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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.

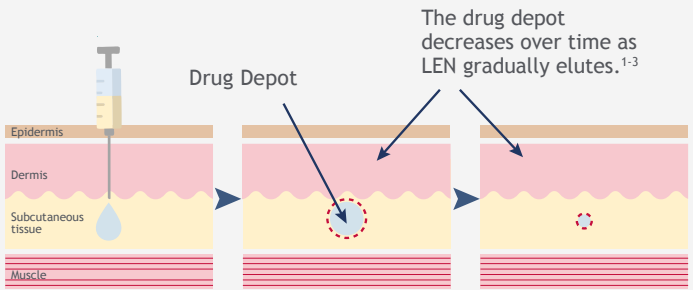
Injection site reactions (ISRs) were the most frequent adverse reactions reported with LEN for PrEP and placebo injections in the PURPOSE 1 & 2 trials.[1]

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

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.[3,6-9]

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

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 subcutaneous (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]

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

While the presence of a nodule may indicate a foreign body reaction to the drug depot, **its absence does not imply that the medication is not working.**[10]

ISRs (All Grades) Reported in ≥2% of Participants Receiving LEN for PrEP in PURPOSE 1 or PURPOSE 2[1-3a]

	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%
Pain	31%	24%	56%	53%
Induration	4%	<1%	16%	10%
Swelling	4%	5%	7%	10%
Pruritus	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).

Key Nodule Data from PURPOSE 1 & PURPOSE 2

	PURPOSE 1	PURPOSE 2
	LEN for PrEP (N=2,140)[1*]	LEN for PrEP (N=2,183)[1†]
Median duration of nodules (Associated with the first injections of LEN for PrEP)	350 days (IQR: 182, 470)	297 days (IQR: 176, 423)
Median diameter of nodules[§] (Maximum observed nodule diameter from each participant)	3.0 cm (IQR: 2.0, 3.5)	3.0 cm (IQR: 2.0, 4.0)

In PURPOSE 1 & 2, the percentage of participants with a nodule decreased with subsequent injections.[4,5]

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).[11]

* PURPOSE 1 is an ongoing 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.[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] ‡ 26 weeks ± 2 weeks from the date of the last injection.
§ There are no available data for approximate depth of nodules.

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

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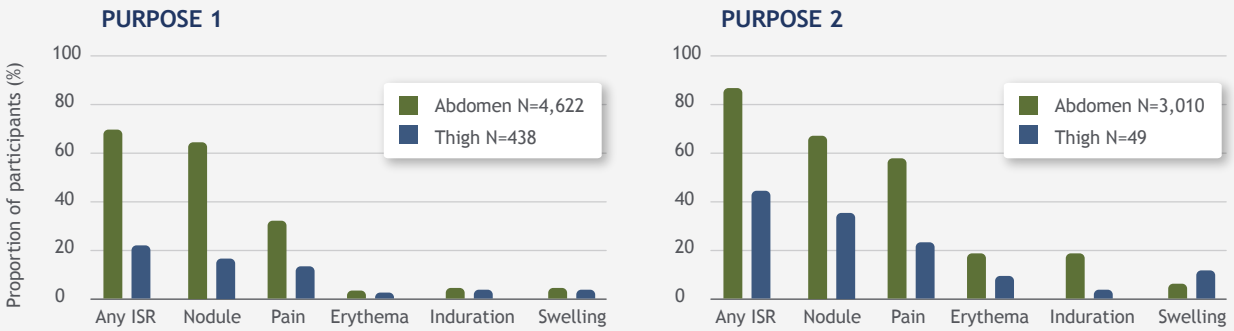
Injection Site Selection

- LEN for PrEP injection is only for SC administration into the **abdomen or thigh** by a healthcare provider. Similar drug exposures are achieved when LEN for PrEP is administered in either anatomic site.[1]
- While not specific to LEN for PrEP, rotating injection sites, when possible, may support ongoing ISR management.[6]

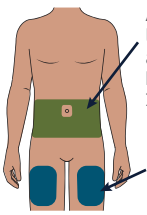
PURPOSE 1 & PURPOSE 2 LEN Randomized Blinded Phase (RBP) and Open-Label Extension (OLE) Site-Specific ISR Data

After the 52-week RBP, approximately 95% of participants chose to continue in the PURPOSE 1 and PURPOSE 2 OLE on LEN for PrEP injections, or switched from oral F/TDF or F/TAF to LEN for PrEP injections after initiation dosing, for an additional 52 weeks. Participants could choose to receive their injections at predetermined sites, including the abdomen and thigh.[10,12]

Percentage of Participants Experiencing ISRs by Injection Site (Abdomen, Thigh)[12]



Acceptable Injection Sites[1,10]



In general, fewer participants reported ISRs in the thigh compared to the abdomen[12]

Incidence and Duration of Nodules by Injection Site (Abdomen, Thigh)[12]

	PURPOSE 1		PURPOSE 2	
	Abdomen (n=4,622)[a]	Thigh (n=438)[a]	Abdomen (n=3,010)[a]	Thigh (n=49)[a]
Total injections[b]	28,891	1,113	19,706	109
Nodules, n (%)[c]	11,899 (41.2%)	108 (9.7%)	10,430 (52.9%)	35 (32.1%)
Resolved, n (%)[d]	7,326 (61.6%)	57 (52.8%)	6,201 (59.5%)	10 (28.6%)
Median time to resolution (Q1, Q3)[e]	260 days (151, 364)	90 days (80, 174)	270 days (176, 367)	116 days (82, 178)

a. Indicates the number of participants who received at least one LEN for PrEP injection in the respective injection site.
b. Total number of LEN for PrEP injections through the 52-week OLE. Each dose was comprised of two injections, and all participants received injections in the abdomen during the RBP except for those in PURPOSE 1 who became pregnant and received injections in the thigh.
c. Bilateral nodules from the same injection visits were counted as separate AEs; each LEN for PrEP dose is given as 2 x 1.5 mL injections.
d. Percent resolved is out of the number of nodules.
e. Duration (days) = stop date minus onset date +1.

Lower incidence of nodules and a shorter median time to resolution were noted with thigh injections as compared with abdominal injections.[12]

ISRs by Injection Site (Abdomen, Thigh)[12]

There was longer follow-up for abdominal injections administered during RBP.[12]

	PURPOSE 1		PURPOSE 2	
	Abdomen (n=4,622)[a]	Thigh (n=438)[a]	Abdomen (n=3,010)[a]	Thigh (n=49)[a]
Any ISR[b], n (%)	3,188 (69%)	95 (21.7%)	2,628 (87.3%)	22 (44.9%)
Any Grade 3 or 4 ISR, n (%)	8 (0.2%)	3 (0.7%)	18 (0.6%)	0 (0%)
Any Serious ISRs, n (%)	0 (0%)	0 (0%)	1 (<0.1%)	0 (0%)
ISRs leading to premature drug discontinuation, n (%)	6 (0.1%)	0 (0%)	27 (0.9%)	0 (0%)

a. Indicates the number of participants who received at least one LEN for PrEP injection in the respective injection site.
b. Any ISR is reflective of all ISRs reported, including those other than the five most commonly reported ISRs presented in the graphs. Bilateral nodules and indurations from the same injection visits were counted as separate AEs; all other ISRs from the same injection visit with the same AE Preferred Term/onset date were counted as one event.

In a limited number of participants who chose to receive LEN for PrEP as a subcutaneous injection in the thigh, no serious ISRs or ISRs that led to study drug discontinuation occurred.[12]

* In the OLE of PURPOSE 1 and PURPOSE 2, participants could choose the site into which LEN for PrEP could be injected based on the options available to them. According to U.S. prescribing information, LEN for PrEP injection is only for SC administration into the abdomen. The thigh can be used as an alternative injection site if preferred.[1,12]

AE=adverse event; F/TAF=emtricitabine/tenofovir alafenamide; F/TDF=emtricitabine/tenofovir disoproxil fumarate; LEN for PrEP=lenacapavir for HIV-1 pre-exposure prophylaxis; ISR=injection-site reaction; SC=subcutaneous.

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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.

Person-centered Injection Counseling

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



1. ISRs were common side effects experienced by people who took LEN for PrEP in the PURPOSE trials.[1]
2. ISRs may include nodule, pain, induration, swelling, pruritus, erythema, bruising and warmth at the injection site. Across PURPOSE 1 and PURPOSE 2, ISRs (excluding nodules and indurations) had median durations of 9 days (IQR: 4–30) and 4 days (IQR: 2–8), respectively.[1,13]
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.[1-3,13]
4. Not feeling a nodule does not indicate that the medication is not working.[1]
5. Serious ISRs were rare (<0.1%) in the PURPOSE trials. Advise individuals receiving LEN for PrEP to tell their healthcare provider if they experience any ISRs or other side effects.[1,12]

Pre-Injection Care

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

Ice

Applying an ice pack **~10 minutes before injection** to both injection sites can help reduce injection-related pain.[8]

Topical Analgesic

If clinically appropriate, applying topical analgesics (e.g., lidocaine or 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 topical analgesic from the injection site with an alcohol swab.[4]

Pain Relief Devices

If clinically appropriate, apply injection pain relief devices.[14]

Injection Preparation and Technique

LEN for PrEP injection is approved only for subcutaneous (SC) administration into the **thigh or abdomen** by a healthcare professional. **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**

LEN for PrEP=lenacapavir for HIV-1 pre-exposure prophylaxis; IQR=interquartile range; SC=subcutaneous.

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Injection Kit Components

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

It is recommended to use the injection needle provided in the kit. This needle has been designed to help optimize the SC injection experience.[10]

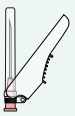
- All necessary components for two 1.5 mL injections (one complete dose), including withdrawal and injection needles, are included in the injection kit.[1]
- If the needle becomes damaged or unusable in some way (e.g., dropped on the floor or otherwise contaminated), do not use that needle. Contact Gilead Sciences to request a replacement needle.[10]



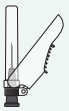
VIAL x 2



SYRINGE x 2



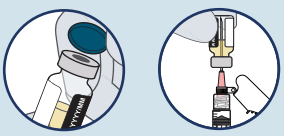
18G, 1.5-inch WITHDRAWAL NEEDLE (with or without safety shield) x 2



22G, 0.5-inch INJECTION NEEDLE x 2

NOTE: All components are for single use.

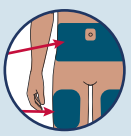
STEP ONE



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.[6]
- Expel air bubbles.[1]
- Prime the needle to 1.5 mL.[1]

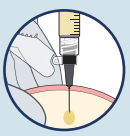
STEP TWO



Select and clean an injection site

- Select an injection site (thigh or abdomen) and clean it.[1]
- You may rotate the injection site from previous injection(s).[6]
- If the abdomen is chosen, injection site should be at least 2 inches from navel.[1]
- Note that the lateral aspects of the abdomen (flank or "love handles") is considered part of the abdomen and can be used as a viable injection site.[10]

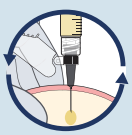
STEP THREE



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.[6]
- **Pause for several seconds** after the injection is complete prior to withdrawing the needle to ensure that the full dose has been administered.[6]
- Engage safety mechanism on needle and dispose immediately.[6]

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.[6]

Needle Removal

- Remove the needle from the skin at the same angle at which it was inserted.[9]

Discharge

- A small amount of drug discharge may occur. Discharge may be absorbed by a small gauze.[6,7,10]
- LEN has a **bright yellow color** so a relatively small amount of drug discharge could appear more noticeable.[1,10]

Bandages

- Gently apply a bandage to injection site, if needed.[15]

Ice

- Post-injection ice may help to reduce pain.[3,8]

Oral Analgesic

- If clinically appropriate, consider acetaminophen or an NSAID after injection if not contraindicated.[8]

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

Individuals receiving LEN for PrEP should consider minimizing strenuous physical activities for the rest of the day after their injections.[10]

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

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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.

REFERENCES

1. LEN for PrEP (lenacapavir) Prescribing Information. Gilead Sciences, Inc. 2026. **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.** Bekker LG, et al. Supplementary appendix. N Engl J Med. 2024;391(13):1179-1192. doi:10.1056/NEJMoa2407001. **5.** Kelley CF, et al. Supplementary appendix. N Engl J Med. 2025;392(13):1261-1276. doi:10.1056/NEJMoa2411858. **6.** Shepherd E. Nursing Times[online];2018;114(9):55-57. **7.** Hunter J. Nurs Stand. 2008;22(21):41-4. doi: 10.7748/ns2008.01.22.21.41. **8.** 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/124166. Accessed May 15, 2025. **9.** Schechter NL, et al. Pediatrics. 2007;119(5):e1184-98. doi: 10.1542/peds.2006-1107. **10.** Data on File. Gilead Sciences, Inc. 2025. **11.** CoinFAQ. Modern U.S. coins [image]. Accessed July 26. 2026. https://coinfaq974389709.wordpress.com/wp-content/uploads/2020/04/modern-us.jpg. **12.** Brites C, et al. Favorable tolerability of lenacapavir for PrEP administered at participant-chosen anatomic sites in PURPOSE 1 and PURPOSE 2. Presented at: AIDS 2026, the 26th International AIDS Conference; July 26-31, 2026; Rio de Janeiro, Brazil. **13.** Castagna A, et al. EACS 2023, Poster eP.A.104. **14.** Sivri Bilgen B, Balcı S. J Korean Acad Nurs. 2019;49(4):486-494. doi: 10.4040/jkan.2019.49.4.486. **15.** 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.

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.

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