GILEAD | Medical Information

Yeztugo® (lenacapavir) Alternative Sites of Administration

This document is in response to your request for information regarding Yeztugo® (lenacapavir [LEN]) and alternative sites of subcutaneous administration other than the abdomen or thigh.

Some data may be outside of the US FDA-approved prescribing information. In providing this data, Gilead Sciences, Inc. is not making any representation as to its clinical relevance or to the use of any Gilead product(s). For information about the approved conditions of use of any Gilead drug product, please consult the FDA-approved prescribing information.

The full indication, important safety information, and boxed warning are available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/yeztugo/yeztugo_pi.

Summary

Product Labeling[1]

- LEN injection is only for subcutaneous administration into the abdomen by a healthcare provider. The thigh can be used as an alternative injection site if preferred.
- Do NOT administer intradermally due to risk of serious injection site reactions.
- Two 1.5 mL injections are required for a complete dose. The second injection is administered at least 4 inches from the first injection site.
- If administering in the abdomen, ensure injections are at least 2 inches away from the navel.

PK Data on SUBQ LEN Alternative Administration Sites

A phase 1, open-label, multicohort study evaluating the PK and safety of LEN SUBQ administered in different sites demonstrated that exposure to LEN administered into the thigh, upper arm, abdomen, and gluteal regions were generally similar.[2,3] Observed PK differences among the different sites were not considered clinically significant.

Data on the Administration of LEN in Different Sites

Phase 1 PK Study: Administration in Different Sites[2]

Study design and demographics

A phase 1, open-label, parallel-design, single-dose, multicohort study evaluated the PK and safety of LEN administered SUBQ in different sites.[2,3] Healthy adult volunteers aged 18 to 55 years who had a BMI of 19 to 30 kg/m2 were enrolled into one of four cohorts (n=10 per cohort). Each cohort of healthy volunteers received a single 927 mg dose of LEN SUBQ administered as two 1.5 mL injections either bilaterally in the thigh, upper arm, or gluteal region or in two different abdominal quadrants, which is the approved administration site

and served as a reference. PK samples from plasma were collected post dose at Hours 0, 2, 4, 6, 8, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, and 216, followed by weekly or biweekly assessments between Days 15 and 210 and monthly assessments through to Day 270.[2] Safety evaluations included injection site examinations on Days 1 to 10 and at each study visit through Day 270 to evaluate the occurrence of ISRs.3 Baseline demographics were generally similar among cohorts (Table 1).[2]

Table 1. Baseline Demographics (Lat et al)[2]

Key Demographics	Abdomen (n=10)	Thigh (n=10)	Upper Arm (n=10)	Gluteal Region (n=10)
Male, %	50	50	60	40
Age, mean (SD), years	44 (11.5)	44 (9.5)	43 (6.7)	40 (9.7)
Race, White/Black or African American, %	70/30	70/30	80/20	100/0
Weight, mean (SD), kg	74.7 (8.7)	77.8 (11.5)	80.3 (13.4)	74.4 (11.6)
BMI, mean (SD), kg/m^2	27 (2.4)	27 (1.6)	27.2 (2.9)	26.9 (2.2)

PK results[2]

Exposures to LEN after SUBQ administration into the thigh, upper arm, and gluteal regions were generally similar or slightly higher than those observed after administration into the abdomen; observed PK differences were not considered clinically significant (Table 2). GM C_{max}, $AUC_{6\ mo}$, and AUC_{last} values were 8% to 15% lower after SUBQ administration into the thigh than those observed for the abdomen (reference comparator) cohort; these PK parameters were 5% to 33% higher in the upper-arm cohort and 18% to 26% higher in the gluteal-region cohort than in the abdomen cohort. The GM $C_{6\ mo}$ in each cohort was greater than the IQ4 (target efficacy concentration) of 15.5 ng/mL.

Table 2. PK Parameters by Administration Site (Lat et al)[2]

Parameters	Abdomen (n=8[a])	Thigh (n=10)	Upper Arm (n=10)	Gluteal Region (n=9[a])
C_{max}, GM (%CV), ng/mL	56.7 (40.7)	52.1 (67.4)	75.6 (57.2)	71.2 (42.7)
T_{max}, median (Q1, Q3), h	2660 (1870, 3250)	2490 (1950, 3120)	1990 (1150, 2490)	2160 (1660, 2580)
$T_{1/2}$, median (Q1, Q3), h	1440 (1180,1920)	1430 (1100, 2080)[b]	1260 (1070, 1500)	1560 (1300, 1810)
$C_{6\ mo}$, GM (%CV), ng/mL	28.6 (60.6)	22.6 (69.9)	18.7 (59.9)	25.2 (68)
$AUC_{6\ mo}$, GM (%CV), ng·h/mL	144,000 (38.2)	122,000 (73.9)[b]	172,000 (45.5)	181,000 (36.9)
AUC_{last}, GM (%CV), ng·h/mL	187,000 (33.3)	164,000 (57.6)[b]	196,000 (43.9)	220,000 (35.9)
AUC_{∞}, GM (%CV), ng·h/mL	223,000 (34.7)	267,000 (26.2)[b]	208,000 (43.8)	247,000 (35.3)

Abbreviations: %CV=geometric % coefficient of variation; AUC_{∞}=area under the concentration-time curve to infinity; Q=quartile; $T_{1/2}$=half-life; T_{max}=time to C_{max}.
[a] Three healthy volunteers (abdomen, n=2; gluteal region, n=1) were lost to follow-up or withdrew prematurely.
[b] AUC_{∞} and $T_{1/2}$, n=6; AUC_{last} and $AUC_{6\ mo}$, n=9.

Safety results[3]

No serious AEs or AEs that resulted in study discontinuation occurred. Treatment-related AEs occurred in 38/40 participants (95%), and all non-ISR treatment-related AEs were Grade 1. Most participants (38/40; 95%) experienced ISRs, and the most common ISRs were pain (90%), induration (73%), erythema (70%), nodules (15%), and swelling (15%; Table 3). All ISRs were Grade ≤2 except for 1 event of erythema in the upper-arm cohort.

Table 3. Most Common ISRs by Administration Site (Saunders et al)[3]

ISR, %	Abdomen (n=10)		Thigh (n=10)		Upper Arm (n=10)			Gluteal Region (n=10)	
	Grade 1	Grade 2	Grade 1	Grade 2	Grade 1	Grade 2	Grade 3	Grade 1	Grade 2
Pain	100	0	90	0	80	0	0	90	0
Induration	50	30	20	60	20	80	0	30	0
Erythema	50	10	30	60	40	30	10	10	40
Nodules	20	0	40	0	0	0	0	0	0
Swelling	30	10	0	0	0	10	0	0	10

Product Labeling[1]

Dosage and Administration

Preparation and administration of SUBQ injection

LEN injection is only for subcutaneous administration into the abdomen by a healthcare provider. The thigh can be used as an alternative injection site if preferred. Do NOT administer intradermally due to risk of serious injection site reactions.

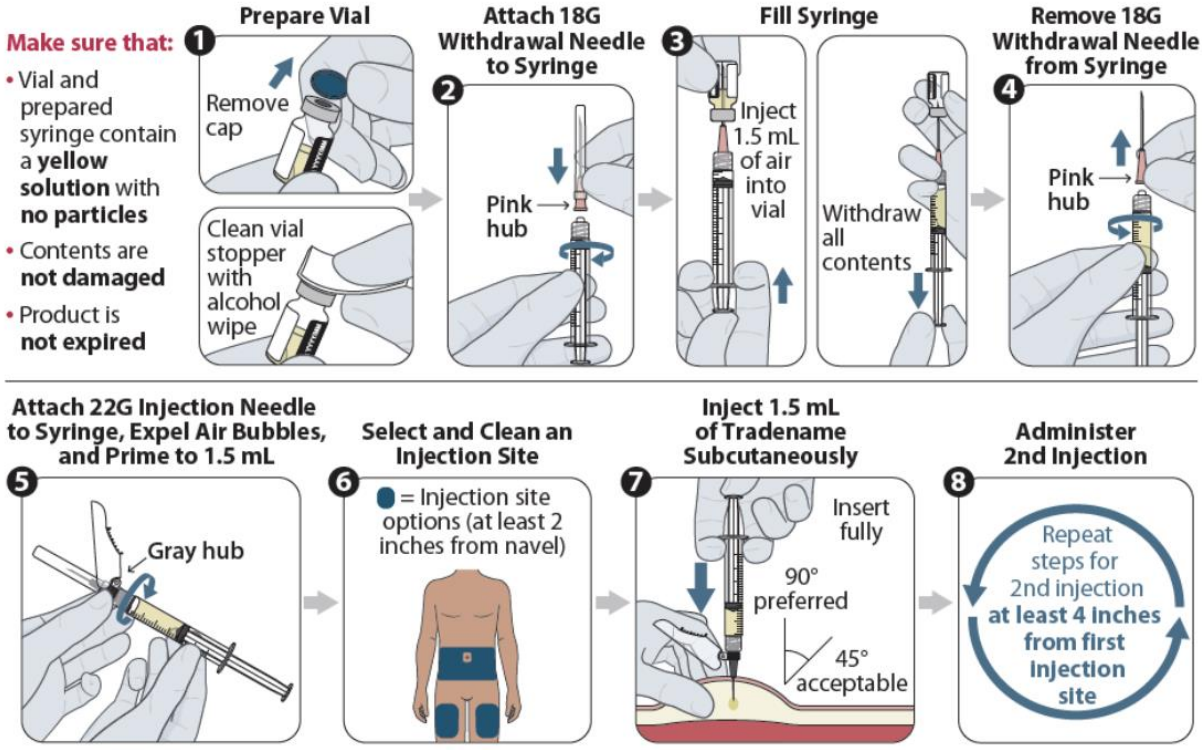
Use aseptic technique. Visually inspect the solution in the vials and prepared syringe for particulate matter and discoloration prior to administration. LEN injection is a yellow solution. Do not use LEN injection if the solution is discolored or if it contains particulate matter. Once the solution is withdrawn from the vials, the subcutaneous injections should be administered as soon as possible.

Figure 1 identifies the components for use in the administration steps for the withdrawal needle injection kit and the administration steps are provided in Figure 2. The 18-gauge needle is for withdrawal only in this kit.

The injection kit components are for single use only. Two 1.5 mL injections are required for a complete dose.

Figure 1. LEN Withdrawal Needle Injection Kit Components

Figure 2. LEN Injection Steps for Withdrawal Needle Injection Kit



Select and clean the injection site. Administer the second injection at least 4 inches apart from the first injection site. If administering in the abdomen, ensure injections are at least 2 inches away from the navel.

SUBQ administered LEN forms a drug depot whereby LEN is slowly released from the site of administration. Advise that, in some individuals, this may lead to a nodule at the injection site. Improper administration (intradermal injection) of LEN has been associated with serious ISRs, including necrosis and ulcer. Ensure LEN is only administered SUBQ.

References

1. Enclosed, Gilead Sciences Inc. YEZTUGO® (lenacapavir) tablets, for oral use. YEZTUGO® (lenacapavir) injection, for subcutaneous use. U.S. Prescribing Information. Foster City, CA.
2. Lat A, Kim A, Zhang H, et al. Impact of Subcutaneous Administration Sites on the Clinical Pharmacokinetics of Lenacapavir , a Long-Acting HIV Capsid Inhibitor: Does Body Site Matter? [Poster Abstract 1542]. Paper presented at: ID Week 2023; October 11-15, 2023; Boston, MA.
3. Saunders G, Mortensen E, Shen G, Kim A. Injection Site Reactions with Subcutaneous Lenacapavir Administration at Alternate Injection Sites [Poster THPEB103]. Paper presented at: 25th International AIDS Conference; July 22-26, 2024; Munich, Germany.

Abbreviations

AE=adverse event
$AUC_{6\ mo}$=area under the concentration-time curve at 6 months
AUC_{last}=area under the concentration-time curve from dosing to last measurable concentration
$C_{6\ mo}$=concentration at 6 months
C_{max}=maximum concentration
GM=geometric mean
ISR=injection site reaction
IQ4=inhibitory quotient-4
LEN=lenacapavir
PK=pharmacokinetic(s)
SUBQ=subcutaneous(ly)

Product Label

For the full indication, important safety information, and boxed warning, please refer to the Yeztugo US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/yeztugo/yeztugo_pi.

Follow-Up

For any additional questions, please contact Gilead Medical Information at:

☎1-866-MEDI-GSI (1-866-633-4474) or 🖱 www.askgileadmedical.com

Adverse Event Reporting

Please report all adverse events to:

Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or
🖱 www.gilead.com/utility/contact/report-an-adverse-event

FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🖱 www.accessdata.fda.gov/scripts/medwatch

Data Privacy

The Medical Information service at Gilead Sciences may collect, store and use your personal information to provide a response to your medical request. We may share your information with other Gilead Sciences colleagues to ensure that your request is addressed appropriately. If you report an adverse event or concern about the quality of a Gilead or Kite product, we will need to use the information you have given us in order to meet our regulatory requirements in relation to the safety of our medicines.

It may be necessary for us to share your information with Gilead's affiliates, business partners, service providers and regulatory authorities located in countries besides your own. Gilead Sciences has implemented measures to protect the personal information you provide. Please see the Gilead Privacy Statement (www.gilead.com/privacy-statements) for more information about how Gilead handles your personal information and your rights. If you have any further questions about the use of your personal information, please contact privacy@gilead.com.