GILEAD | Medical Information

Sunlenca® (lenacapavir) Injection Site Reactions

This document is in response to your request for information regarding the use of subcutaneous (SUBQ) Sunlenca® (lenacapavir [LEN]) for the treatment of HIV-1 and injection site reactions (ISRs). This response was developed according to principles of evidence-based medicine and contains data from clinical trials and real-world studies (N≥75).

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 warnings are available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/sunlenca/sunlenca_pi.

Summary

Product Labeling[1]

Administration of LEN may result in local ISRs. If clinically significant ISRs occur, evaluate and institute appropriate therapy and follow-up.

Improper administration (intradermal injection) has been associated with serious ISR reactions, including necrosis and ulcer. Ensure LEN is only administered SUBQ in the abdomen.

The most common adverse reactions (all grades) reported in ≥3% of participants in CAPELLA were nausea and ISRs.

Please refer to the LEN US FDA-approved product labeling for complete product information.

Clinical Data on SUBQ LEN and ISRs

In CAPELLA, an ongoing phase 2/3 study of LEN use in HTE PWH (N=72), 97.2% of ISRs (383/394) through Week 156 were Grade 1 or 2 in severity. Four Grade ≥3 TEAEs of ISRs and 1 report of abdominal abscess were reported. Two participants (2.8%) discontinued LEN due to Grade 1 injection site nodule.[2]

In CALIBRATE, a phase 2 study of LEN use in ARV-naive PWH (N=105), 103 participants received ≥1 SUBQ LEN injection through Week 132. Overall, 69 participants (67%) reported an ISR of any grade, and most ISRs were Grade 1 or 2 in severity. Two Grade 3 TEAEs of ISRs were reported (injection site nodule, n=1; injection site abscess, n=1); neither resulted in LEN discontinuation. LEN discontinuations were reported in 3 participants due to Grade 1 injection site induration and in 1 participant due to both Grade 1 injection site erythema and Grade 1 injection site swelling.[3]

Real-World Data on SUBQ LEN and ISRs

In LENAddOn, an observational, retrospective study in France (N=77), ISRs were reported by 53.2% and 46.6% after the first and second SUBQ LEN injections, respectively. Two Grade 3 ISRs (pain ± erythema) were reported after the first SUBQ LEN injection and did not lead to LEN discontinuation. Two additional Grade 3 ISRs were reported after the second injection at Month 6.[4]

Clinical Data on SUBQ LEN and ISRs

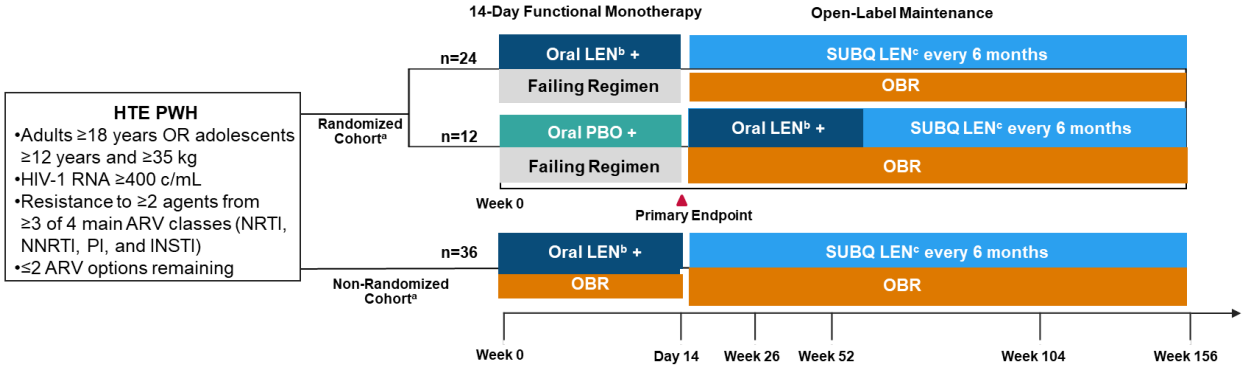
CAPELLA: LEN in HTE PWH

Study design and demographics

CAPELLA (NCT04150068) is an ongoing, phase 2/3, randomized, PBO-controlled clinical study designed to evaluate LEN as add-on therapy to a failing regimen in HTE PWH with multidrug resistance (N=72). Participants in both cohorts receive either oral LEN or PBO for 14 days in addition to their failing regimen or OBR. Both cohorts then enter the maintenance phase, which is evaluating the safety and efficacy of SUBQ LEN administered every 6 months in combination with an OBR (Figure 1).[2]

Overall baseline demographics and characteristics were as follows: median (range) age, 52 (23–78) years; female sex at birth, 25%; Black race, 38%; Hispanic/Latinx ethnicity, 21%; median (range) weight, 70.5 (41.4–126) kg; median (range) BMI, 25 (14.9–42.6) kg/m^2.[5]

Figure 1. CAPELLA: Study Design[2,6,7]



Abbreviations: ATV=atazanavir; COBI=cobicistat; INSTI=integrase strand transfer inhibitor; NNRTI=non-nucleoside reverse transcriptase inhibitor; NRTI=nucleoside reverse transcriptase inhibitor; PI=protease inhibitor; RTV=ritonavir.

[a]Participants with <0.5 $\log_{10}$ decline in HIV-1 RNA and HIV-1 RNA ≥400 c/mL were enrolled in the randomized cohort. Participants were enrolled in the non-randomized cohort if they had ≥0.5 $\log_{10}$ decline in HIV-1 RNA and/or had HIV-1 RNA <400 c/mL or were enrolled after the randomized cohort was fully recruited.

[b]Oral LEN dosing schedule: Day 1, 600 mg; Day 2, 600 mg; and Day 8, 300 mg.

[c]SUBQ LEN dosing schedule: 927 mg (2 × 1.5 mL) on Day 15 and then every 6 months.

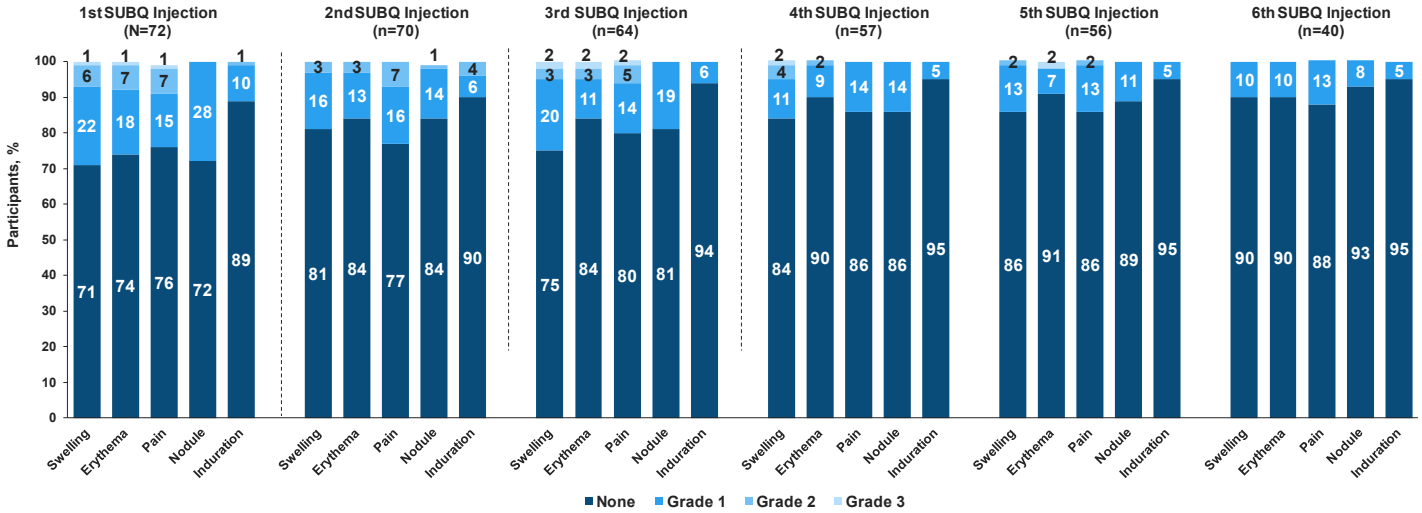
Note: ATV, ATV/COBI, ATV/RTV, efavirenz, etravirine, nevirapine, and tipranavir were not permitted for use in OBR.

ISR data

The median (IQR) duration of follow-up was 165 (146–178) weeks. Through Week 156, 97.2% of ISRs (383/394) were Grade 1 or 2 in severity (Figure 2). The frequency of LEN-related ISRs decreased over time; they were reported in 61.1% of participants after the

first injection visit at Day 15, 45.7% after the second visit at Week 26, and 37.5% after the third visit at Week 104.[2]

Figure 2. CAPELLA Study: ISRs Related to SUBQ LEN After First Six Injections[2,6a]



[a]Percentage denominators are the number of participants who received an injection at that visit. Percentages may not total 100% due to rounding.

TEAEs of ISRs and the median durations of each type of ISR are presented in Table 1.

Table 1. CAPELLA: Types, Frequencies, and Median Durations of ISRs Through Week 156[2]

ISRs, n (%)	LEN (N=72)	Median (IQR) Duration, Days
Injection site swelling	34 (47.2)	8 (4–15)
Injection site nodule	28 (38.9)	288 (155–548)
Injection site pain	28 (38.9)	3 (2–5)
Injection site erythema	26 (36.1)	5 (3–8)
Injection site induration	11 (15.3)	190 (67–410)

Four of the 6 Grade ≥3 treatment-related TEAEs were ISRs. Through Week 156, 2 participants (2.8%) discontinued LEN due to Grade 1 injection site nodules.[2]

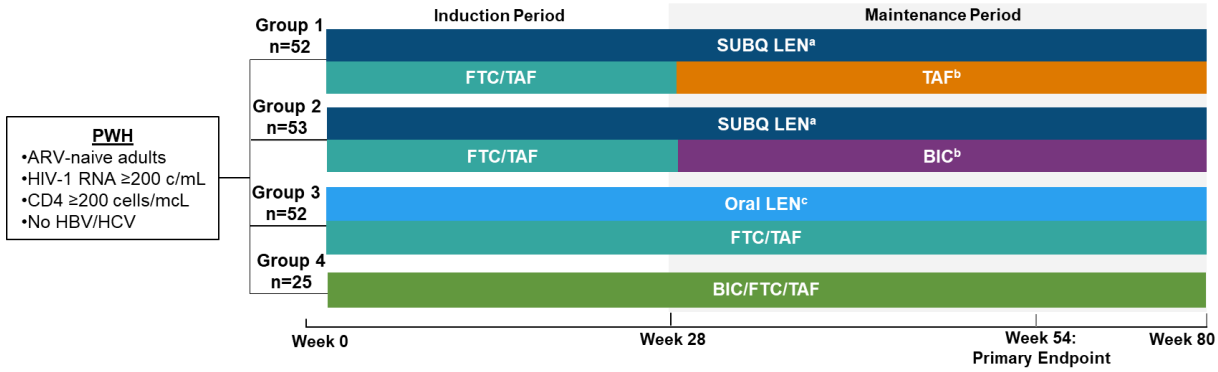
CALIBRATE: LEN in ARV-Naive PWH

Study design and demographics

CALIBRATE (NCT04143594) was a phase 2, randomized, open-label, active-controlled clinical study that evaluated the safety and efficacy of LEN in ARV-naive PWH (N=182). Participants received SUBQ or oral LEN in combination with other oral ARV agents or BIC/FTC/TAF alone.[3]

Baseline demographics and characteristics were generally balanced between treatment groups: median (range) age, 30 (19–61) years; female sex at birth, 6%; Black race, 46%; Hispanic/Latinx ethnicity, 44%; median (range) weight, 77.1 (47.6–163.8) kg; median (range) BMI, 25.2 (17.5–51.1) kg/m^2.[5]

Figure 3. CALIBRATE: Study Design[3,8]

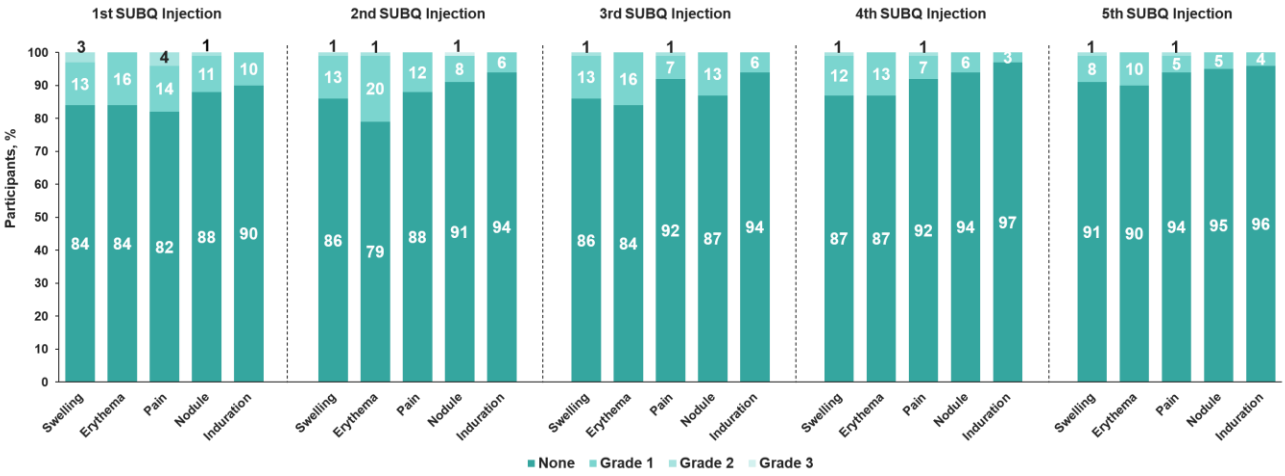


Abbreviation: CD4=cluster of differentiation 4.
[a]The LEN dosing schedule included an oral lead-in phase (Day 1: 600 mg; Day 2: 600 mg; Day 8: 300 mg) followed by SUBQ LEN 927 mg (2 × 1.5 mL) on Day 15 and every 6 months (26 weeks) thereafter.
[b]Participants were required to have HIV-1 RNA <50 c/mL at Weeks 16 and 22 to initiate treatment with a two-agent regimen at Week 28. Those with HIV-1 RNA ≥50 c/mL discontinued the study at Week 28.
[c]The oral LEN dosing schedule was as follows: 600 mg on Day 1, 600 mg on Day 2, and 50 mg on Day 3 and onwards.
Note: FTC/TAF (200/25 mg), TAF (25 mg), BIC (75 mg), and BIC/FTC/TAF (50/200/25 mg) were administered as daily oral doses.

ISR data[3]

The median (IQR) duration of exposure to LEN + ARVs was 156 (147–172) weeks in Group 1 and 154 (118–164) weeks in Group 2. Through Week 132, 103 participants overall received ≥1 SUBQ LEN injection (Group 1, n=51; Group 2, n=52); of these, 69 participants (67%) reported an ISR of any grade. The frequency of LEN-related ISRs decreased over time, with reports of 43% after the first injection visit, 52% after the second, 46% after the third, 32% after the fourth, and 30% after the fifth. Most ISRs were Grade 1 or 2 in severity (Figure 4).

Figure 4. CALIBRATE Study: ISRs Related to SUBQ LEN After the First Five Injections (Treatment Groups 1 and 2, n=105)[3]



Note: The denominator was 105, which included 2 participants who did not receive a LEN SUBQ injection. LEN SUBQ injection 1 occurred at Day 15, injection 2 at Week 28, injection 3 at Week 54, injection 4 at Week 80, and injection 5 at Week 106.

TEAEs of ISRs and the median durations of each type of ISR are presented in Table 2 .

Table 2. CALIBRATE: Types, Frequencies, and Median Durations of ISRs Through Week 132[3]

ISRs, n (%)	LEN Group 1 (n=51)	LEN Group 2 (n=52)	Overall Median (IQR) Duration, Days
Injection site swelling	17 (33)	18 (35)	10 (5–15)
Injection site erythema	25 (49)	18 (35)	5 (2–9)
Injection site pain	15 (29)	14 (27)	2 (1–6)
Injection site inflammation	12 (24)	4 (8)	–
Injection site induration	11 (22)	11 (21)	192 (143–400)
Injection site nodule	10 (20)	13 (25)	219 (84–372)

Two Grade 3 treatment-related TEAEs of ISRs were reported, consisting of 1 event of injection site nodules on Day 194 that resolved on Day 265 and 1 event of injection site abscess on Day 395 that resolved on Day 449; neither resulted in LEN discontinuation. Overall, LEN discontinuations were reported in 3 participants due to Grade 1 injection site induration and in 1 participant due to both Grade 1 injection site erythema and Grade 1 injection site swelling.

Real-World Data on SUBQ LEN and ISRs

LENAddOn Study[4]

LENAddOn is an observational, retrospective, multicenter study in France that aims to characterize PWH who initiate LEN in the commercial setting, assess LEN continuation rates at Months 6 and 12, and describe reasons for LEN discontinuation (N=77). The median (IQR) age is 57 (44–63) years, 67.5% are cisgender men, the median (IQR) time from HIV diagnosis was 30 (21–34) years, and 61% have had an AIDS-defining event. Overall, 21 participants (27.3%) received a fully injectable ARV regimen (LEN + CAB, n=16; LEN + CAB + RPV, n=5).

After the first SUBQ LEN injection, ISRs were reported by 53.2% of participants (41/77), of which 26% were Grade 1, 24% were Grade 2, and 3% were Grade 3. The 2 Grade 3 ISRs were pain ± erythema and did not lead to LEN discontinuation. After the second SUBQ LEN injection at Month 6, ISRs were reported by 46.6% of participants (34/73); 22% of these ISRs were Grade 1, 22% were Grade 2, and 3% were Grade 3. No additional information was provided on the 2 Grade 3 ISRs at Month 6.

References

1. SUNLENCA, Gilead Sciences Inc. SUNLENCA® (lenacapavir) tablets, for oral use. SUNLENCA® (lenacapavir) injection, for subcutaneous use. US Prescribing Information. Foster City, CA
2. Ogbuagu O, Wiznia A, McGowan JP, et al. Subcutaneous Lenacapavir in People With Multidrug-Resistant HIV-1: 156 Week Results of the CAPELLA Study. *Open Forum Infect Dis.* 2025;13(1):ofaf763.
3. Hagins D, Berhe M, Crofoot GE, et al. Final efficacy and safety of twice-yearly subcutaneous lenacapavir in treatment-naive people with HIV. *AIDS.* 2026;40(3):302-311.
4. Palich R, Ghosn J, Valantin M-A, et al. Real world use of lenacapavir in France: a national, observational study.[Poster #eP101]. Paper presented at: 20th European AIDS Conference (EACS); October 15-18, 2025; Paris, France.

5. Kumar P, Gupta S, Segal-Maurer S, et al. Injection-Site Reaction Experience in Clinical Studies of People Using Lenacapavir For HIV Treatment [Poster EPB184]. Paper presented at: AIDS 2022; 29 July-2 August, 2022; Montreal, Quebec, Canada.
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7. Segal-Maurer S, DeJesus E, Stellbrink HJ, et al. Capsid Inhibition with Lenacapavir in Multidrug-Resistant HIV-1 Infection [Supplement]. *N Engl J Med.* 2022;386(19):1793-1803.
8. Gupta SK, Berhe M, Crofoot G, et al. Lenacapavir administered every 26 weeks or daily in combination with oral daily antiretroviral therapy for initial treatment of HIV: a randomised, open-label, active-controlled, phase 2 trial [main article + supplementary]. *Lancet HIV.* 2023;10(1):e15-e23.

Abbreviations

ARV=antiretroviral
BIC=bictegravir
c/mL=copies per mL
CAB=cabotegravir
FTC=emtricitabine
HTE=heavily treatment-experienced
ISR=injection site reaction
LEN=lenacapavir
OBR=optimized background regimen
PBO=placebo
PWH=people with HIV
RPV=rilpivirine
SUBQ=subcutaneous
TAF=tenofovir alafenamide
TEAE=treatment-emergent adverse event

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Sunlenca US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/sunlenca/sunlenca_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

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