WARD 86 LONG-ACTING PRE-EXPOSURE PROPHYLAXIS (PREP) GUIDELINES

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WARD 86 HIV CLINIC: Ward 86, established in January 1983, is a large HIV clinic based at San Francisco General Hospital at the University of California, San Francisco (UCSF). Since 2012, when oral pre-exposure prophylaxis (PrEP) was approved by the FDA, Ward 86 has served publicly insured, undocumented and underinsured people at risk of HIV acquisition within the city of San Francisco. With a focus on gay and bisexual men, other men who have sex with men, women at risk for HIV, transgender individuals, and people who use drugs, the Ward 86 Prevention Program offers preventative interventions as part of a comprehensive sexual health program. The approval of long-acting injectable PrEP with cabotegravir in 2021 provided a novel treatment strategy to manage HIV risk. The addition of lenacapavir for PrEP in 2025 has increased options further for patients. This protocol describes procedures developed at Ward 86 to use long acting cabotegravir and lenacapavir for HIV PrEP.

Purpose of this document

- Provide guidance to clinicians on patients eligible for long-acting injectable cabotegravir (CAB LA) and lenacapavir (LEN LA).
- Provide guidance to clinicians on initiation and management of patients initiating and continuing CAB LA and LEN LA
- Provide guidance to clinicians on education for patients initiating CAB LA or LEN LA
- Provide guidance to clinicians on discontinuation of CAB LA or LEN LA
- Provide guidance on care coordination for patients on CAB LA or LEN LA

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WARD 86 LONG-ACTING PREP PROTOCOL

The following details Ward 86's protocol on initiating CAB LA OR LEN LA in patients for HIV prevention.

BACKGROUND

Long-acting (LA) cabotegravir (CAB) and lenacapavir (LEN) are injectable prescription medicines to prevent HIV-1 infection in adolescents and adults weighing at least 35 kg (77.2 lbs).

CAB LA consists of an extended-release injectable formulation of cabotegravir, an integrase strand transfer inhibitor (INSTI). CAB LA is administered as an intramuscular (IM) gluteal injection and must be administered by a licensed health care professional. Per a US FDA update, oral lead-in dosing with oral cabotegravir prior to initiating CAB LA injection is optional and has been completely dropped from the Ward 86 guidelines.

Cabotegravir:

CAB LA for HIV pre-exposure prophylaxis (PrEP) has been studied in two major clinical trials: HPTN 083 and HPTN 084, both of which proceeded to open label extension studies.

HPTN 083 was a phase 2b/3 double blind safety and efficacy study of CAB LA compared to daily oral tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) as HIV PrEP for cisgender men and transgender women who have sex with men. Participants were randomized to one of two study arms and included three steps: Step 1 consisted of 5 weeks of daily oral CAB and a TDF/FTC placebo (CAB LA arm) or 5 weeks of daily oral TDF/FTC and an oral CAB placebo (TDF/FTC arm); Step 2 consisted of 148 weeks of intramuscular CAB LA 600 mg every 8 weeks plus daily oral TDF/FTC placebo (CAB- LA arm) or 148 weeks of daily oral TDF/FTC plus an intramuscular CAB LA placebo every 8 weeks (TDF/FTC arm); and Step 3 consisted of an open-label daily oral TDF/FTC for 48 weeks after participants completed Step 2. In May of 2020, HPTN 083 ended the blinded arm of the study early due to successfully meeting its objectives. Data demonstrated that CAB LA administered every 8 weeks was statistically superior to oral TDF/FTC in preventing HIV acquisition. A total of 52 new HIV infections occurred in HPTN 083: 39 new HIV infections in the once daily TDF/FTC arm and 13 HIV new HIV infections in the CAB LA arm, demonstrating that once daily oral TDF/FTC had an HIV acquisition rate 3 times that of injectable CAB.[1]

HPTN 084 (The Life Study) was a phase 3 double blind safety and efficacy study comparing CAB LA to once daily oral TDF/FTC for HIV PrEP in HIV-uninfected cisgender women in sub-Saharan Africa. Participants were randomized into one of two arms and included three steps, which directly mirrored the HPTN 083 study design. In November 2020, HPTN 084 also halted the blinded phase of the trial due to data indicating superior efficacy of CAB LA over oral TDF/FTC. In HPTN 084, a total of 40 new HIV infections were observed among study participants: 36 new HIV infections in the once daily TDF/FTC arm and 4 new HIV infections in the CAB LA arm. This once again demonstrated that CAB LA is superior to oral TDF/FTC at preventing HIV.[2]

In December 2021, based on the findings from HPTN 083 and 084, the FDA approved the use of CAB LA for HIV PrEP.[3]

Lenacapavir

LEN LA for PrEP is an HIV-1 capsid inhibitor and is indicated in at-risk adolescents and adults weighing at least 35 kg for PrEP to reduce the risk of sexually acquired HIV-1 Infection. Individuals must have a negative HIV-1 test prior to initiating LEN LA for PrEP.

Approval of LEN LA for PrEP was based on 2 randomized, double-blind, active-controlled, multinational trials, PURPOSE 1 was performed in cisgender adolescent girls and young women between 16 and 25 years of age in South Africa and Uganda and PURPOSE 2 was in cisgender men, transgender women, transgender men, and gender nonbinary individuals 16 years of age and older.

- In PURPOSE 1, the efficacy endpoint was the rate of incident HIV-1 infections per 100 person-years in participants randomized to LEN LA compared with the rate of incident HIV-1 infections per 100 person-years in participants randomized to tenofovir disoproxil fumarate/emtricitabine (TDF/FTC). LEN LA demonstrated superiority with a 100% reduction in the risk of incident HIV-1 infection over TDF/FTC. In the FDA label, 2 incident HIV infections were subsequently reported in PURPOSE 1; 1 individual who was lost to follow-up and had no LEN resistance; 1 individual who was diagnosed with a viral load <200 copies/mL, with a failed genotype.
- In PURPOSE 2, the efficacy endpoint was the rate of incident HIV-1 infections per 100 person-years in participants randomized to LEN LA compared with the rate of incident HIV-1 infections per 100 person-years in participants randomized to TDF/FTC. LEN LA demonstrated superiority with an 89% reduction in the risk of incident HIV-1 infection over TDF/FTC. There were 3 incident infections total, with 1 occurring after the primary endpoint. The post-primary case did not have viral load data reported, the other two cases had viral loads of 934,000 c/mL and 14,100 c/mL at diagnosis. All 3 individuals had resistance with N74D (2) and Q67H/K70R (1) reported. Per data presented at EACS 2025, annual persistence on lenacapavir was approximately twice that on oral PrEP in the study.

CLINICAL CONSIDERATIONS AND RECOMMENDATIONS FOR STARTING PATIENTS ON LA PREP

GENERAL CONSIDERATIONS AND RECOMMENDATIONS PRIOR TO INITIATING LA PREP

- Patient is at risk of HIV exposure and weighs at least 35kg
- Patient expresses willingness to attend regularly scheduled appointments and complete regularly scheduled laboratory testing
- Patient demonstrates understanding of CAB LA or LEN LA administration and expresses willingness to receive an injection in gluteal muscles or subcutaneously according to schedule

- Patient demonstrates understanding of, and agrees to take, an oral PrEP regimen or alternate long-acting regimen if CAB LA or LEN LA PrEP is interrupted or discontinued
- Patient demonstrates understanding of the potential for integrase or capsid Inhibitor resistance should HIV be acquired while on CAB LA or LEN LA PrEP for HIV PrEP, as residual concentrations may remain in systemic circulation of individuals for a prolonged period following administration (up to 12 months or longer)
- Patient has reliable means of communication (e.g., working phone or other consistent means of communication) and provides additional method(s) of contact (e.g., family member(s), friend(s), or case manager) should direct means of communication fail
- If the patient is within 72 hours of their last exposure, consider initiating PEP with dolutegravir and tenofovir alafenamide/emtricitabine or bictegravir/tenofovir alafenamide/emtricitabine and then transitioning to PrEP (i.e. PEP to PrEP) once HIV testing is negative.

Drug-Drug Interactions:

- The patient's current prescribed and over the counter medications should be reviewed and assessed for potential drug-drug interactions using the Liverpool HIV Drug Interactions database and referring to the FDA package insert
- If planning to initiate cabotegravir, patient is not taking the following medications, which are contraindicated with CAB LA prevention due to potential interactions with cabotegravir:
    - Anticonvulsants: carbamazepine, oxcarbazepine, phenobarbital, phenytoin
    - Antimicrobials: rifampin, rifapentine, rifabutin (*NB: monthly CAB-LA dosing with rifabutin may be considered as per the FDA label)*
    - Herbal: St. John's Wart
- Lenacapavir is a substrate and moderate inhibitor of cytochrome P450 (CYP3A4) and a substrate of P-glycoprotein (P-gp), there is a risk of LEN LA increasing the levels of CYP3A4 substrates and there is a risk of reduced LEN drug concentrations when combined with both moderate and strong CYP3A4 inducers such as carbamazepine, oxcarbazepine, phenobarbital, primidone, phenytoin, and rifamycins.
    - Refer to LEN for PrEP product information for recommended supplemental doses of LEN LA and PO for PrEP when using with rifampin and rifabutin; specifically, administer an additional 927mg subcutaneous injection of LEN with two additional oral loading LEN doses with rifampin (600mg po LEN on day 1 of rifampin and 600mg po LEN on day 2 of rifampin). With rifabutin, add an additional half-dose of the injectable LEN (463.5mg of LEN) on day 1 of rifabutin (both lasting 6 months).
    - There is no interaction with gender affirming hormone therapy or oral contraceptive therapy based on PURPOSE 1 and 2 data reported at ID Week 2025
    - Avoid ketamine while on lenacapavir as lenacapavir may potentiate its effects
    - Consider starting oxycodone at a half dose and monitoring for effects

- Fentanyl levels may be moderately increased, caution patients who use fentanyl recreationally
    - In PURPOSE 2, adherence and safety issues were favorable among people who use drugs in spite of this interaction
- Concentrations of PDE5 inhibitors (i.e. sildenafil) and statins may be increased with lenacapavir: a maximum dose of 25mg of sildenafil or 10mg of tadalafil; and 40mg of atorvastatin has been recommended by the manufacturer
- Drug Interactions may occur for 9 months following injection

Patients who meet overall clinical criteria and are interested in starting CAB or LEN based PrEP should be evaluated by a clinician prior to initiating the injectable PrEP medication and should be screened for the following:

- HIV testing should be performed and resulted no more than 1 week *before* administration of first CAB LA or LEN LA initiation dose. Ward 86 recommends HIV RNA testing on the day LA PrEP is initiated. So, testing includes
    - HIV Ab/Ag within 7 days before 1st dose
      OR
    - POC HIV Ab/Ag with lab HIV Ab/Ag if same day start
      AND
    - HIV RNA testing on the day of initiation
- Signs and/or symptoms of acute HIV infection (ARS) should be evaluated and ruled out with an HIV RNA if appropriate
- For subsequent HIV testing after initiation of the LA LEN or CAB, Ward 86 recommends serum HIV Ag/Ab testing with each administration (with HIV RNA testing only if acute retroviral syndrome symptoms of seroconversion are present)
- Patients with prior hypersensitivity to cabotegravir or lenacapavir should not be initiated on that specific regimen

Initiation Phase Procedures

Any team member may identify a patient who is at risk for HIV, interested in PrEP start/restart or oral or injectable medication, or interested in PrEP follow-up. Interested patient can be directed to drop-in to Ward 81/The Lobby on Mon-Fri from 1-4pm or text the Ward 86 PrEP phone to set up a more specific time at: 415-696-4836

If a patient is seeking primary care and would prefer scheduled visits over a drop-in model, they can be referred to a primary care provider at Ward 86.

Registration

- Register patient: confirm or create patient's ZSFG medical record number and demographics/contact information.

- Confirm patient has active insurance coverage (Medical and/or Health SF).
- For Ward 81 Register the patient for a drop-in visit under “POP-UP” and “LOBBY MEDICAL”
- For Ward 86 schedule patient with social worker for an intake appointment

Clinician Intake (Either RN or Provider)

- Explain/review PrEP options available to patient: oral daily tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC), oral tenofovir alafenamide (TAF)/FTC for nonvaginal sex, 2-1-1 dosing of TDF/FTC if applicable, CAB-LA, and LEN-LA for PrEP
- Order CAB or LEN for PrEP initiation labs and ensure completed by the patient
    - Eventual plan will be for an Order Set to be available that will include:

Labs at Initial Dose
HIV Ab/Ag within 7 days before 1st dose
POC HIV Ab/Ag with lab HIV Ab/Ag if same day start
HIV RNA testing on day of initiation
Comprehensive STI screening (syphilis and 3 site GC/CT testing)
HBsAg, HBsAb, HBcAb (if non-immune and not done in past 12 months); or note, Hepatitis B vaccination when indicated HCV Ab (if not done in past 12 months), Consider CMP
Urine Pregnancy Test (when applicable)

Document Intake using the following dot phrases in EPIC

- Oral PrEP or undecided: .W86PREPINTAKE
- Injectable CAB for PrEP only: .W86CABPREPINTAKE
- Injectable LEN for PrEP: .W86LENPREPINTAKE

Nursing: on day of initiation visit

- Pull medications from medication room
- Review patient's current prescription and non-prescription medication history to determine risk for drug-drug interactions
- Prepare and administer:
    - CAB or LEN LA injection for PrEP
- HAP Clinic: Confirm patient has had at least one face-to-face visit with HAP Provider, and if not, have HAP provider see patient before leaving today
- Ward 86: Confirm patient has had as least one encounter with PCP or that there is a visit scheduled
- Provide patient with 30-day prescription TDF/FTC oral PrEP 'bridge' with 1 refill
- Confirm pt listed on HAP LA PrEP patient list or Ward 86 LA PrEP list as appropriate
- For LEN specifically: Observe patient taking first dose of 2 tablets of lenacapavir 300 mg (total 600mg)
    - Document injection administration and dosing of oral dose on the MAR
    - Document nurse initiation visit using the following dot phrase in EPIC: .W86LENSTART
    - Schedule telephone follow up visit for next day to confirm 2nd dose of 2 tablets of lenacapavir 300 mg are ingested by patient
    - Schedule telephone follow up visit at 3 months
        - Nurse to reach out to patient to confirm current contact information
        - See if patient interested in coming in for routine STI testing
    - Schedule the next 26-week injection visit for LEN LA for PrEP; ideally should receive PCP visit on the same day
- For CAB specifically:
    - Document injection administration on the MAR
    - Document nurse initiation visit using the following dot phrase in EPIC: .W86CABSTART
    - Schedule the next 8-week injection visit for CAB LA for PrEP with STI testing when indicated; ideally should receive PCP visit every 3 injections or every 6 months

ADDITIONAL CLINICAL CONSIDERATIONS AND RECOMMENDATIONS FOR INITIATING CAB-LA PREVENTION

- **Pregnancy:** Based on recent data from the HPTN 084 presented at the 2024 AIDS conference, in which maternal and fetal outcomes were similar when comparing cabotegravir to TDF/FTC across 367 pregnancies, cabotegravir is considered an acceptable alternative to tenofovir disoproxil fumarate/emtricitabine during pregnancy and Ward 86 does not restrict its use in pregnancy

- Pregnancy Exposure Registry: There is a pregnancy exposure registry that monitors pregnancy outcomes in individuals exposed to CAB LA for PrEP during pregnancy. Healthcare providers are encouraged to register individuals by calling the Antiretroviral Pregnancy Registry (APR) at 1-800-258-4263.

- **Lactation:** Cabotegravir concentrations in breast milk are very low, only a small amount transferring from the mother's blood into breast milk, averaging about 1.4% of maternal blood levels. Measuring drug concentrations in infants' blood, the relative infant dose was a median of 5%. Adverse effects in breastfed infants have not been observed.

- Drug-resistant HIV-1 variants have been identified with use of CAB for HIV-1 PrEP by individuals with undiagnosed HIV-1 infection. CAB LA for HIV PrEP should not be initiated until clinical assessment and laboratory confirmation rules out likelihood of frank HIV infection. Individuals who become infected with HIV while on CAB LA therapy should be transitioned to a complete antiretroviral therapy (ART) immediately with a regimen not containing an INSTI until resistance is excluded (e.g., darunavir/cobicistat/tenofovir alafenamide/emtricitabine).

- The time from initiation of CAB LA to adequate serum concentration for protection against HIV infection is unknown. The available evidence based on animal models suggests that 50% of people will achieve protective blood levels 1 day after the first injection, 90% of people 3 days after the first injection, and 95% of people 7 days after the first injection. Clinicians may consider providing patients an oral PrEP regimen during the first 7 days of CAB LA therapy, particularly if they will be exposed to HIV in this period.

ADDITIONAL CLINICAL CONSIDERATIONS AND RECOMMENDATIONS FOR INITIATING LEN-LA THERAPY

- **Pregnancy:** There were 509 pregnancies reported among 487 participants in PURPOSE 1; 193 in the LEN group. There was no drug-related risk for miscarriage, adverse maternal outcomes, or adverse fetal outcomes compared to the comparators of TAF/FTC and TDF/FTC, and the rate of birth defects was similar to the background prevalence. In animal reproduction studies, no adverse developmental effects were observed when lenacapavir was administered to rats and rabbits at exposures (AUC) ≥7 times the exposure in humans at the recommended human dose. Ward 86 does not restrict the use of LEN for PrEP in pregnancy.
    - Pregnancy Exposure Registry: There is a pregnancy exposure registry that monitors pregnancy outcomes in individuals exposed to LEN LA for PrEP during pregnancy. Healthcare providers are encouraged to register individuals by calling the Antiretroviral Pregnancy Registry (APR) at 1-800-258-4263.
- **Lactation:** Lenacapavir is present in human milk and was detected at very low levels in infants breastfed by individuals receiving LEN LA for PrEP (2% of maternal blood concentration in infants). Adverse effects in breastfed infants have not been observed.

- **Injection Site:** The FDA label recommends the abdomen or the thigh as an alternate injection site. However, phase 1 data is available showing similar drug levels with upper arm or gluteal injection so these can be considered alternate sites at Ward 86, although they are not currently recommended on the label.

Mitigating Injection Site Reactions[2]

In PURPOSE 1 (cisgender women), 59% experienced injection site reactions (ISR) vs. 35% in the placebo, with induration lasting a median of 173 days and nodules a median of 350 days; there were 4 discontinuations due to ISRs (0.2%) but most ISRs were mild or moderate severity (69%). In PURPOSE 2 (cisgender men, transgender men and women), 83% experienced an ISR vs. 69% in the placebo group. Induration lasted a median of 151 days and nodules a median of 297 days; there were 26 discontinuations due to ISRs (1.2%); but most ISRs were mild or moderate severity (83%). In both studies, ISRs decreased with subsequent injections.

- Apply ice pack to planned injections sites for 10 minutes
- Administer the injection subcutaneously at 90°
- Continue to apply ice packs post-injection
- Apply topical lidocaine or prilocaine cream to both injection sites 30 minutes prior to injection
- Oral analgesics (acetaminophen, NSAIDs) before or after injection
- To prevent leakage, pause for several seconds after injection is complete prior to withdrawing needle
- Bandage may be applied
- It is recommended not to massage the injection site
- Some leakage is expected, but if there is excessive leakage, consider alternate PrEP option

RECOMMENDATIONS FOR ROUTINE CAB-LA AND LEN-LA DOSING

RECOMMENDED INITIATION AND MAINTENANCE DOSING FOR CABOTEGRAVIR

Cabotegravir:
Initiation and maintenance dosing for CAB-LA are outlined in Table 1 below. Testing at initiation is covered in the prior section.

Testing for maintenance dosing should include the following: antigen/antibody-based HIV testing should be collected at the time of maintenance dosing, but may be pending at the time of administration to avoid gaps in coverage. Based on the analysis of HIV testing data from HPTN 083 from Landovitz et al. at AIDS 2024, HIV viral load testing after the initiation visit is considered optional due to the potential for frequent false positive tests during the cabotegravir maintenance phase. In the case of potential false positive viral load results, we recommend discussing with the clinical lab if re-testing can be performed, and collecting a separate sample to repeat testing, as well as send outs for qualitative HIV

RNA and HIV DNA. We also recommend contacting the SeroPrEP team (seroPrEP.ucsf.edu), for more in-depth investigation. In addition, at follow-up visits (or at least every other visit), we recommend 1-3-site STI testing (per the patient's described sexual practices) and blood-based syphilis testing.

See **Appendix C** for manufacturer's instructions for LEN handling and administration

TABLE 1: RECOMMENDED DOSING SCHEDULE FOR CAB LA IM INJECTIONS

Drug	**Initiation Injection Dosing (Two Doses, Q 4-Weeks Apart)**	**Maintenance Injection Dosing (Q 8-Weeks Maintenance Dosing)**
Cabotegravir	600 mg (3 mL)	600 mg (3 mL)

RECOMMENDED INITIATION AND MAINTENANCE DOSING FOR LENACAPAVIR

Dosing Schedule

Initiation	
Day 1	927 mg 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 subcutaneous injection (2 x 1.5 mL injections) every 26 weeks +/- 2 weeks	

Missed Oral Dose

If Day 2 initiation dose of LEN (600mg) is missed, it should be taken as soon as possible.

See **Appendix C** for manufacturer's instructions for LEN

RECOMMENDATIONS FOR MANAGEMENT OF MISSED CAB-LA AND LEN-LA DOSES

RECOMMENDED RESPONSES TO UNPLANNED MISSED CAB LA DOSES

If a patient misses a scheduled CAB LA dose that is unplanned, a local response, such as an active outreach to the patient, should be initiated immediately. If the patient is not reachable directly, the patient's listed contacts should be contacted. If the patient and their contacts are not reachable, the prescribing medical provider should be alerted and a care plan for the patient's return to care attempted.

To pre-emptively manage a potential interruption in CAB LA therapy, prescribing medical providers should consider prescribing 30 days of oral PrEP with 1 refill to patients starting CAB LA therapy (pill-in-pocket approach).

If a scheduled CAB LA dose (initiation or maintenance dose) is missed or delayed by more than seven days from scheduled dosing, oral PrEP should be initiated where possible. Following an interruption in CAB LA therapy, if a patient wishes to continue injectable CAB LA, the prescribing medical provider should resume CAB LA injections according to Table 2.

TABLE 2: RECOMMENDED MANAGEMENT OF LATE OR MISSED DOSE FOR PERSONS ON CAB LA THERAPY

Time Since Scheduled Dosing	**Recommended Actions**
<=1 month after scheduled injection	• Obtain HIV Ag/Ab testing and HIV viral load testing (rapid resulting prior to injection preferred if possible) • **If HIV test is negative, resume maintenance dosing or CAB LA (600mg doses, Q-8 Weeks apart)**
>1 month after scheduled injection	• Obtain HIV Ag/Ab testing and HIV viral load testing (rapid resulting prior to injection preferred if possible) • **If HIV test is negative, reinitiate initiation injection dosing schedule for CAB LA (Q-4 Weeks apart then resumption of Q-8 week dosing)**

RECOMMENDED MANAGEMENT FOR PLANNED MISSED CAB LA DOSES

If a patient plans to miss a scheduled CAB LA dose by more than seven days, the patient should be provided with an oral PrEP regimen to replace the injection. Patient should be given education on HIV risk and importance of oral adherence, either continuous or episodic (i.e., 2-1-1 oral dosing). Daily oral PrEP should begin on the date of the scheduled CAB-LA dose that is being missed.

Please see Table 2 about instructions for dosing when restarting cabotegravir. In brief, if an injection is more than 4 weeks late, the patient should receive re-loading with two 600mg CAB LA doses administered one month apart.

RECOMMENDED MANAGEMENT FOR PLANNED MISSED LEN LA DOSES

If injection will not be administered within 26-28 weeks of last injection:

LEN 300mg orally every 7 days can be given on a temporary basis for up to 6 months.

LEN LA injection can be resumed within 7 days of the last oral dose.

RECOMMENDED RESPONSES TO UNPLANNED MISSED LEN LA DOSES

If more than 28 weeks have elapsed since last injection, and LEN tablets have not been taken, assess for HIV-1 infection and follow initiation dosing schedule:

Re-Initiation	
Day 1	927 mg 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)

Followed by continuation dosing.

Continuation
927 mg subcutaneous injection (2 x 1.5 mL injections) every 26 weeks +/- 2 weeks

RECOMMENDATIONS REGARDING DISCONTINUATION OF CAB LA OR LEN LA PREP

When CAB or LEN LA PrEP is to be discontinued, the patient should be provided with education about HIV risk factors and provided with oral PrEP while the patient remains at risk of HIV and for at least 2 days after they are no longer at risk. Alternatively, they could be started on alternate injectable PrEP while they remain at risk. In general, providers should err on the side of recommending coverage of the cabotegravir and lenacapavir tail for at least one year, given that patients may be inaccurate in estimating their own future risk of HIV.

- Patients who discontinue CAB LA during the initiation period (i.e., after receiving a single dose of CAB LA) should start oral PrEP 28 days after the last injection dose of CAB LA.
- Patients who discontinue CAB LA during the maintenance period (i.e., after receiving both initiation doses) should start oral PrEP 56 days after the last injection dose of CAB LA.
- Patients who discontinue LEN LA should start oral PrEP 26 weeks after their last injection
    - On the Outpatient Pharmacy Order for LEN LA PrEP please leave LEN active for 9 months after last administration. This will allow drug-drug interaction alerts to be fired while drug is still at levels that have the potential of increasing other medications.
- Laboratory monitoring should continue for at least 12 months after discontinuation with HIV viral load and Ag/Ab testing done quarterly. Given the possibility of false positive HIV RNA tests demonstrated with CAB PrEP, viral load tests within 6 months of cabotegravir exposure, results should be interpreted with caution.

Review the following with the patient:

- After stopping the injections, the medication can still be present in the body for up to 12 months or longer. These levels are not high enough over time to prevent HIV acquisition.
- If the patient is still at risk for acquiring HIV during that time offer oral PrEP or alternate long-acting option for PrEP.
- If the patient does acquire HIV during the 12 months after stopping the injections, there is a risk for drug resistant HIV
- All patients should be educated about nonoccupational post-exposure prophylaxis (nPEP)

CONSIDERATIONS FOR USE OF CAB LA OR LEN LA IN UNHOUSED COMMUNITIES

WPIC/MARIA X. MARTINEZ AND WARD 86 THE LOBBY OPEN ACCESS CLINICS: BACKGROUND

The Whole Person Integrated Care (WPIC)/Maria X. Martinez (MXM) Health Resource Center, Ward 86 The Lobby, and associated satellite clinical sites deliver care and coordinate services for unstably housed individuals in San Francisco who are disproportionately affected by homelessness, substance use, mental illness, and HIV. These programs are committed to eliminating barriers to high-quality health services for patients experiencing homelessness or unstable housing, including HIV prevention and treatment services through a very low-barrier (e.g., no-appointment) clinics

SPECIAL CONSIDERATIONS/ALTERATIONS TO STANDARD PROTOCOL

Eligibility:

- Consideration of HIV exposure risk factor: CAB or LEN LA have not been explicitly studied for persons who inject drugs (PWID), however, many PWID are also at risk of HIV through sexual activity, and it is plausible that CAB or LEN LA would offer some protection against HIV transmission through sharing of injection equipment, as has been shown for daily TDF in one prior study in conjunction with available methadone treatment for opioid use disorder (Choopanya et al. Lancet 2013). While daily TDF/FTC is the preferred HIV prevention option for people who inject drugs who share injection equipment based on the available data, adherence to a daily medication may not be feasible for some PWID, and in this case, CAB or LEN LA should be considered.

Visit schedule:

- In addition to the visits outlined in this protocol, a pre-initiation visit with an MD or NP to discuss CAB or LEN LA benefits, expectations, risks, and alternatives should be considered, either before or on the day of initiation. This should include a discussion of contingency planning in case of missed/late injections, which may be more tailored to patients experiencing homelessness including:
    - Update housing status, locations of residence in the community, patient phone numbers and/or email addresses (if applicable) in the EMR
    - Request phone numbers and/or email addresses of 1-5 community contacts (i.e., case manager(s), navigators, OTP counselors, family, friends, etc.) and document in EMR
    - Confirm with patient whether we may contact these individuals in case attempting to locate them for late injections.
    - Review missed/late injection protocol with the patient

Medication Ordering Specifics:

- No PA is required for MediCal recipients; however, may be required for patients with other forms of insurance.

Special Situations with Missed Doses: Hospitalization/Incarceration

- If a patient is hospitalized or incarcerated when an injection is due:
    - Ask the inpatient or Jail Health team if able to order LA-CAB IM 600mg or LA-LEN 927 mg subcutaneous injection for inpatient administration.
    - If LA-CAB or LA-LEN is unavailable and there are no contraindications, recommend to the inpatient or Jail Health provider that the patient start TDF/FTC 1 tab po daily or TAF/FTC 1 tab po daily until able to follow up with provider

EXAMPLE PROCESS FOR INTERNAL WORKFLOW FOR VARIOUS PATIENT VISIT TYPES

See Appendix A

MANUFACTURER'S INSTUCTIONS FOR CAB/RPV LA ADMINISTRATION

See Appendix B

APPENDIX A: EXAMPLES OF PATIENT VISIT OUTLINES

LA PREP ASSESSMENT AND INITIATION VISIT (TWO SEPARATE VISITS IF RAPID HIV TESTING IS NOT AVAILABLE):

Note: If patient is interested and meets criteria (see "Clinical Considerations and Recommendations for Starting Patients on LAI PrEP" section above), prescribe and obtain CAB or LEN LA prior to initiation visit.

- Patient meets with Registered Nurse or other Health Care Provider to conduct LA PrEP counseling and assessment.
    - Assess for recent potential HIV exposures within <72 hours
        - If patient has HIV exposure, visit will continue as a PEP visit
    - Assess oral PrEP adherence prior to visit if patient is switching from oral to CAB LA
    - If the patient is new to clinical operation, or if they are not already added to the PrEP registry, they will be added at this time. Complete PrEP intake flowsheet.
- Laboratory testing should be completed during this encounter
    - Point of care rapid HIV Ab test (e.g., STAT PAK) should be done if possible
    - Serum HIV Ab/Ag, HIV RNA, CMP, HBsAg, HBsAb, HBcAb (if there is no record of HBV vaccination status), HAV Ab (if no record of Hepatitis A vaccination status), HCV Ab
    - Comprehensive STI screening (syphilis and three site GC/CT testing; trich if appropriate)
- Presumptive STI treatment should be initiated if indicated
- Doxycycline Post-exposure Prophylaxis for STI prevention should be discussed if indicated.
- If rapid HIV test is negative and the patient has not had any potential HIV exposures within the preceding 72 hours, and the patient wishes to proceed with CAB or LEN LA:
    - Convert visit to provider visit (alternatively, schedule RN visit with labs separately and an evaluation and initiation visit with provider within three days of RN visit).
    - Patient will meet with a provider for evaluation, including acute retroviral syndrome (ARS) rule out, discussion of injection site reactions, and procedures that can be done to mitigate them (e.g. taking OTC pain meds, warm/cold compress).
    - In patients who have gluteal fillers interested specifically in CAB, various strategies can be considered:
        - Ultrasound evaluation for location of fillers to see if ventrogluteal administration can still be considered
            - As an alternative: thigh (vastus lateralis) injections have been studied in an ATLAS-2M substudy among people living with HIV and a Phase 1 study. In these studies, absorption was quicker with a small reduction in bioavailability (~10%). Thigh injections may be considered if ventrogluteal injection is not feasible after discussion of risks and benefits with a provider.

        - Consider subcutaneous LEN instead of CAB
    - Following provider evaluation, an initiation dose of CAB LA (600 mg cabotegravir IM) OR LEN LA LEN 927mg subcutaneous injection [2 x 1.5mL injections] AND LEN 600mg orally [2x300mg tablets] is administered).
    - Obtain HIV RNA on day of cabotegravir or lenacapavir initiation.
    - Consider prescribing 30 days + 1 refill of TDF/FTC (or other oral PrEP regimen) as A backup measure should patient miss a future scheduled LA PrEP dose. Counsel patient on importance of injection schedule and transition to oral PrEP if needed.
- Follow-up:
    - CAB: Patient should be scheduled an appointment for second CAB LA initiation dose four weeks (28 days) from administration of first initiation dose.
        - Telephone or in-person appointment with RN/provider should be scheduled within seven days of first CAB LA or LEN LA initiation dose to assess for tolerability and potential side effects.
    - LEN: Patient is provided 600mg of LEN (2 x 300mg tablets) to take on the following day
        - If the patient misses this dose, they should take it as soon as possible
        - Schedule telephone follow up visit for next day to confirm 2nd dose of 2 tablets of lenacapavir 300 mg are taken by patient
        - Schedule telephone follow up visit at 3 months
            - Nurse to reach out to patient to confirm current contact information
            - See if patient interested in coming in for routine STI testing
        - Schedule next injection visit 26 weeks for LEN LA for PrEP
            - Nurse/administrative staff/pharmacy technician to confirm visit with patient 2 weeks prior to injection visit so that LEN LA. After confirmation, medication can be ordered from pharmacy
        -

Prescription and Clinic Administered Medication Orders

Diagnosis Code

On Pre-exposure prophylaxis for HIV
ICD 10 code Z79.899
Diagnosis ID 1840124
Note that you can search by name or ID code 1840124. If you search by ICD-10 code, it brings up a lot of diagnoses.

Pharmacy and Clinic Administered Medication (CAM) Orders for LEN

Eventual plan will be for an Order Set/SmartSet to be available that will include:

Prescriptions for Pharmacy

Lenacapavir (Yeztugo®) 300 mg Tablets

Take 2 tablets (600 mg) by mouth 1 time each day for 2 doses.

Disp # 4 tablets and 0 refills

Lenacapavir (Yeztugo®)) 309 mg/mL soln for injection

Inject 3 mL (927 mg total) under the skin once every 26 weeks. (2 x 1.5 mL subcutaneous injections in the abdomen or thigh)

Disp #3 mL 1 refill

Orders for Clinic Administered Medications (CAM)

Lenacapavir (Yeztugo®) 300 mg tablets

Take 2 tablets (600 mg) by mouth 1 time each day for 2 doses.

☐ Patient supplied medication should be checked

Starting Date should be scheduled in the future as this is one time dose and will expire off the profile

Patient will take the first dose of two tablets in clinic when receiving the injections.

Lenacapavir (Yeztugo®) 309 mg/mL soln for injection

Inject 3 mL (927 mg total) under the skin once every 26 weeks. (2 x 1.5 mL subcutaneous injections in the abdomen or thigh)

☐ Patient supplied medication should be checked

Until Orderset/SmartSet is created, It is recommended that users save the above orders in their Preference List for easy/quick ordering.

CAB LA ASSESSMENT AND INITIATION VISIT:

- Ward 86 does not recommend the oral lead-in dosing for CAB

- Cabotegravir (Apretude®) concentration is 200 mg/mL. Inject 3 ml (600mg total) intramuscularly in the gluteal region

CAB LA SECOND INITIATION VISIT (4-WEEKS FROM FIRST INITIATION DOSE):

- Patient meets with RN or Medical Provider to assess for ARS symptoms, medication tolerability, assess for side effects, review concerns and/or questions, and set up future injection appointments.
- Laboratory testing should be completed during this encounter:
    - Point of care rapid HIV Ab test (e.g., STAT PAK) should be done if possible
    - Serum HIV Ab/Ag
    - Comprehensive STI screening (syphilis and three site GC/CT testing, plus trich if appropriate)
- Presumptive STI treatment should be initiated if indicated
- A follow-up telephone appointment should be scheduled seven days after second initiation injection
- Following evaluation, if rapid HIV test is negative and/or if the patient does not have signs/symptoms of acute HIV, a second initiation dose of CAB LA (600 mg *cabotegravir* IM) is administered

CAB OR LEN LA FIRST MAINTENANCE INJECTION VISIT (Q 8-WEEKS FROM SECOND CAB-LA INITIATION DOSE Q 26-WEEKS FROM LAST LEN INJECTION):

- At first maintenance injection visit, scheduled Q-8 weeks following second initiation dose for cabotegravir, and 26 weeks following the following the LEN initiation dose, the patient is evaluated for acute HIV and a comprehensive STI evaluation is performed.
- Laboratory testing should be completed during this encounter:
    - Point of care rapid HIV Ab test (e.g., STAT PAK) should be done if possible
    - Serum HIV Ab/Ag
    - Comprehensive STI screening (syphilis and three site GC/CT testing, plus trich if appropriate)
- Presumptive STI treatment should be initiated if indicated

Subsequent Maintenance Visits

- **CAB:** At every subsequent CAB LA maintenance injection visit, patient should be screened for HIV and STIs if indicated, but no less than Q 16-weeks (i.e., every other CAB LA injection visit).

- **LEN:** At every subsequent LEN LA maintenance injection visit, the patient should be screened for HIV and STIs. More frequent STI testing should be considered, generally every 3 months for those at risk.

Primary Care Provider visits, and other medical evaluations, can be conducted in parallel to this schedule.

LEN specific Nursing and Pharmacy Protocol:

Pharm Tech/Nursing Two Weeks Prior to Injection Visit Date (at week 24)

- Pharmacy tech or nurse start the process of reaching out to patient to confirm they would like to continue LEN LA for PrEP
- Once verbal/text/MyChart confirmation is received Pharmacy Technician will order LEN LA for PrEP Injection from pharmacy

Nursing on Q26 Week Injection Visits

- RN to pull med form 81 medication room
- Assess patient for symptoms/STIs and partner symptoms and treat as needed
- Order HIV Ab/Ag and other STI screens as noted above
- Prepare and administer LEN LA for PrEP
- Document nurse follow up visit using the following .dot phrase in EPIC: .W86LENSTART
- Schedule nurse telephone follow up visit at 3 months
    - Nurse to reach out to patient to confirm current contact information
    - See if patient interested in coming in for routine STI testing
- Schedule the next 26-week injection visit for LEN LA for PrEP in the LAI PREP INJECTION schedule

Discontinuation Phase Procedures

On the Outpatient Pharmacy Order for LEN LA PrEP for 9 months after last administration. This will allow drug-drug interaction alerts to be fired while drug is still at levels that have the potential of increasing other medications.

If patient decides to stop LEN LA for PrEP, review the following with the patient

- After stopping the injections, the medication can still be present in the body for up to 12 months or longer but at levels that are not enough to prevent HIV acquisition.
- If the patient is still at risk for acquiring HIV during that time offer oral PrEP or CAB LA for PrEP.
- If the patient does acquire HIV during the 12 months after stopping the injections, there is a risk for drug resistant HIV

EPIC STRUCTURE AND MAINTENANCE

- *Patient List Function*
    - All patients who start on CAB or LEN LA are placed on a dedicated *patient list* in Epic. The columns have demographics and upcoming injection appointment. This allows

preemptive work to happen (e.g., have CAB or LEN LA dose delivered prior to scheduled appointment) and allows for panel management work (e.g., reminder calls and follow up if missed appointments). For optimal utility of *patient list*, consider the following:

- Schedule future injection appointment during – or close to completion of – injection appointment.
- Use consistent and specific visit type within the Epic department (e.g., *INTAKE*)
- Modify a column on *patient list* to display next injection appointment (if not enabled, place a service ticket and ask for build of column showing next upcoming appointment patient has with set visit type).
- Assign a care team member to view upcoming appointments in *patient list* and prepare accordingly (order medication delivery, perform reminder calls, etc.)
- *Schedule*
    - Consider creating a generic/resource provider within Epic department for CAB and LEN LA and schedule all injection appointments into this template. This will provide structure for visits and allow care team an overview of upcoming appointments when viewing the daily/weekly/monthly schedule. The overall purpose is broader than the *patient list* function as it groups appointments within the daily appointment interface and allows care team members to see and anticipate appointments and, importantly, notify core team if patients miss appointments for follow up outreach.
- *Clinical Notes*
    - In addition to clinical findings and local charting practices, consider adding a cumulative CAB and LEN LA dosing summary to all clinical notes documenting CAB and LEN LA administrations. A simple summary will allow clinical users to quickly identify patient's CAB and LEN LA history: if each injection appointment is scheduled using a specific visit type, this will be easily identifiable in *Encounters* tab within *Chart Review.* In turn, this will provide a quick summary to clinical team member seeing a patient for CAB or LEN LA administration (this can be particularly helpful for clinical operations that assign multiple team members to medication administration as Epic does not provide a simple overview of cumulative history of clinic administered medications). A cumulative dosing summary could be simple or more detailed (see example tables A and B below). During each visit, clinical care team member administering CAB or LEN LA would copy table from previous note, document administration of CAB or LEN LA administered during visit, and add a row for date of next dose.
- Document injection administration on MAR in Epic
    - Administration records can be viewed on Epic under Chart review -> Misc Reports -> Long Acting Med Administration History

TABLE A: EXAMPLE OF SIMPLE CUMULATIVE CAB OR LEN LA DOSING SUMMARY FOR CLINICAL DOCUMENTATION

CAB Dose	Scheduled	Administered
1st Initiation	7/1/22	7/1/22
2nd Initiation	7/28/22	7/28/22
1st Maintenance	9/22/22	9/22/22
2nd Maintenance	11/17/22	

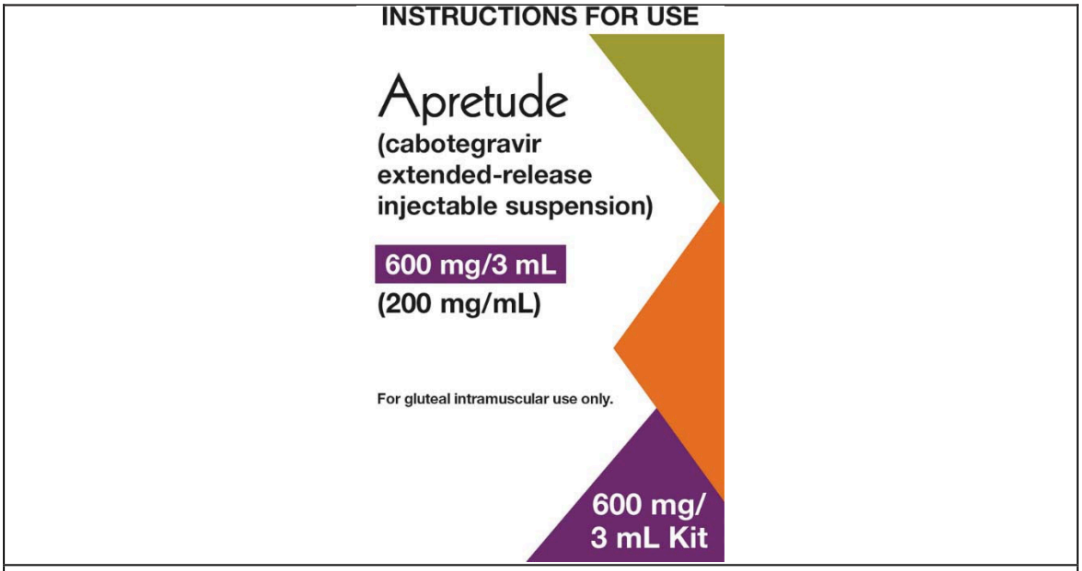
LEN Dose	Scheduled	Administered
Initiation	8/1/25	8/1/25
1st Maintenance	1/30/26	1/30/26
2nd Maintenance	7/31/26	

TABLE B: EXAMPLE OF A DETAILED CUMULATIVE CAB OR LEN LA DOSING SUMMARY FOR CLINICAL DOCUMENTATION

CAB Dose	Scheduled	Administered	HIV Test	RPR	GC/CT	STI treatment
1st Initiation	7/1/22	7/1/22	☑	☑	☑ Rectal ☑ Pharyngeal ☑ Urine	☐ Gonorrhea ☑ Chlamydia ☐ Syphilis
2nd Initiation	7/28/22	7/28/22	☑	☑	☐ Rectal ☐ Pharyngeal ☐ Urine Notes: Declined	☐ Gonorrhea ☐ Chlamydia ☑ Syphilis
1st Maintenance	9/22/22	9/22/22	☑	☑	☑ Rectal ☑ Pharyngeal ☐ Urine	☐ Gonorrhea ☐ Chlamydia ☐ Syphilis
2nd Maintenance	11/17/22		☐	☐	☐ Rectal ☐ Pharyngeal ☐ Urine	☐ Gonorrhea ☐ Chlamydia ☐ Syphilis

LEN Dose	Scheduled	Administered	HIV Test	RPR	GC/CT	STI treatment
Initiation	8/1/25	8/1/25	☑	☑	☑ Rectal ☑ Pharyngeal ☑ Urine	☐ Gonorrhea ☑ Chlamydia ☐ Syphilis
STI Check-in	10/31/25	N/A	N/A	☑	☑ Rectal ☑ Pharyngeal ☑ Urine	☐ Gonorrhea ☑ Chlamydia ☐ Syphilis
1st Maintenance	1/30/26	1/30/26	☑	☑	☐ Rectal ☐ Pharyngeal ☐ Urine Notes: Declined	☐ Gonorrhea ☐ Chlamydia ☑ Syphilis
2nd Maintenance	7/31/26		☑	☑	☑ Rectal ☑ Pharyngeal ☐ Urine	☐ Gonorrhea ☐ Chlamydia ☐ Syphilis

APPENDIX B: STORAGE, HANDLING AND ADMINISTRATION (MANUFACTURER INSTRUCTIONS FOR CAB-LA)



Overview:

A complete dose of APRETUDE requires 1 injection: 600 mg (3 mL) of cabotegravir.

APRETUDE is a suspension that does not need further dilution or reconstitution.

APRETUDE is for gluteal intramuscular use only.

Note: The ventrogluteal site is recommended.

Storage information

Store at 2°C to 25°C (36°F to 77°F). Exposure up to 30°C (86°F) permitted.

Do not freeze.

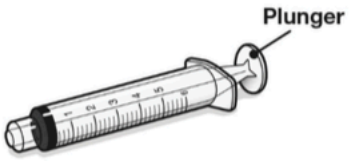
Prior to administration:

- If the pack has been stored in the refrigerator, the vial should be brought to room temperature prior to administration (not to exceed 30°C [86°F]).
- Once APRETUDE has been drawn into the syringe, the medication can remain in the syringe for up to 2 hours before injecting. The filled syringes should not be placed in the refrigerator. If the medicine remains in the syringe for more than 2 hours, the filled syringe and needle must be discarded.

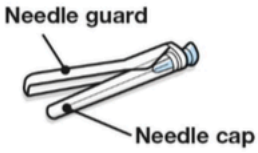
APRETUDE vial

Vial adapter

Syringe



Injection needle



Your pack contains:

- 1 vial of APRETUDE
- 1 vial adapter
- 1 syringe
- 1 injection needle (23 gauge, 1½ inch)

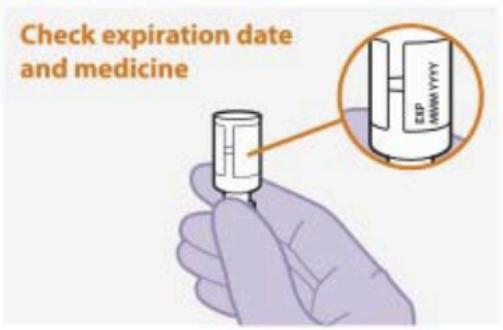
Consider the individual's build and use medical judgment to select an appropriate injection needle length.

You will also need:

- Non-sterile gloves
- 2 alcohol wipes
- 2 gauze pads
- A suitable sharps container

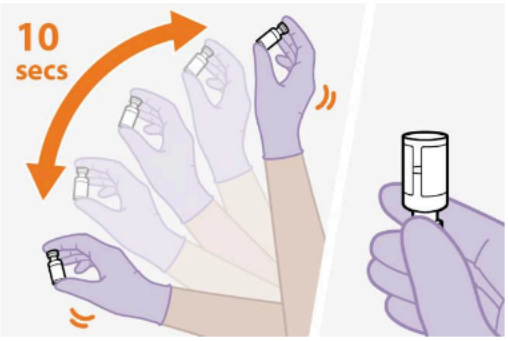
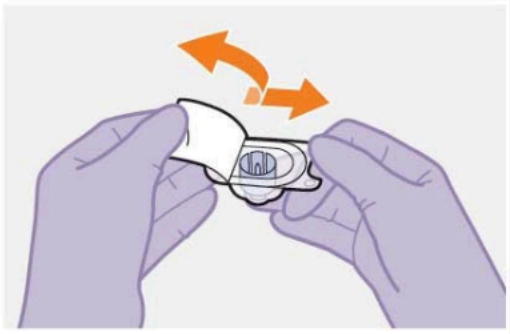
Preparation:

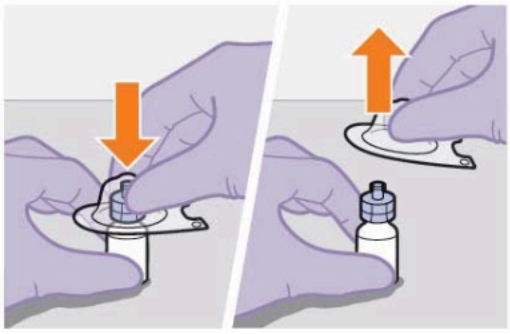
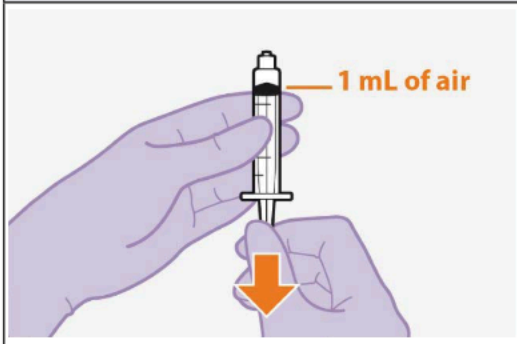
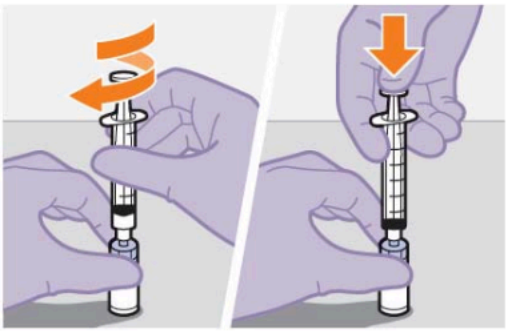
1. Inspect the vial.

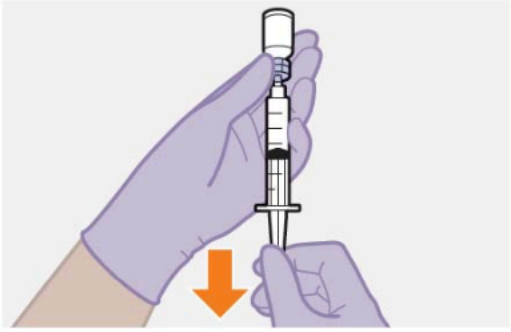
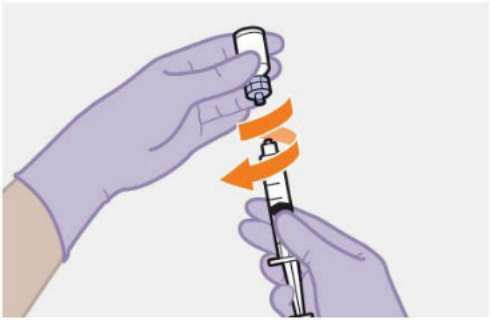
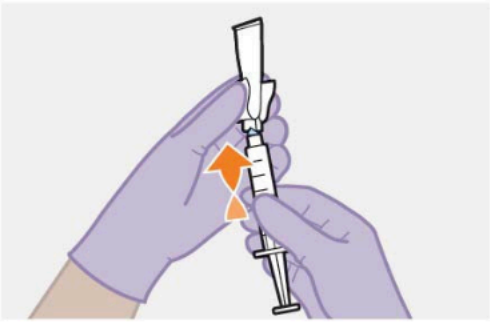


- Check that the expiration date has not passed. **See Figure A.**
- Inspect the vial immediately. If you can see foreign matter, do not use the product.

Note: The vial has a brown tint to the glass.
Do not use if the expiration date has passed.

Figure A	• If the pack has been stored in the refrigerator, allow the medication to come to room temperature.
2. Shake the vial vigorously.	
 **Figure B**	• Hold the vial firmly, and vigorously shake for a full 10 seconds. **See Figure B.** • Invert the vial and confirm the suspension is uniform. It should look uniform. • If the suspension is not uniform, shake the vial again. • It is also normal to see small air bubbles.
3. Remove the vial cap.	
 **Figure C**	• Remove the cap from the vial. **See Figure C.** • Wipe the rubber stopper with an alcohol wipe. **Do not** allow anything to touch the rubber stopper after wiping it.
4. Peel open the vial adapter.	
 **Figure D**	• Peel off the paper backing from the vial adapter packaging. **See Figure D.** **Note:** Keep the adapter in place in its packaging for the next step.

5. Attach the vial adapter.	
 **Figure E**	• Press the vial adapter straight down onto the vial using the packaging, as shown. The vial adapter should snap securely into place. • When you are ready, lift off the vial adapter packaging as shown. **See Figure E.**
6. Prepare the syringe.	
 **Figure F**	• Remove the syringe from its packaging. • Draw 1 mL of air into the syringe. This will make it easier to draw up the medicine later. **See Figure F.**
7. Attach the syringe.	
 **Figure G**	• Hold the vial adapter and vial firmly, as shown. • Screw the syringe firmly onto the vial adapter. • Press the plunger all the way down to push the air into the vial. **See Figure G.**

8. Slowly draw up the dose.	
 **Figure H**	• Invert the syringe and vial and slowly withdraw as much of the medicine as possible into the syringe. There may be more medicine than the dose amount. **See Figure H.**
9. Unscrew the syringe.	
 **Figure I**	• Unscrew the syringe from the vial adapter, holding the vial adapter as shown. **See Figure I.** **Note:** Keep the syringe upright to avoid leakage. Check that the suspension looks uniform and milky white.
10. Attach the needle and affix syringe label.	
 **Figure J**	• Peel open the needle packaging part way to expose the needle base. • Keeping the syringe upright, firmly twist the syringe onto the needle. • Remove the needle packaging from the needle. **See Figure J.**

Injection:

11. Prepare the injection site.

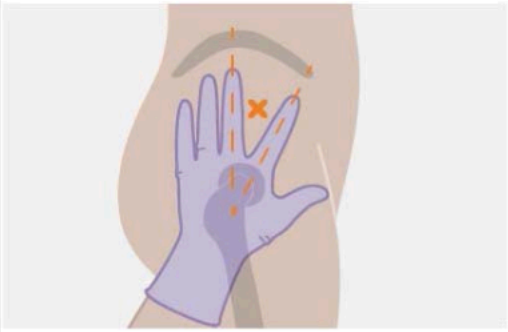


Figure K

APRETUDE must be administered to a gluteal site. **See Figure K.**

Select from the following areas for the injection:

- Ventrogluteal, as shown (recommended)
- Dorsogluteal, not shown (upper outer quadrant)

Note: For gluteal intramuscular use only. **Do not** inject intravenously.

12. Remove the cap.

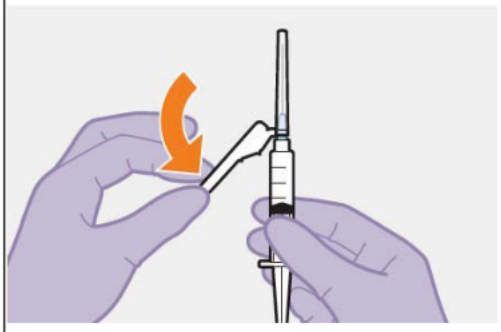


Figure L

- Fold the needle guard away from the needle. **See Figure L.**
- Pull off the injection needle cap.

13. Remove extra liquid from the syringe.

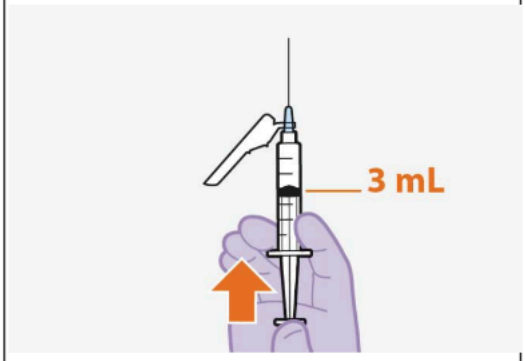
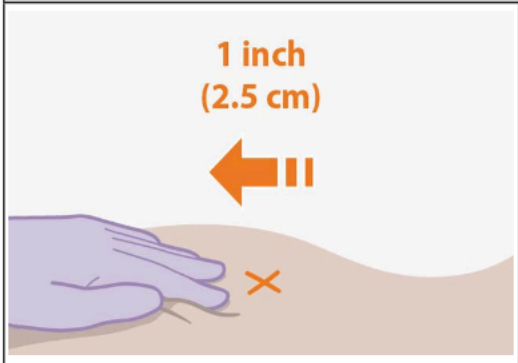
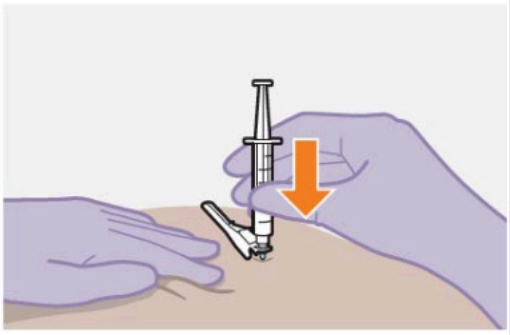
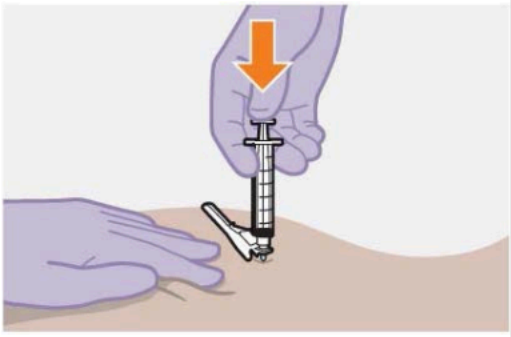


Figure M

- Hold the syringe with the needle pointing up. Press the plunger to the 3-mL dosing mark to remove extra liquid and any air bubbles. **See Figure M.**

Note: Clean the injection site with an alcohol wipe. Allow the skin to air dry before continuing.

14. Stretch the skin.	
 **Figure N**	Use the z-track injection technique to minimize medicine leakage from the injection site. • Firmly drag the skin covering the injection site, displacing it by about an inch (2.5 cm). **See Figure N.** • Keep it held in this position for the injection.
15. Insert the needle.	
 **Figure O**	• Insert the needle to its full depth, or deep enough to reach the muscle. **See Figure O.**
16. Inject the dose of medicine.	
 **Figure P**	• Still holding the skin stretched – slowly press the plunger all the way down. **See Figure P.** • Ensure the syringe is empty. • Withdraw the needle and release the stretched skin immediately.

17. Assess the injection site.

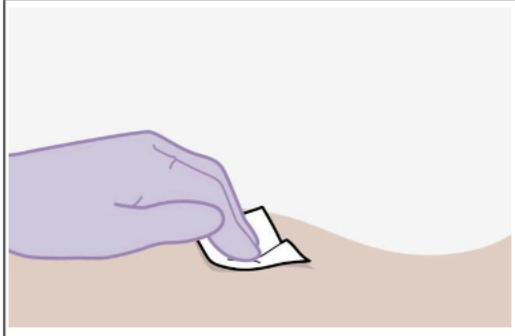


Figure Q

- Apply pressure to the injection site using a gauze pad. **See Figure Q.**
- A small bandage may be used if bleeding occurs.

Do not massage the area.

18. Make the needle safe.

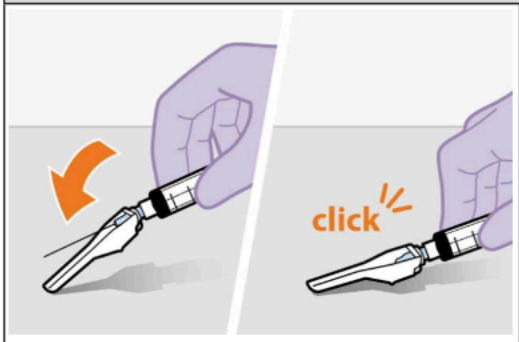


Figure R

- Fold the needle guard over the needle.
- Gently apply pressure using a hard surface to lock the needle guard in place.
- The needle guard will make a click when it locks. **See Figure R.**

After injection:

19. Dispose safely.

Figure S

- Dispose of used needle, syringe, vial, and vial adapter according to local health and safety laws. **See Figure S.**

Questions and Answers

1. **If the pack has been stored in the refrigerator, is it safe to warm the vial up to room temperature more quickly?**
   The vial should be brought to room temperature before you are ready to give the injection, but make sure the vial does not get above 30°C (86°F).
   Do not use any heating methods, other than using the warmth of your hands.
2. **How long can APRETUDE be left in the syringe?**
   It is best to inject (room temperature) APRETUDE as soon as possible after drawing it up. However, APRETUDE can remain in the syringe for up to 2 hours before injecting.
   If the medicine remains in the syringe for more than 2 hours, the filled syringe and needle must be discarded.
3. **Why do I need to inject air into the vial?**
   Injecting 1 mL of air into the vial makes it easier to draw up the medicine into the syringe. Without the air, some liquid may flow back into the vial unintentionally, leaving less medicine than intended in the syringe.
4. **Why is the ventrogluteal administration approach recommended?**
   The ventrogluteal approach into the gluteus medius muscle is recommended because it is located away from major nerves and blood vessels. A dorsogluteal approach into the gluteus maximus muscle is acceptable, if preferred by the healthcare professional. The injection should not be administered in any other site.

Manufactured for:
ViiV Healthcare
ViiV Healthcare
Research Triangle Park, NC 27709

by:
GlaxoSmithKline
Research Triangle Park, NC 27709

APR:xIFU

This Instructions for Use has been approved by the U.S. Food and Drug Administration. Issued: 12/2021

APPENDIX C: STORAGE, HANDLING AND ADMINISTRATION (MANUFACTURER INSTRUCTIONS FOR LEN LA)

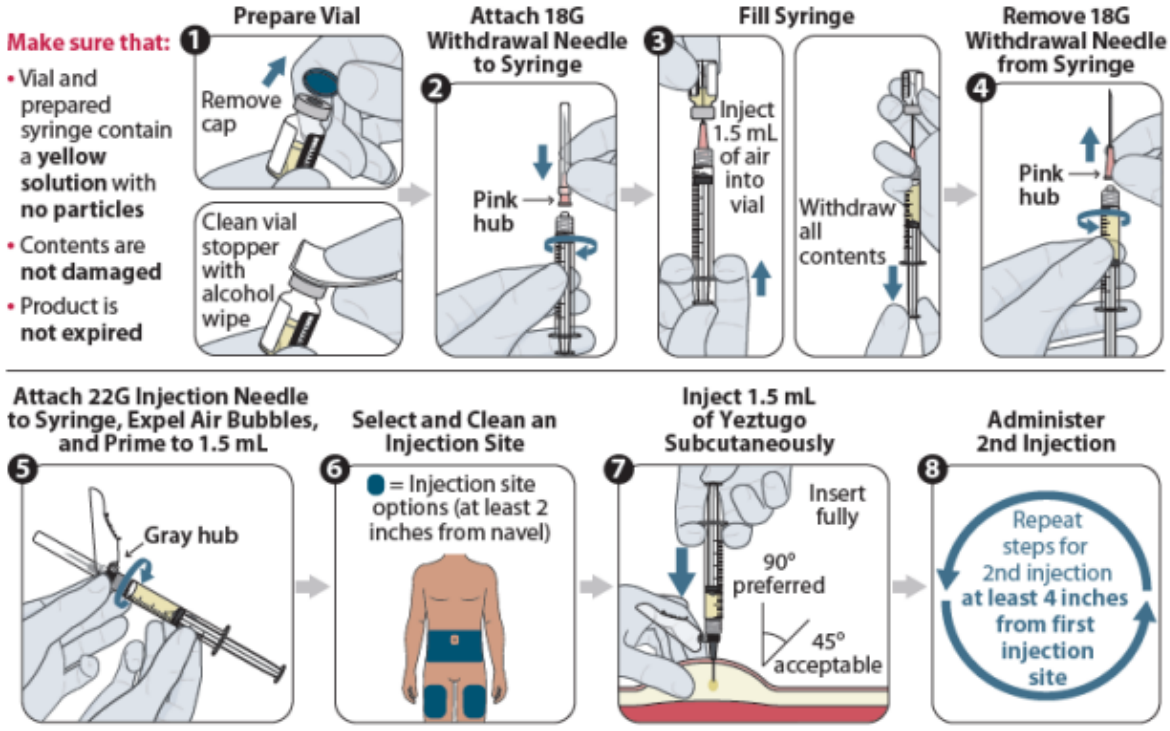
Lenacapavir Administration

LEN LA for PrEP should only be administered into the abdomen by a healthcare provider; the thigh can be used as an alternative injection site (one injection in the right thigh, the other in the left).

Figure 1 YEZTUGO Withdrawal Needle Injection Kit Components

NOTE: all components are for single use.

Figure 2 YEZTUGO Injection Steps for Withdrawal Needle Injection Kit



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