLAXIS (PrEP) IN UNDIAGNOSED HIV-1 INFECTION

Individuals must be tested for HIV-1 infection prior to initiating LEN for PrEP, and with each subsequent injection of LEN for PrEP, using a test approved or cleared by the FDA for the diagnosis of acute or primary HIV-1 infection. Drug-resistant HIV-1 variants have been identified with the use of LEN for PrEP by individuals with undiagnosed HIV-1 infection. Do not initiate LEN for PrEP unless negative infection status is confirmed. Individuals who acquire HIV-1 while receiving LEN for PrEP must transition to a complete HIV-1 treatment regimen.[1]

These highlights do not include all the information needed to use LEN for PrEP safely and effectively. Please see YEZTUGO full Prescribing Information, including Boxed Warning, at Gilead.com.

See additional safety information in subsequent portions of this brochure.

Approved for Use on 08 Sep 2025

1. YEZTUGO Prescribing Information. Gilead Sciences, Inc. 2025.

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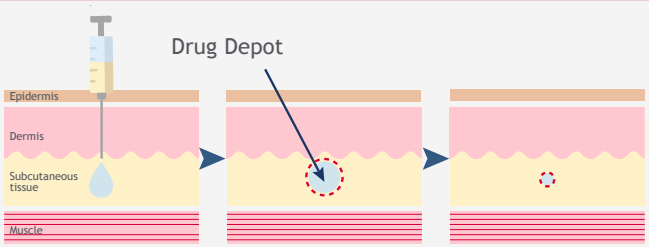
The most common adverse drug reactions (all grades) reported in at least 5% of participants receiving LEN for PrEP in either PURPOSE 1 or PURPOSE 2 were ISRs, headache, and nausea.[1]

Nodules were the most commonly reported ISR. Additional ISRs reported include pain, induration, swelling, pruritus, erythema, bruising, and warmth.[1-3]

It is important to understand LEN's mechanism of depot formation to set expectations for individuals receiving LEN.[1]

Following routine clinical care techniques (e.g., proper injection method, ice application, and administering analgesics for pain) before, during, and after injection may help address ISRs.[3-7]

Twice-yearly SC LEN for PrEP Injection Forms a Drug Depot



For illustrative purposes only.

The LEN for PrEP dosing schedule consists of a **required initiation dosing** with a combination of SC injections and oral tablets, followed by twice-yearly‡ **continuation dosing** with SC injections.[1] See full Prescribing Information for details on dosing and administration.

When LEN for PrEP is injected, a **drug depot** forms in the SC tissue whereby lenacapavir is slowly released into the systemic circulation over time. This allows for a twice-yearly continuation injection schedule.[1]

The drug depot can lead to a possible reaction.[1]

In some individuals, but not all, this may lead to a palpable – although not usually visible – **nodule** at the injection site.[1]

The absence of a nodule does not imply the medication is not working.[1]

Nodules are expected to reduce in size over time.[1-3]

Injection-site Reactions (All Grades) Reported in ≥2% of Participants Receiving LEN for PrEP in PURPOSE 1 or PURPOSE 2[1a]

	PURPOSE 1		PURPOSE 2	
	LEN for PrEP (N=2,140)[1,2*]	F/TDF[b] or F/TAF[b] (N=3,205)[1,2*]	LEN for PrEP (N=2,183)[1,3†]	F/TDF[b] (N=1,088)[1,3†]
Injection site reactions	69%	34%[c]	83%	69%
Nodule	64%	17%	63%	39%
Median duration of nodules (days) (Associated with the first injections of LEN for PrEP)	350 (IQR: 182, 470)	N/A	297 (IQR: 176, 423)	N/A
Median diameter of nodules (cm)[§] (Maximum observed nodule diameter from each participant)	3.0 (IQR: 2.0, 3.5)	N/A	3.0 (IQR: 2.0, 4.0)	N/A
Pain	31%	24%	56%	53%
Induration	4%	<1%	16%	10%
Swelling	4%	5%	7%	10%
Pruritis	2%	1%	3%	3%
Erythema	1%	1%	17%	19%
Bruising	<1%	<1%	3%	4%
Warmth	<1%	<1%	2%	2%
Discontinuations due to ISRs (participants) (None of the ISRs were serious, and the incidence of reported ISRs decreased with subsequent injections)[1-3]	4 (0.2%)	0/0	26 (1.2%)	3 (0.3)

a. Frequencies are based on all injection site reactions attributed to study drug (or to the procedure) by the investigator.
b. Participants received placebo subcutaneous injections (polyethylene glycol 400).
c. Only includes F/TDF (N=1,070)

In PURPOSE 1 & 2, nodule frequency decreased with subsequent injections.[1-3]

Nodules resolved more slowly than other ISRs.[1]

A nodule of 3.0 cm (just under 1.2 inches) is slightly larger than the diameter of a U.S. quarter (25 cent coin).

Preparing for an Injection

Healthcare providers should use their clinical judgment to make a medically appropriate decision for individuals receiving a SC LEN for PrEP injection.

Pre-Injection Care

These techniques for injection site pain are **commonly used in routine clinical care** and are not specific to LEN for PrEP.

Person-centered Injection Counseling

Individuals receiving LEN for PrEP should be informed about what to expect during and after injections.[1]

1. ISRs are common side effects experienced by most people who take LEN for PrEP.[1]
2. ISRs may include pain, erythema, and swelling at the injection site, and may resolve within days.[1,8]
3. Long-acting LEN for PrEP forms a drug depot and can lead to a possible reaction, where some individuals may feel a "bump" (nodule). Nodules may take longer to go away than other ISRs.[1-3,8]
4. Not feeling a nodule does not indicate that the medication is not working.[1]
5. None of the ISRs in the PURPOSE 1 and PURPOSE 2 trials were serious. Individual results may vary. Advise individuals receiving LEN for PrEP to tell their healthcare provider if they experience any ISRs or other side effects.[1]

Ice

Applying an ice pack **~10 minutes before injection** to both injection sites can help reduce injection-related pain.[6]

Topical Analgesic

If clinically appropriate, applying topical analgesics (e.g., lidocaine-prilocaine EMLA cream, not patches) can help reduce injection-related pain.[6,7] Apply at least **30 minutes** before injection to both injection sites, if not contraindicated.[6,7] Before injecting, wipe off the cream from the injection site with an alcohol swab.[4]

Pain Relief Devices

If clinically appropriate, applying injection pain relief devices that use pressure or vibration can block pain signals.[9]

* PURPOSE 1 is a phase 3, double-blind, active-controlled, multicenter, randomized study of twice-yearly SC LEN for PrEP, daily oral emtricitabine/tenofovir alafenamide (F/TAF) or emtricitabine/tenofovir disoproxil fumarate (F/TDF) for HIV prevention in cisgender women in South Africa and Uganda. The HIV incidence in adolescent girls and young women not receiving PrEP in these countries was at least 3.5/100 person-years in recent trials.[2] † The PURPOSE 2 study is a phase 3, double-blind, active-controlled, multicenter, randomized trial designed to evaluate safety and efficacy of twice-yearly subcutaneous LEN for PrEP for HIV prevention in cisgender gay, bisexual, and other men, transgender women, transgender men, and gender non-binary individuals who have condomless receptive anal sex with partners assigned male at birth.[3] ‡From the date of the last injection.[1] § There is no available data for approximate depth of nodules.

HIV=human immunodeficiency virus; IQR=interquartile range; ISR=injection-site reaction; LEN for PrEP=lenacapavir for HIV-1 pre-exposure prophylaxis; SC=subcutaneous.

1. YEZTUGO Prescribing Information. Gilead Sciences, Inc. 2025. **2.** Bekker L, et al. *New Engl J Med*. 2024; 391(13):1179-1192. doi: 10.1056/NEJMoa2407001. **3.** Kelley C, et al. *New Engl J Med*. 2025;392(13):1261-1276. doi: 10.1056/NEJMoa2411858. **4.** Shepherd E. *Nursing Times*[online];2018;114(9):55-57. **5.** Hunter J. *Nurs Stand*. 2008;22(21):41-4. doi: 10.7748/ns2008.01.22.21.41. **6.** Kroger A, et al. General Best Practice Guidelines for Immunization: Best Practice Guidance of the Advisory Committee on Immunization Practices (ACIP) 2023. Available at: https://stacks.cdc.gov/view/cdc/124166. Accessed May 15, 2025. **7.** Schechter NL, et al. *Pediatrics*. 2007;119(5):e1184-98. doi: 10.1542/peds.2006-1107. **8.** Castagna A, et al. EACS 2023, Poster eP.A.104. **9.** Sivri Bilgen B, Balcı S. *J Korean Acad Nurs*. 2019;49(4):486-494. doi: 10.4040/jkan.2019.49.4.486.

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Injection Preparation and Technique

LEN for PrEP injection is only for subcutaneous (SC) administration into the abdomen by a healthcare provider. The thigh may be used as an alternate site if preferred. **Injecting too superficially could lead to improper administration into the dermis.** Intradermal injection of lenacapavir has been associated with serious ISRs, including necrosis and ulcer. Ensure LEN for PrEP is only administered subcutaneously.[1]

Prior to injection, make sure that:[1]

- Vial and prepared syringe contain a **yellow solution** with **no particles**
- Contents are **not damaged**
- Product is **not expired**

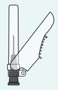
Injection Kit Components

- All necessary components for two 1.5 mL injections (one complete dose of LEN for PrEP), including withdrawal and injection needles, are included in the injection kit.[1]


VIAL
x 2


SYRINGE
x 2


18G, 1.5-inch
WITHDRAWAL NEEDLE
x 2


22G, 0.5-inch
INJECTION NEEDLE
x 2

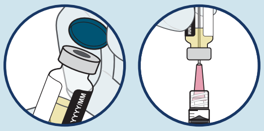
NOTE: All components are for single use.

- If the needle becomes damaged or unusable in some way (e.g., dropped on the floor or otherwise contaminated), do not use that needle. Rather contact Gilead Sciences to request a replacement needle.[2]

For replacement needles contact 1-800-GILEAD-5 (1-800-445-3235), and select option #2.

At this time, we recommend using the injection needle provided in the kit. This needle has been designed to help optimize the SC injection experience.[2]

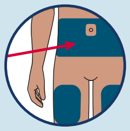
STEP ONE



Prepare vial and syringe for the injection

- Remove cap from the vial.[1]
- Clean vial stopper with alcohol wipe.[1]
- Attach the **18G, 1.5-inch withdrawal needle** with the pink hub to the syringe.[1]
- Insert the withdrawal needle into the rubber stopper of vial.[1]
- Inject 1.5 mL of air into the vial.[1]
- Fill the syringe by withdrawing all contents.[1]
- Replace the withdrawal needle with the **22G, 0.5-inch injection needle.**[1] Dispose of the withdrawal needle immediately.[3]
- Expel air bubbles.[1]
- Prime the needle to 1.5 mL.[1]

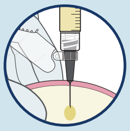
STEP TWO



Select and clean an injection site

- Select an injection site and clean it.[1] You may rotate the injection site from previous injection(s).[3]
- Injection site should be at least 2 inches from navel if injecting into the abdomen.[1]
- The thigh may be used as an alternate site if preferred.[1]

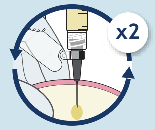
STEP THREE



Inject 1.5 mL of LEN for PrEP SC

- Gently pinch the skin.[1]
- Ensure the needle is **fully inserted** for proper SC administration. Injecting too superficially may increase the chance of a serious ISR.[1]
- Inject the whole content SC at an angle to the site (**90° is preferred** but 45°- 90° range is acceptable).[1] Be **cautious not to withdraw** the needle while injecting.[3]
- **Pause for several seconds** after the injection is complete prior to withdrawing the needle to ensure that the full dose has been administered.[3]
- Engage safety mechanism on needle and dispose immediately.[3]

STEP FOUR



Administer 2nd injection

- Choose a second injection site at least 4 inches from the first injection site and 2 inches from the navel if injecting into the abdomen.[1]
- Repeat the injection instructions for the second injection using the new withdrawal needle, injection needle, and syringe provided for the second injection.[1]

Post-injection Care

The injection site should not be massaged or subjected to pressure post-injection.[3]

Needle Removal

- Remove the needle from the skin at the <u>same angle</u> at which it was inserted.[4]

Leakage

- A small amount of drug leakage may occur. Leakage may be absorbed by a small gauze.[2,3,5]
- LEN has a **bright yellow color** so a relatively small amount of drug leakage could appear more noticeable.[1]

Bandages

- Gently apply a bandage to injection site, if needed.[6]

Ice

- Post-injection ice may help to reduce pain.[7,8]

Oral Analgesic

- If clinically appropriate, consider acetaminophen or an NSAID after injection if not contraindicated.[6]

These post-injection care strategies are not specific to LEN for PrEP.

ISRs=injection site reactions; LEN for PrEP=lenacapavir for HIV-1 pre-exposure prophylaxis; NSAID=non-steroidal anti-inflammatory drug; PrEP=pre-exposure prophylaxis; SC=subcutaneous.

1. YEZTUGO Prescribing Information. Gilead Sciences, Inc. 2025. **2.** Data on file. Gilead Sciences, Inc. 2025. **3.** Shepherd E. *Nursing Times*[online];2018;114(9):55-57. **4.** Schechter NL, et al. *Pediatrics*. 2007;119(5):e1184-98. doi: 10.1542/peds.2006-1107. **5.** Hunter J. *Nurs Stand*. 2008;22(21):41-4. doi: 10.7748/ns2008.01.22.21.41. **6.** CDC Epidemiology and Prevention of Vaccine-Preventable Diseases. Hall E., Wodi A.P., Hamborsky J., et al., eds. 14th ed (2021) Chapter 6 pg 83. **7.** Kroger A, et al. General Best Practice Guidelines for Immunization. Best Practices Guidance of the Advisory Committee on Immunization Practices (ACIP) 2023. Available at: https://stacks.cdc.gov/view/cdc/124456. Accessed May 15, 2025. **8.** Kelley C, et al. *New Engl J Med*. 2025;392(13):1261-1276. doi: 10.1056/NEJMoa2411858. **9.** Bekker L, et al. *New Engl J Med*. 2024; 391(13):1179-1192. doi: 10.1056/NEJMoa2407001.

Highlights of Prescribing Information (Cont.)[1]

These highlights do not include all the information needed to use LEN for PrEP safely and effectively. See full prescribing information for YEZTUGO.

YEZTUGO® (lenacapavir) tablets, for oral use

YEZTUGO® (lenacapavir) injection, for subcutaneous use

DOSAGE AND ADMINISTRATION

- **HIV-1 screening:** Screen all individuals for HIV-1 infection prior to initiating LEN for PrEP, prior to each injection of LEN for PrEP, and additionally as clinically appropriate.
- **Dosing schedule:** Initiation dosing (injection and tablets) followed by once every 6-months continuation injection dosing. Tablets may be taken without regard to food.

  Initiation
  Day 1 927 mg by subcutaneous injection (2 x 1.5 mL injections) and 600 mg orally (2 x 300 mg tablets)
  Day 2 600 mg orally (2 x 300 mg tablets)

  Continuation
  927 mg by subcutaneous injection (2 x 1.5 mL injections) every 6 months (26 weeks) from the date of the last injection +/-2 weeks.
- **Anticipated delayed injections:** If scheduled injection is anticipated to be delayed by more than 2 weeks, LEN for PrEP tablets may be used on an interim basis (for up to 6 months if needed) until injections resume. Dosing schedule for delayed injection is 300 mg orally once every 7 days.
- **Missed injections:** If more than 28 weeks have elapsed since the last injection and LEN for PrEP tablets have not been taken, restart initiation from Day 1 if clinically appropriate.
- Dosage modifications (supplemental doses) of LEN for PrEP are recommended when initiating strong or moderate CYP3A inducers.
- LEN for PrEP injection is for subcutaneous administration only. Two 1.5 mL injections are required for a complete dose.

DOSAGE FORMS AND STRENGTHS

- **Tablets:** 300 mg of lenacapavir
- **Injection:** 463.5 mg/1.5 mL (309 mg/mL) of lenacapavir in single-dose vials

CONTRAINDICATIONS

- Unknown or positive HIV-1 status.

WARNINGS AND PRECAUTIONS

- Comprehensive management to prevent HIV-1 acquisition.
- Potential risk of developing resistance to lenacapavir if an individual acquires HIV-1 either before or when receiving LEN for PrEP or following discontinuation of LEN for PrEP. Test before each injection and additionally as clinically appropriate to confirm HIV-1 negative status.
- Residual concentrations of lenacapavir may remain in systemic circulation for up to 12 months or longer.
- Improper administration (intradermal injection) has been associated with serious injection site reactions.

ADVERSE DRUG REACTIONS

- Most common adverse drug reactions (incidence greater than or equal to 5%, all grades) are injection site reactions, headache,and nausea.

To report SUSPECTED ADVERSE DRUG REACTIONS, contact Gilead Sciences, Inc. at 1-800-GILEAD-5 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Consult the full Prescribing Information for important drug interactions with LEN for PrEP.

To report an adverse event, call 1-800-GILEAD-5 (1-800-445-3235), and select option #3, available 24 hours a day, 7 days a week.

1. YEZTUGO Prescribing Information. Gilead Sciences, Inc. 2025.

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