WARD 86 LONG-ACTING INJECTABLE ANTIRETROVIRAL GUIDELINES

PURPOSE OF THIS GUIDELINE

- Provide guidance to clinicians on long-acting injectable cabotegravir/rilpivirine (CAB/RPV LA) for their patients
- Establish a workflow for referral, initiation, and management of patients starting CAB/RPV LA
- Provide guidance to clinicians on education to patients who will receive CAB/RPV LA
- Provide guidance on care coordination, including clinic appointments and follow ups, for patients on CAB/RPV LA

BACKGROUND

CAB/RPV LA is an injectable prescription medicine to treat HIV-1 infection in adults. CAB/RPV LA contains two different medications: *cabotegravir*, an integrase strand transfer inhibitor (INSTI) and *rilpivirine*, a non-nucleoside reverse transcriptase inhibitor (NNRTI). CAB/RPV LA is administered as intramuscular (IM) gluteal injection only and must be administered by a licensed health care professional. On March 24, 2022, the FDA changed the CAB/RPV LA injection, labeling to take out the need for oral lead-in dosing with cabotegravir 30mg daily and rilpivirine 25mg daily.

Direct to inject (no oral lead-in), regardless of viral load, is preferred at Ward 86. This decision (consistent with FDA relabeling guidelines on March 24, 2022) is based on data from the FLAIR study, in which participants in the ABC/3TC/DTG arm were allowed to choose direct to inject at 100 weeks; 110/111 (99%) maintained suppression at Week 24, compared to 113/121 (93%) in the oral lead-in arm. The FLAIR study also found no difference in initial plasma CAB/RPV LA concentrations following first injections as direct-to-inject and after the oral lead-in dosing. There was no difference in tolerability.

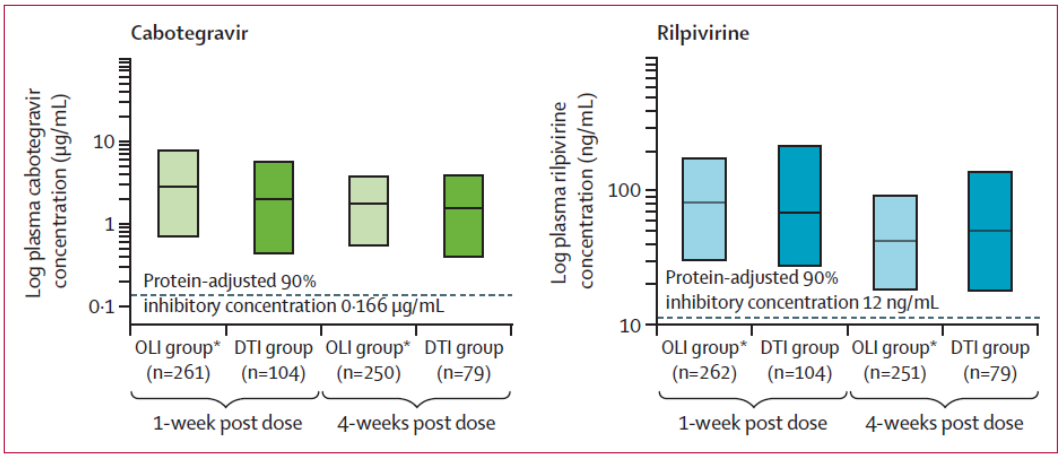


Figure 2: **Initial plasma cabotegravir and rilpivirine concentrations following first injections as DTI and after OLI**

Data are median (5th and 95th percentiles). DTI=direct-to-injection. OLI=oral lead-in. *Historical data: participants who were randomly assigned to receive long-acting cabotegravir plus rilpivirine in the maintenance phase.

WARD 86 CAB/RPV LONG-ACTING PROTOCOLS

The following are Ward 86 recommendations for clinicians initiating CAB/RPV LA in patients with HIV infection. Ward 86 recommends starting all adult patients on an every 4-week (Q 4-week) injection dosing schedule (prior to going to an every 8 week schedule if desired). Further, Ward 86 recommends a minimum of 3-6 months continuous history of Q 4-weeks injection dosing prior to considering a switch to an every 8-week (Q 8-week) injection dosing schedule.

Clinical Considerations and Recommendations for Starting Patients on CAB/RPV LA Therapy:

Clinical Considerations and Recommendations for Initiating a Q 4-Weeks CAB/RPV LA Therapy in Adults

- Patient expresses willingness and demonstrates ability to attend regularly scheduled appointments every four weeks at first to receive CAB/RPV LA injections.
- Patient demonstrates understanding of CAB/RPV LA administration and expresses willingness to receive two injections in gluteal muscles according to schedule.
- Patient understands and agrees to take a fully suppressive oral antiretroviral regimen if CAB/RPV LA therapy is interrupted.
- Patient has a reliable phone number(s), and/or other consistent means of communication, and provides additional method of contact, such as family member(s), friend(s), or case manager.
- While patients with CrCl <30mL/min should not be excluded from CAB/RPV LA therapy consideration, patients with CrCl <30mL/min should be monitored closely for adverse effects after initiation of CAB/RPV LA therapy.
- While HIV viral suppression prior to CAB/RPV LA therapy initiation is preferred, patients who have detectable HIV viral loads should not be excluded from CAB/RPV LA therapy considerations. CAB/RPV LA therapy should be considered for patients who are unable to achieve HIV viral suppression on oral therapy due to adherence challenges.
- Patients who have chronic hepatitis B (HBV) infection should not be considered for CAB/RPV LA therapy except in select cases where patients who have a detectable HIV viral load and HBV co-infection are unable to attain HIV viral suppression due to adherence challenges to oral antiretroviral therapy (ART). For these patients, however, additional HBV treatment will be required. Provider should ensure current Hepatitis B status is updated by sending HepBsAb, HepBsAg, HepBcAb within the last 6 months if not performed.
- Patients who have a history of known or suspected drug resistance that would compromise CAB/RPV LA therapy should not be considered for CAB/RPV LA therapy. Patients with virus with any NNRTI mutations or INSTI mutations that could compromise either RPV or CAB in past genotypes should not be started on the long-acting regimen.
    - *Rilpivirine*: L100I; K101E; V106I and A; V108I; E138K and A, G, Q, R; V179F and I; Y181C and I; V189I; G190E; H221Y and H/L; F227C; M230I and L; K103N+K238T, K103N+E138G+K238T; Y188L
    - *Cabotegravir*: Q146L; S153Y; I162M; T124A; Q148H, K; C56S; V72I; L74M; V75A; T122N; E138K; G140S; G149A; M154I; N155H
- Patients who have a known hypersensitivity to *cabotegravir* or *rilpivirine* should not be considered for CAB/RPV LA therapy.
- Patients who are currently taking the following medications should not be considered for CAB/RPV LA therapy due to potential for decreased drug levels of *cabotegravir* or *rilpivirine*:
    - Anticonvulsants: *carbamazepine, oxcarbazepine, phenobarbital, phenytoin*

- Antimycobacterials: *rifabutin, rifampin, rifapentine*
- Systemic glucocorticoids: more than short-term use of *dexamethasone*
- Herbal: *St John's Wort*

Additional Clinical Considerations and Recommendations for Initiating a Q 8-Weeks CAB/RPV LA Therapy in Adults

Patients who are on Q 4-Weeks CAB/RPV LA Therapy, have demonstrated a 3-6 month history of consistent on-time dosing, and who have achieved HIV viral suppression, can be considered for a switch to a Q 8-week CAB/RPV LA dosing schedule. However, clinical consideration of the following is recommended prior to switching patients from Q 4-week to Q 8-Weeks CAB/RPV LA dosing schedules:

Three risk factors for rare *cabotegravir/rilpivirine* failure were identified in clinical trials (FLAIR, ATLAS and ATLAS 2M): HIV-1 A1/A6 strains; two proviral (on archive testing) rilpivirine resistance associated mutations; and BMI >30 kg/m^2. Lower *cabotegravir* levels in patients with BMI >30 kg/m^2 can be overcome by using a 2-inch administration needle to inject the medication. Finally, given recent data from CROI 2023 that showed low cabotegravir and rilpivirine concentrations when LA ART was used initially in patients with high BMI without the oral lead-in, we also recommend using an oral ART regimen overlapping with the LA CAB/RPV for the first two weeks in patients with BMI >30 kg/m^2

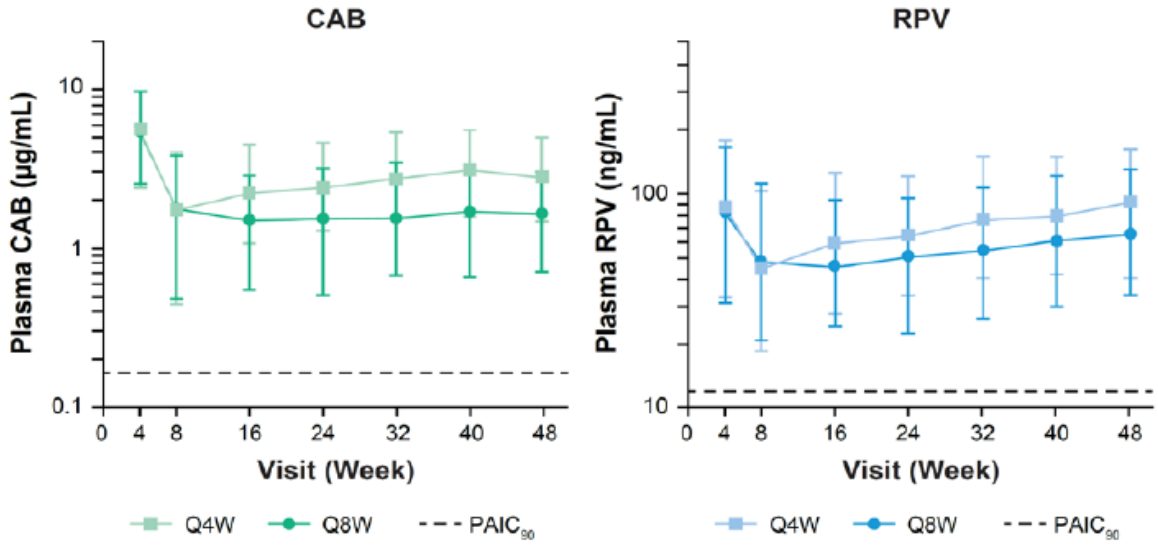
Rationale for Recommending a Demonstration of Success on Q-4-Weeks CAB/RPV LA Dosing Schedule Prior to Considering a Switch to Q 8-Weeks CAB/RPV LA Dosing Schedule:

ATLAS 2M included those who had 52 weeks on oral SOC, 52 weeks on Q 4-weeks injections, and newly recruited patients on stable ART ≥6 months and VS ≥12 months. In the first 48 weeks of ATLAS 2M, there were 8 confirmed virologic failures in the Q 8-weeks arm and 2 in the Q 4-weeks arm. Notably,

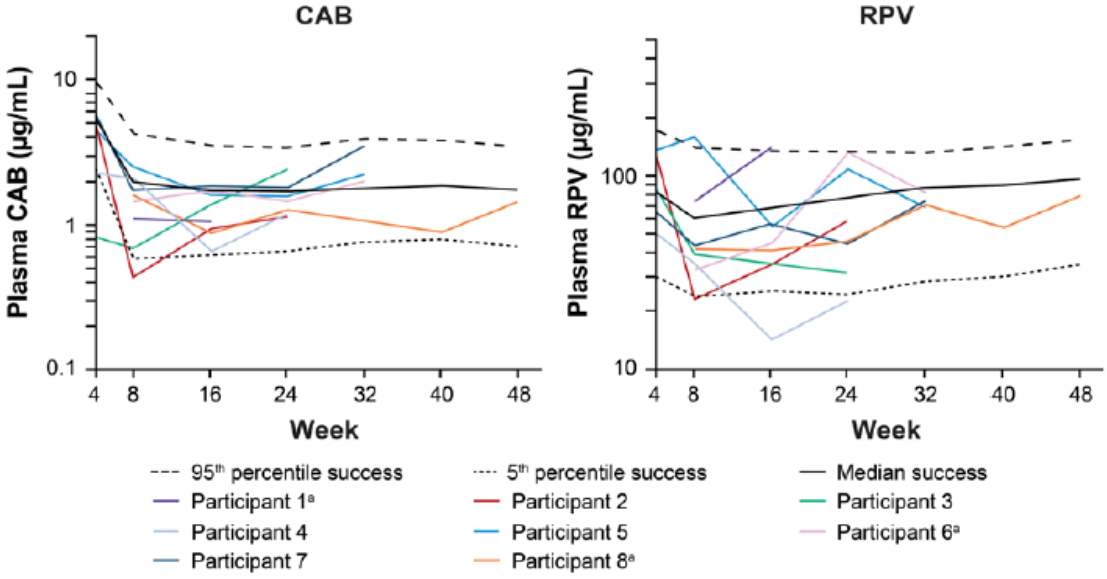
- 7/8 in the Q 8-weeks arm had CVF in the first 24 weeks
- 5/8 had *rilpivirine* RAMs at baseline
- 7/10 had no prior *cabotegravir* or *rilpivirine* exposure and the other 3 (all in the Q 8-weeks arm) with exposure from ATLAS had cumulative exposures of 16, 33, and 61 weeks

Median troughs in those without prior CAB/RIL exposure, though above the necessary concentration, are lower in Q 8-weeks dosing compared to Q 4-weeks dosing.

Figure S4. Median (5th and 95th percentile) evaluable trough plasma concentration–time profiles for participants with no prior exposure to CAB+RPV (following 4-week oral lead-in period)



Moreover, the 8 participants in the Q 8-weeks arm with confirmed virologic failures had troughs at 8-24 weeks that tended to be below the median level for success.



Given these data, Ward 86 favors a conservative approach and recommends starting all adult patients who meet clinical criteria for CAB/RPV LA therapy on a Q 4-week CAB/RPV LA dosing schedule. Clinical recommendations prior to considering a switch to Q 8-week CAB/RPV LA dosing schedule, include (a) demonstrated 3-6 month history of consistent on-time Q 4-week CAB/RPV LA dosing, and (b) sustained HIV viral suppression.

Injection Dosing Recommendations:

Table 1: Recommended Q 4-Weeks CAB/RPV LA IM Injection Dosing Schedule in Adults

Drug	**Initiation Injection Dosing (Q 4-Weeks Initiation Dosing)**	**Maintenance Injection Dosing (Q 4-Weeks Maintenance Dosing)**
Cabotegravir	600 mg (3 mL)	400 mg (2 mL)
Rilpivirine	900 mg (3 mL)	600 mg (2 mL)

*Table 2: Dosing Recommendation When Switching from Q 4-Weeks to Q 8-Weeks CAB/RPV LA IM Injection Dosing Schedule in Adults (recommended after 3-6 months continuous history of Q 4-weeks dosing)**

Drug	**Initial Injection Dosing at Switch to Q 8-Weeks Dosing (Q 8-Weeks Initiation Dosing)**	**Maintenance Injection Dosing (Q 8-Weeks Maintenance Dosing)**
Cabotegravir	600 mg (3 mL)	600 mg (3 mL)
Rilpivirine	900 mg (3 mL)	900 mg (3 mL)

* While not recommended by Ward 86 nor advised by the FDA any longer, oral lead-in for cabotegravir and rilpivirine can be considered at the following doses for a Q-8 week schedule

Drug	Oral Lead-in (Up to 30 Days)	Initial and Maintenance Injection Dosing (At Week 4, Week 8, and Then Q 8-Weeks Onwards)
Cabotegravir	30 mg once daily with a meal	600 mg (3 mL)
Rilpivirine	25 mg once daily with a meal	900 mg (3 mL)

Recommended Response to Missed CAB/RPV LA Doses:

Recommended Responses to Unplanned Missed CAB/RPV LA Doses
If a patient misses a scheduled CAB/RPV LA dose, a local response, such as an active outreach to patient, should be initiated immediately. If patient is not reachable directly, patient's listed contacts should be contacted. If patient and contacts are not reachable, prescribing medical provider should be alerted and a care plan for patient's return to care is recommended.

If CAB/RPV LA Q 4-weeks injection is missed or delayed by more than seven days from scheduled dosing, and oral therapy has not been taken in the interim, prescribing medical provider should clinically reassess the patient to determine if resumption of CAB/RPV LA injection dosing remains appropriate. The patient should be started on a fully suppressive oral antiretroviral regimen as soon as possible.

Table 3: Recommended Response to Late or Missed Doses for Adults on Q 4-Weeks CAB/RPV LA IM Injection Dosing Schedule

Time Since Scheduled Dosing	**Recommended Actions**
8-9 days after scheduled injection	• **Administer Q 4-Weeks Maintenance CAB/RPV LA dose (400mg/600mg) IM**

	• Obtain HIV VL (rapid resulting preferred)
10-14 days after scheduled injection	• **Administer Q 4-Weeks Maintenance CAB/RPV LA dose (400mg/600mg) IM** • Obtain HIV VL (rapid resulting preferred) and HIV genotype • Schedule patient to return to clinic/practice next day ▪ If HIV VL is detectable, start patient on DRV/c/FTC/TAF until genotype results become available
15-30 days or longer after scheduled injection	• **Administer Q 4-Weeks Initiation CAB/RPV LA dose (600mg/900mg) IM** • Obtain HIV VL (rapid resulting preferred) and HIV genotype • Schedule patient to return to clinic/practice next day ▪ If HIV VL is detectable, start patient on DRV/c/FTC/TAF until genotype results become available

Table 4: Recommended Response to Late or Missed Doses for Adults Who are Transitioning from Q 4-Weeks to Q 8-Weeks CAB/RPV LA IM Injection Dosing Schedule

Note: The following recommendation applies when a patient misses first or second scheduled Q 8-weeks doses.	
Time Since Scheduled Dosing	**Recommended Actions**
8-14 days after scheduled injection	• **Administer Q 8-Weeks Initiation CAB/RPV LA dose (600mg/900mg) IM** • Obtain HIV VL (rapid resulting preferred) • Continue to follow Q 8-weeks injection dosing schedule (*see* Table 2)

15-30 days after scheduled injection	• **Administer Q 8-Weeks Initiation CAB/RPV LA dose (600mg/900mg) IM**
	• Obtain HIV VL (rapid resulting preferred) and HIV genotype
	• Schedule patient to return to clinic/practice next day
	  ▪ If HIV VL is detectable, start patient on DRV/c/FTC/TAF until genotype results become available
	  ▪ If HIV VL is undetectable, administer Q-8 Weeks Initiation CAB/RPV LA dose (600mg/900mg) IM 4 weeks later and continue to follow Q 8-week injection dosing schedule (*see* Table 2)

Table 5: Recommended Response to Late or Missed Doses for Adults on Q 8-Weeks CAB/RPV LA IM Injection Dosing Schedule

Note: The following recommendations applies when a patient misses third, or subsequent, scheduled Q 8-weeks doses.	
Time Since Scheduled Dosing	**Recommended Actions**
8-42 days after scheduled injection*	• **Administer Q 8-Weeks Initiation CAB/RPV LA dose (600mg/900mg) IM** • Obtain HIV VL (rapid resulting preferred) • Continue to follow Q 8-weeks injection dosing schedule (*see* Table 2)
43 days or later after scheduled injection°	• **Administer Q 8-Weeks Initiation CAB/RPV LA dose (600mg/900mg) IM** • Obtain HIV VL (rapid resulting preferred) ▪ If HIV VL is undetectable, administer Q-8 Weeks Initiation CAB/RPV LA dose (600mg/900mg) IM 4 weeks later and continue to follow Q 8-week injection dosing schedule (*see* Table 2)

*Modelling data of missed cabotegravir and rilpivirine injections suggests that an interval of 60 days is sufficient. However, to be conservative, Ward 86 allows an interval that is shorter by 42 days

Recommended Responses to Panned Missed CAB/RPV LA Doses

If a patient plans to miss a scheduled CAB/RPV LA dose by more than seven days, the patient should be given a fully suppressive oral antiretroviral regimen to replace injection. The following recommendations should be considered:

1. The first dose of a fully suppressive oral antiretroviral regimen should be taken 28 days after patient's last injection dose of CAB/RPV LA. Oral antiretroviral regimen should be continued until the patient resumes scheduled CAB/RPV LA dosing.
2. Follow recommended actions in Tables 3-5 above for resuming treatment with CAB/RPV LA.
3. If patient is taking oral *cabotegravir* and *rilpivirine* as bridge therapy and on Q 4-Weeks CAB/RPV LA IM Injection Dosing Schedule, they can receive Q 4-Weeks Maintenance CAB/RPV LA dose (400mg/600mg) if CAB/RPV LA treatment interruption has been less than or equal to 8 weeks.

Recommendations Regarding Discontinuation of CAB/RPV LA Therapy

When CAB/RPV LA therapy is to be discontinued, the patient should be transitioned to a fully suppressive oral antiretroviral regimen. Oral regimen should be initiated 28 days after patient's last injection dose of CAB/RPV LA.

Example of Patient Education Package:

See Appendix A

Example Process for Internal Referral Workflow, CAB/RPV LA Therapy Initiation, CAB/RPV LA Storage and Handling at Ward 86 (which has the EPIC medical record system):

See Appendix B

Appendix A:
Example of Patient Education Package

WARD 86
DIVISION OF HIV, INFECTIOUS DISEASES AND GLOBAL MEDICINE
UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
ZUCKERBERG SAN FRANCISCO GENERAL

CABENUVA
INFORMATION GUIDE

WHAT IS CABENUVA?

Cabenuva is an injectable prescription medication to treat HIV infection in adults. Cabenuva contains two different medications: Cabotegravir and Rilpivirine.

Cabenuva is given as two injections into the muscle, one on each side of your buttocks, once a month.

WHAT SHOULD YOU KNOW BEFORE STARTING CABENUVA?

- Cabenuva injections will be given in clinic every month
- You ***may*** be given starter pills before beginning injections so you and your provider can see how your body responds to the two medications in Cabenuva
- It is important to attend your planned appointments to receive your Cabenuva injections
- **If you miss or plan to miss a scheduled monthly injection of Cabenuva, call Ward 86 right away to discuss your options**
- Your contact information must be updated and two alternative contacts will need to be provided in the event that your provider is unable to reach you
- If you stop treatment with Cabenuva, you will need to take other medicines to treat your HIV to reduce the risk of developing viral resistance

COMMON SIDE EFFECTS

Cabenuva is generally well-tolerated. The most common side effects include:

- Injection site reactions
- Flu-like symptoms
- Fatigue
- Muscle pain
- Headache
- Nausea

Pain at the injection site can be relieved by using a hot/cold pack, going for a walk, avoid sitting for prolonged periods on injection day, and taking an OTC pain relievers.
Contact us if you develop rash, warm, or painful swelling.

WHO SHOULD NOT RECEIVE CABENUVA?

Do not receive Cabenuva if you are taking any of the following medications: carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifampin, rifapentine, dexamethasone (more than a single-dose treatment), St. John's wort (*Hypericum perforatum*)

QUESTIONS?
CALL: (628)206-2414 | (628)206-2421
TEXT: (415)361-8577

Appendix B:
Example Process for Internal Referral Workflow, CAB/RPV LA Therapy Initiation, and CAB/RPV LA Storage and Handling

Internal Referral Workflow and CAB/RPV LA Therapy Initiation

- Referral is placed to Ward 86 Pharmacy staff via email, staff message, or electronic health record (Epic) documentation (telephone encounter)
- Standardized questionnaire, including specific questions about current and past HIV antiretroviral regimen(s), HIV resistance history, and patient's HBV status, is sent to referring medical provider to complete
- Once standard questionnaire is completed by referring medical provider, Clinical Pharmacist reviews clinical criteria with CAB/RPV LA Therapy clinical committee, including HIV treatment and resistance history.
- Outcome of referral is documented in Epic
  - If patient does not meet clinical criteria, referring medical provider is notified of outcome
  - If a patient meets criteria, Pharmacy Team initiates insurance coverage query
    - CAB/RPV LA to be billed as a pharmacy benefit
- Clinical Pharmacist reaches out to patient to review CAB/RPV LA
- If patient to receive oral lead-in, it is ordered from Theracom Pharmacy and sent to patient or clinic, based on patient preference
- If direct to inject, patient is scheduled for CAB/RPV LA initiation injection

  <u>CAB/RPV Oral Lead-in Follow Up (if performed)</u>
- Telephone visit with Clinical Pharmacist is scheduled within a week post start of oral lead-in to assess adherence and tolerability
  - If intolerant or non-adherent to oral lead-in treatment, referring medical provider will be alerted and CAB/RPV LA initiation injection will not be scheduled
  - If patient tolerates oral lead-in and demonstrates adherence to regimen CAB/RPV LA initiation dose is ordered by the Clinical Pharmacist

  <u>Ordering CAB/RPV LA Initiation Injection</u>

  - For Q 4-weeks injections, CAB/RPV LA 600-900mg x 1 dose initiation prescription is sent to pharmacy and ordered as clinic administered medication
  - For Q 8-weeks injections (note, this is not Ward 86 protocol but FDA approved dosing schedule):
    - CAB/RPV LA 600-900mg should be ordered with the instructions: *inject once a month for 2 months, then every 2 months thereafter*
    - Clinic administered medication will be ordered as:
      - CAB/RPV LA 600-900mg inject every 28 days x 2 doses
    - Once the initial 2 doses have been administered, clinic administered medication will be ordered as:
      - CAB/RPV LA 600-900mg inject every 56 days
  - Pharmacy Team schedules CAB/RPV LA initiation injection appointment in Ward 86 Injection Clinic (INJECTION) template
    - Appointment will be scheduled as:
      - Visit type "INJECTION"

        - With "CAB/RPV LA 600-900 **Initiation** Inj" in appointment notes
    - The following labs will be obtained on day of CAB/RPV LA initiation injection:
        - HIV VL, CMP, CBC
- Pharmacy Team contacts patient by phone the day before injection appointments
- If patient has BMI >30 kg/m^2, the injection should be administered with a longer needle (e.g., 2-inch IM needle).

CAB/RPV Initiation Injection Follow Up

- Telephone visit is scheduled within seven days of patient receiving CAB/RPV initiation injection to assess for tolerability
- If patient tolerates treatment and patient is on Q 4-weeks injection dosing:
    - CAB/RPV LA 400-600mg maintenance prescription is sent to pharmacy and ordered as clinic administered medication on a 28-day cycle
    - Pharmacy staff schedules a future appointment on a 28-day cycle
    - Appointment is scheduled as
        - Visit type "INJECTION"
        - With "CAB/RPV LA 400-600mg **Maintenance** Inj" in notes
    - Patient will have the following labs repeated at first and second maintenance injection:
        - HIV VL
    - If patient had detectable HIV VL on initial injection
        - HIV VL repeated every 4 weeks until <30 copies/mL
        - HIV Genotype will be ordered on first maintenance injection
    - Patients may be given CAB/RPV LA up to seven days before or after the date the patient is scheduled to receive Q 4-weeks injections (i.e., subsequent dose is to be within 21-35 day window)

- If patient tolerates treatment and patient is to get every Q 8-weeks dosing, patient is scheduled for CAB/RPV LA 600-900mg, injection 28 days from first injection, then every 56 days thereafter

Monitoring on CAB/RPV LA Maintenance Injections

- Once patient has completed their first three injections, HIV VL is to be monitored at a minimum of every three months (i.e., during every third CAB/RPV LA maintenance injection appointment)
- If patient is switched to Q 8-weeks dosing, HIV VL is to be drawn at every injection for the first six doses and then can transition to less frequent VL follow-up (e.g., every 6 months)
- Primary care provider will assess patient one month after first injection and at minimum every three months for six months following initiation

Documentation and Tracking

- Documentation will be conducted in Epic using developed smartphrases
- A list of patients on active CAB/RPV LA therapy will be maintained in Epic for ongoing monitoring and management

- Every two weeks, Pharmacy Team and leadership will clinically review patients on CAB/RPV LA therapy to monito clinical status, including potential for virologic failures and adverse effects
- Pharmacy Team maintains a list of patients who are on CAB/RPV LA therapy, ensures that future appointments and labs are scheduled appropriately, and conducts reminder calls to patients for all CAB/RPV LA related appointments
- Pharmacy Team coordinates CAB/RPV LA inventory and ensures CAB/RPV LA is available prior to injection appointments

Storage, Handling, and Administration

- See below manufacturer instructions
- Note: If patient has BMI >30 kg/m^2, the injection should be administered with a longer needle (e.g., 2-inch IM needle).

INSTRUCTIONS FOR USE

CABENUVA
(kab' en ue vah)

Cabotegravir extended-release injectable suspension
400 mg/2 mL (200 mg/mL)

co-packaged with

Rilpivirine extended-release injectable suspension
600 mg/2 mL (300 mg/mL)

For gluteal intramuscular use only.
Healthcare Professional administration only.

Overview:

A complete dose of CABENUVA requires two injections: 400 mg (2 mL) of cabotegravir and 600 mg (2 mL) of rilpivirine.

Cabotegravir and rilpivirine are suspensions that do not need further dilution or reconstitution.

The preparation steps for both medicines are the same.

Cabotegravir and rilpivirine are for gluteal intramuscular use only. Each injection must be administered to separate gluteal intramuscular sites (on opposite sides or at least 2 cm apart). The administration order is not important.

Note: The ventrogluteal site is recommended.

Storage information

- Store in refrigerator at 2°C to 8°C (36°F to 46°F)

Do not freeze.

Prior to administration:

- Before preparing the injections, the vials may sit in the carton at room temperature (maximum temperature of 25°C [77°F]) for up to 6 hours. If not used within 6 hours, the medication must be discarded.
- Once the medicines have been drawn into the syringe, the medication can remain in the syringes for up to 2 hours before injecting. If 2 hours are exceeded, the medication, syringes, and needles must be discarded.
- It is recommended to label the syringe with the time that the medication has been drawn into the syringe if the medication is not administered immediately.

INSTRUCTIONS FOR USE

CABENUVA
(kab' en ue vah)

Cabotegravir extended-release injectable suspension
600 mg/3 mL (200 mg/mL)

co-packaged with

Rilpivirine extended-release injectable suspension
900 mg/3 mL (300 mg/mL)

For gluteal intramuscular use only.

Healthcare Professional administration only.

Overview:

A complete dose of CABENUVA requires two injections: 600 mg (3 mL) of cabotegravir and 900 mg (3 mL) of rilpivirine.

Cabotegravir and rilpivirine are suspensions that do not need further dilution or reconstitution.

The preparation steps for both medicines are the same.

Cabotegravir and rilpivirine are for gluteal intramuscular use only. Each injection must be administered to separate gluteal intramuscular sites (on opposite sides or at least 2 cm apart). The administration order is not important.

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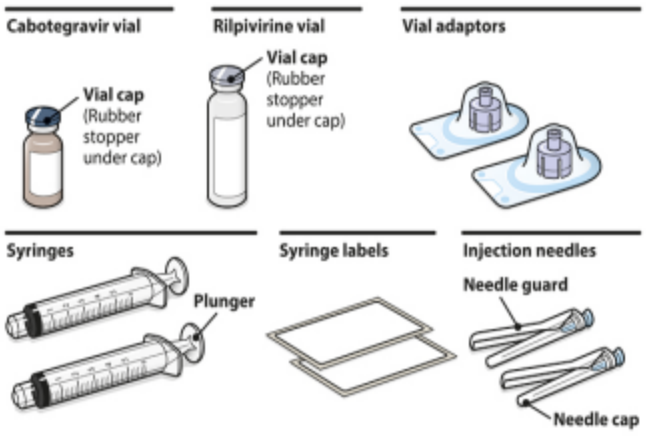
- It is recommended to label the syringe with the time that the medication has been drawn into the syringe if the medication is not administered immediately.



Your pack contains:

- 1 vial of Cabotegravir
- 1 vial of Rilpivirine
- 2 vial adaptors
- 2 syringes
- 2 syringe labels
- 2 injection needles (23 gauge, 1½ inch)

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

You will also need:

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

Preparation:

1. Inspect both vials.

Figure A

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

Note: The Cabotegravir vial has a brown tint to the glass.

Do not use if the expiration date has passed.

2. Wait 15 minutes.

Figure B

- Wait at least 15 minutes before you are ready to give the injection to allow the medication to come to room temperature. **See Figure B.**

3. Shake the vial vigorously.

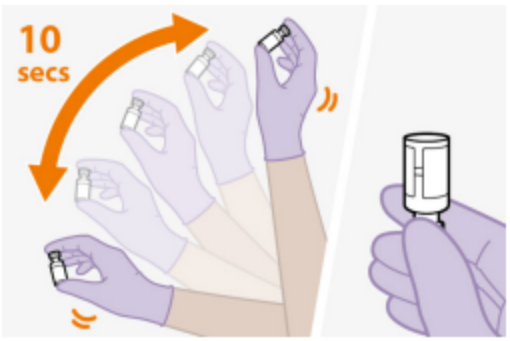


Figure C

- Hold the vial firmly, and vigorously shake for a full 10 seconds. **See Figure C.**
- Invert the vial and confirm the suspension is uniform.
- If the suspension is not uniform, shake the vial again.
- It is also normal to see small air bubbles.

4. Remove the vial cap.

Figure D

- Remove the cap from the vial. **See Figure D.**
- Wipe the rubber stopper with an alcohol wipe.

> **Do not** allow anything to touch the rubber stopper after wiping it.

5. Peel open the vial adaptor.

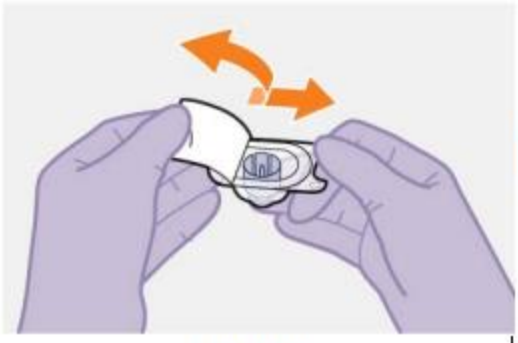


Figure E

- Peel off the paper backing from the vial adaptor packaging. **See Figure E.**

Note: Keep the adaptor in place in its packaging for the next step.

6. Attach the vial adaptor.

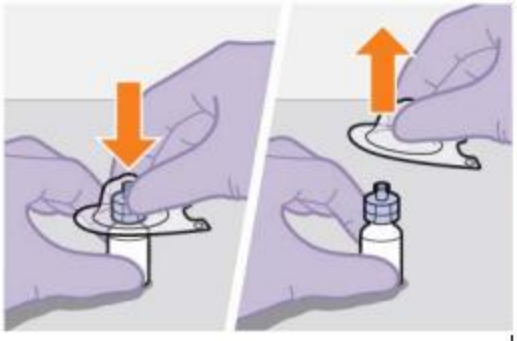


Figure F

- Press the vial adaptor straight down onto the vial using the packaging, as shown.
  The vial adaptor should snap securely into place.
- When you are ready, lift off the vial adaptor packaging as shown.

See Figure F.

7. Prepare the syringe.

Figure G

- 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 G.**

8. Attach the syringe.

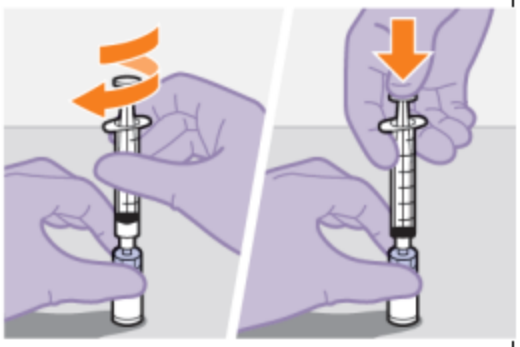


Figure H

- Hold the vial adaptor and vial firmly, as shown.
- Screw the syringe firmly onto the vial adaptor.
- Press the plunger all the way down to push the air into the vial.

See Figure H.

9. Slowly draw up the dose.

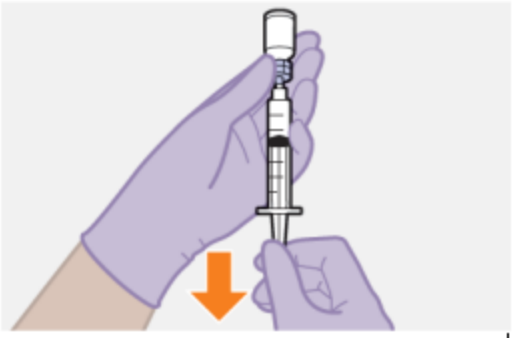


Figure I

- 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 I.**

10. Unscrew the syringe.

Figure J

- Unscrew the syringe from the vial adaptor, holding the vial adaptor as shown.

See Figure J.

Note: Keep the syringe upright to avoid leakage. Check that the suspension looks uniform and milky white.

11. Attach the needle and affix syringe label.

Figure K

- 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.
- Write the name of the medicine on the syringe label. Affix the label to the syringe making sure the gradations remain visible.

See Figure K.

Injection:

12. Prepare the injection site.

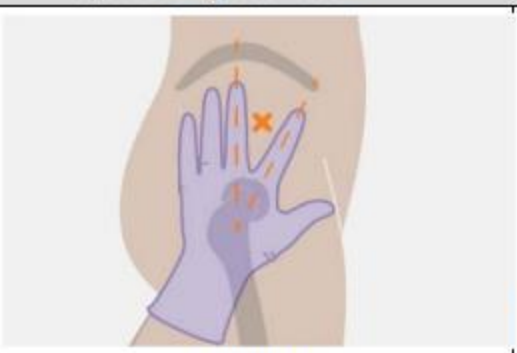


Figure L

Injections must be administered to the gluteal sites. **See Figure L.**

Select from the following areas for the injection:

- Ventrogluteal, as shown (recommended)
- Dorsogluteal (upper outer quadrant)

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

13. Remove the cap.

Figure M

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

14. Remove extra liquid from the syringe.

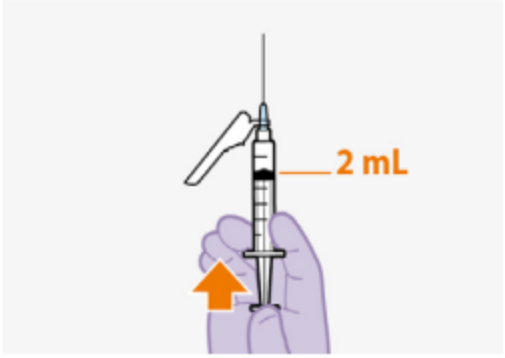


Figure N

- Hold the syringe with the needle pointing up. Press the plunger to the 2-mL dosing mark to remove extra liquid and any air bubbles. **See Figure N.**

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

15. Stretch the skin.

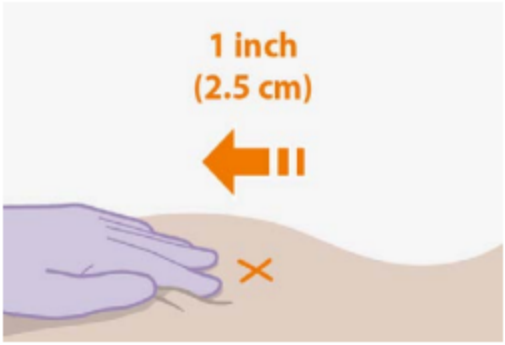


Figure O

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 O.**
- Keep it held in this position for the injection.

16. Insert the needle.

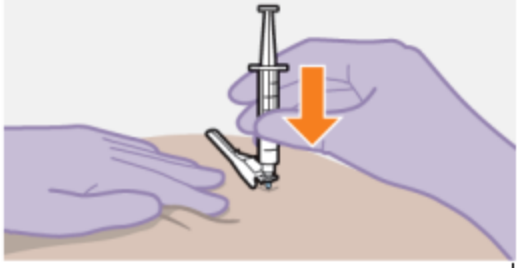


Figure P

- Insert the needle to its full depth, or deep enough to reach the muscle. **See Figure P.**

17. Inject the dose of medicine.

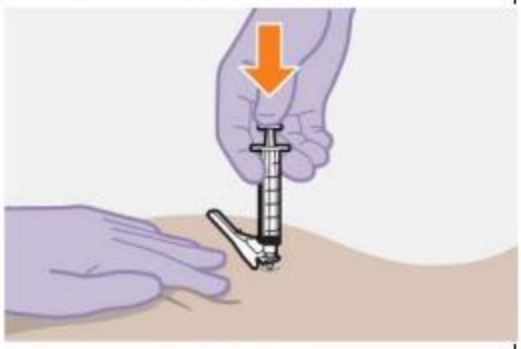


Figure Q

- Still holding the skin stretched – slowly press the plunger all the way down. **See Figure Q.**
- Ensure the syringe is empty.
- Withdraw the needle and release the stretched skin immediately.

18. Assess the injection site.

Figure R

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

Do not massage the area.

19. Make the needle safe.

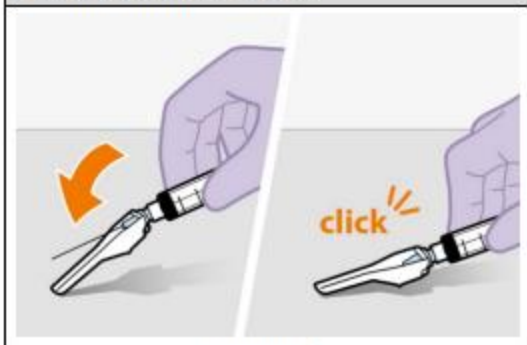


Figure S

- 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 S.

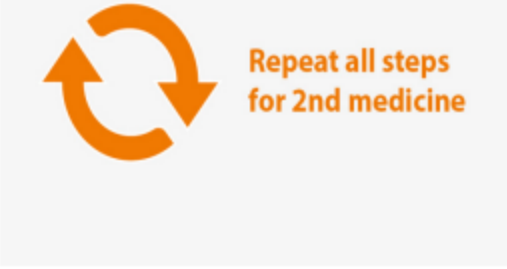
After injection:

20. Dispose safely.

Figure T

- Dispose of used needles, syringes, vials, and vial adaptors according to local health and safety laws. **See Figure T.**

Repeat for 2nd medicine.



- If you have not yet injected both medicines, use the same steps for preparation and injection of the other medicine.
- The second medicine must be injected into a separate gluteal intramuscular site (on opposite sides or at least 2 cm apart).

Questions and Answers

1. How long can the medicine be left out of the refrigerator?

It is best to inject the medicine as soon as it reaches room temperature. However, the vials may sit in the carton at room temperature (maximum temperature of 25°C [77°F]) for up to 6 hours. If not used within 6 hours, the medication must be discarded.

2. How long can the medicine be left in the syringe?

It is best to inject the (room temperature) medicine as soon as possible after drawing it up. However, the medication can remain in the syringe for up to 2 hours before injecting.

If 2 hours are exceeded, the medication, syringes, and needles 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. Does the order in which I give the medicines matter?

No, the order is unimportant.

5. Is it safe to warm the vials up to room temperature more quickly?

It is best to let the vials come to room temperature naturally. However, you can use the warmth of your hands to speed up the warm-up time, but make sure the vials do not get above 25°C (77°F).

Do not use any other heating methods.

Manufactured for:

ViiV Healthcare

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by:
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This Instructions for Use has been approved by the U.S. Food and Drug Administration. Issued: 01/2021