USE OF INJECTABLE CAB/RPV LA AS REPLACEMENT ART IN VIRALLY SUPPRESSED ADULTS

NYSDOH AIDS INSTITUTE HIV CLINICAL GUIDELINE AUGUST 2022

ALL RECOMMENDATIONS P.1

Patients for Whom CAB/RPV LA Is Not Recommended

- Before recommending a switch to CAB/RPV LA, clinicians should determine patients' hepatitis B status (hepatitis B surface antigen, core antibody, surface antibody, and HBV DNA if indicated); CAB/RPV LA should not be recommended for patients with active HBV coinfection without concurrent oral therapy for HBV. (A*)
- Before recommending CAB/RPV LA for patients who have been treated previously with INSTIs or NNRTIs, clinicians should review results of prior resistance testing and ART treatment history or consider baseline genotypic resistance testing if no prior results are available; genotypic resistance testing should include both the reverse transcriptase and integrase genes. (A3)
- Clinicians should not recommend CAB/RPV LA in patients with known or suspected INSTI or NNRTI RAMs, excluding the K103N mutation in isolation, at baseline. (A1)
- Because there are no currently available data on the safety and efficacy of this regimen in children or adolescents or during pregnancy or breast-feeding, clinicians should not recommend treatment with CAB/RPV LA for these patients. (A*)
- Preexisting CAB and RPV RAMs have been associated with virologic failure; therefore, clinicians should obtain proviral DNA genotypic resistance testing before switching to CAB/RPV LA in any patient for whom historical resistance test results are not available. (B2)

Administration

- CAB/RPV LA should be administered by a licensed and trained healthcare professional. (A*)
- To prepare and administer CAB/RPV LA, clinicians should follow the protocols detailed in Box 2 and in the medication package inserts. (A1)

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ALL RECOMMENDATIONS *(continued from P.1)* P.2

Dosing Strategy and Managing Missed Injections

- If an oral lead-in is chosen to assess medication tolerability, the clinician should prescribe up to 4 weeks of oral CAB/RPV. (A3)
- Once a dosing schedule is decided upon, clinicians should administer CAB/RPV LA as detailed in Table 2 or Table 3; a bimonthly (every 8 weeks) dosing schedule is preferred. (A1)
- If a patient plans to miss or delay a monthly CAB/RPV LA injection by >7 days, the clinician should arrange for oral medication (CAB 30 mg and RPV 25 mg daily) to be available in advance in an adequate supply (up to 2 months/8 weeks) to cover the gap in injections.
- Clinicians should resume CAB/RPV LA in patients who miss injections as detailed in *Managing Missed or Delayed Injections*. (A3)

Discontinuing CAB/RPV LA

- Clinicians should discontinue CAB/RPV LA in patients with confirmed virologic failure (defined as 2 consecutive plasma HIV-1 RNA measurements ≥200 copies/mL) or evidence of INSTI or NNRTI RAMs, excluding the K103N mutation in isolation, on subsequent genotype testing. (A1)
- Clinicians should discontinue CAB/RPV LA in patients with evidence of INSTI or NNRTI RAMs (excluding the K103N mutation in isolation) on subsequent proviral DNA–based genotype testing (which may be performed for another clinical indication or following a viral blip), regardless of viral load suppression status, including an undetectable viral load (defined as plasma HIV-1 RNA measurement <50 copies/mL). (B3)
- When extended or frequent gaps occur between injections, resulting in prolonged periods of subtherapeutic drug concentrations, the risk of drug resistance increases; to avoid this risk, clinicians should encourage patients to adhere to the injection schedule and should switch to oral therapy for patients who cannot maintain the injection schedule. (A3)
- If CAB/RPV LA is discontinued, the clinician should initiate a fully suppressive oral ART regimen no later than 1 month (4 weeks) following the final CAB/RPV LA monthly injection or 2 months (8 weeks) following final CAB/RPV LA bimonthly injection. (A2)

Laboratory Testing and Monitoring

- Clinicians should perform baseline and routine monitoring of patients receiving injectable ART according to the recommendations in the following NYSDOH AI guidelines (A3): *Virologic and Immunologic Monitoring in HIV Care* and *Laboratory Monitoring for Adverse Effects of ART*.

BOX 1: Summary of Benefits, Limitations, and Risks of CAB/RPV LA

Benefits:

- Improved patient satisfaction
- Monthly (every 4 weeks) or bimonthly (every 8 weeks) administration
- Directly observed
- Noninferior to oral ART
- Potential option for patients who have ongoing substance use, mental health concerns, neurocognitive disorders, disclosure concerns, or other challenges associated with adherence to oral ART, including difficulty swallowing pills
- Removes the daily reminder of HIV status that is associated with taking pills

Potential Risks:

- Potential injection site reactions and other adverse effects, including pyrexia
- Potential for resistance to develop if doses are missed outside the 7-day window period, given the long half-life ("tail") of CAB and RPV

Limitations:

- Cannot be used if a patient has prior resistance to INSTIs or NNRTIs, excluding the K103N mutation in isolation
- Lack of data on use during pregnancy or breastfeeding and in children and adolescents
- Does not treat HBV coinfection
- Lack of data on use in patients with prior virologic failure
- Treatment with 4 weeks of oral CAB and RPV (oral lead-in) may be used before the first injection to assess for unexpected reactions or allergies to CAB or RPV
- Requires oral medications as bridging therapy when injections are missed
- Medication storage requirements (2° C to 8° C [36° F to 46° F])
- Requires 6 to 12 in-person visits with a healthcare provider per year

→ **Use this code with your phone's QR code reader to go directly to a mobile-friendly version of the guideline.**

This ¼-Folded Guide is a companion to the New York State Department of Health AIDS Institute guideline *Use of Injectable CAB/RPV LA as Replacement ART in Virally Suppressed Adults*. The full guideline is available at www.hivguidelines.org.

Managing Missed or Delayed Injections

Planned: If a patient plans to miss or delay a scheduled injection by >7 days, oral therapy can be taken for up to 2 consecutive months (8 weeks). Alternatively, a patient's previous suppressive oral ART regimen may be considered as a bridge if it was well tolerated, with care to assess for potential drug interactions with coadministered medications. Oral therapy should be started approximately 1 month (4 weeks) after the last monthly injection or 2 months (8 weeks) after the last bimonthly injection and continued until injections are resumed.

Unplanned, monthly (every 4 weeks) injection schedule: If a patient who is not taking oral bridging CAB/RPV misses a monthly injection by >7 days and will resume injectable therapy, restart injections as follows:

- If last injection was ≤2 months (≤8 weeks) prior, resume as soon as possible with a maintenance dose injection of CAB 400 mg (2 mL)/RPV 600 mg (2 mL) IM.
- If last injection was >2 months prior, resume as soon as possible with a high-dose injection of CAB 600 mg (3 mL)/RPV 900 mg (3 mL) IM once followed by monthly (every 4 weeks) maintenance dosing 400 mg (2 mL)/RPV 600 mg (2 mL) IM.

Unplanned, bimonthly (every 8 weeks) injection schedule: If a patient who is not taking oral bridging CAB/RPV misses an injection and will resume injectable therapy, restart injections as soon as possible: within 2 months (8 weeks) if the second initial injection was missed or within 3 months (12 weeks) if any other bimonthly (every 8 weeks) maintenance injection was missed. If outside of those windows, a second dose should be administered 1 month (4 weeks) following reinitiation of injections, with subsequent return to bimonthly (every 8 weeks) dosing.

GOOD PRACTICE

- Follow up by phone within 1 week after initiation of oral therapy lead-in, if used, and within 3 days after a patient receives the initial loading dose of injectable ART to assess the patient's tolerance.

Abbreviations: ART, antiretroviral therapy; CAB, cabotegravir; CAB/RPV LA, injectable long-acting cabotegravir/rilpivirine; CVF, confirmed virologic failure; HBV, hepatitis B virus; IM, intramuscular; INSTI, integrase strand transfer inhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor; RAM, resistance-associated mutation; RPV, rilpivirine.

DOSING STRATEGIES

TABLE 2: Optional Lead-in, Initiation, and Maintenance for MONTHLY (every 4 weeks) CAB/RPV LA Dosing

Timing	Dosing and Administration	Comments
Optional oral lead-in: Therapy initiation: Week 0 (aka month 0)	CAB 30 mg/RPV 25 mg once daily by mouth with a meal x 4 weeks	Oral medication lead-in
Week 4 (aka month 1)	CAB 600 mg (3 mL)/RPV 900 mg (3 mL) IM injection	**Initiation dose:** Administer on last day of oral lead-in or prior suppressive ART regimen
Week 8 (aka month 2) and every 4 weeks (aka every 1 month) thereafter	CAB 400 mg (2 mL)/RPV 600 mg (2 mL) IM injection	**Maintenance dose:** Administer within 7 days before or after scheduled date (see *Managing Missed or Delayed Injections*)

TABLE 3: Optional Lead-in, Initiation, and Maintenance for BIMONTHLY (every 8 weeks) CAB/RPV LA Dosing

Timing	Dosing and Administration	Comments
Optional oral lead-in: Therapy initiation: Week 0 (aka month 0)	CAB 30 mg/RPV 25 mg once daily by mouth with a meal x 4 weeks	Oral medication lead-in
Week 4 (aka month 1)	CAB 600 mg (3 mL)/RPV 900 mg (3 mL) IM injection	**Initiation dose:** Administer on last day of oral lead-in or prior suppressive ART regimen
Week 8 (aka month 2)	CAB 600 mg (3 mL)/RPV 900 mg (3 mL) IM injection	**Maintenance dose:** Administer within 7 days before or after scheduled date (see *Managing Missed or Delayed Injections*)
Week 16 (aka month 4) and every 8 weeks (aka every 2 months) thereafter	CAB 600 mg (3 mL)/RPV 900 mg (3 mL) IM injection	**Maintenance dose:** Administer within 7 days before or after scheduled date (see *Managing Missed or Delayed Injections*)

TABLE 4: Advantages and Limitations of CAB/RPV LA Dosing Strategies

Advantage or Limitation	Monthly (every 4 weeks) Dosing	Bimonthly (every 8 weeks) Dosing
Required annual visits	12	6
Injection site pain [a]	Less	More
CVF despite on-time dosing [b]	Rare	Rare
Risk of CAB and/or RPV RAMs if CVF	Common	Common
Patient satisfaction	High	Preferred
Staffing, administration time, and cost	More	Less

Notes:

a. In the ATLAS-2M trial, 3% of participants in the monthly injection arm and 2% in the bimonthly injection arm discontinued treatment because of injection site pain.

b. In the ATLAS-2M trial, <1% of participants in the monthly injection arm and 2% in the bimonthly injection arm had CVF.

BOX 2: Preparation and Administration of Initial and Maintenance Doses of CAB/RPV LA [a]

1. Bring the vials [a] of CAB LA and RPV LA to room temperature for at least 15 minutes and for a maximum of 6 hours.
2. Prepare 2 syringes [a]. Once CAB/RPV LA has been drawn into the syringes, they must be used within 2 hours.
3. For aspiration, use a vial adaptor or general-use sterile 21 gauge × 1½ inch hypodermic needle [b]. Shake the vial vigorously for at least 10 seconds before aspiration.
4. For injection, use a general-use sterile 23 gauge × 1½ inch hypodermic needle [b]. Administer the injection within 2 hours of syringe preparation. A patient's build or body mass index may be considered when selecting an appropriate injection needle length.
5. Inject into the gluteus medius muscle [c] at a 90° angle, ventrogluteal (preferred) or dorsogluteal (upper-outer quadrant of the buttock), with care that the compound is not injected into a vein.

Notes:

a. The same preparation and administration are used for both initial and maintenance doses of CAB/RPV LA. Follow sterile technique at all points while preparing syringes and injecting compounds. Use 3 mL vials/syringes for the initial dose and 2 mL vials/syringes for maintenance doses.

b. The hypodermic needle must be long enough to inject the medication into the muscle mass without penetrating underlying nerves, blood vessels, or bone.

c. Inject CAB LA into the gluteus medius muscle and RPV LA into the contralateral gluteus medius muscle. Injections can be given on opposite sides or on the same side, 2 cm apart.

d. For more detail, see instructions for use in the CAB/RPV LA package insert.