HIV CLINICAL RESOURCE ¼-FOLDED GUIDE

VISIT **HIVGUIDELINES.ORG** TO LEARN MORE OR VIEW COMPLETE GUIDE

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

NYSDOH AIDS INSTITUTE HIV CLINICAL GUIDELINE JULY 2021

ALL RECOMMENDATIONS P.1

Initiation and Maintenance of CAB/RPV LA as ART

- Clinicians should initiate injectable long-acting cabotegravir/rilpivirine (CAB/RPV LA) only after a patient has completed 4 weeks of therapy with daily oral CAB 30 mg and RPV 25 mg. (A1)
- To prepare and administer CAB/RPV LA, clinicians should follow the protocols detailed below and in the medication package inserts. (A1)

Limitations of Use

- Clinicians should not prescribe injectable CAB/RPV LA for patients with active hepatitis B virus (HBV) coinfection without concurrent oral therapy for HBV. (A*)
- Clinicians should not initiate CAB/RPV LA in patients with known or suspected integrase strand transfer inhibitor (INSTI) or nonnucleoside reverse transcriptase inhibitor (NNRTI) resistance-associated mutations (RAMs), excluding the K103N mutation in isolation, at baseline. (A1)
- Clinicians should discontinue CAB/RPV LA in patients with confirmed virologic failure (defined as 2 consecutive plasma HIV-1 RNA measurements ≥200 copies/mL) and 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)
- Because there are no currently available data on the safety and efficacy of this regimen in children or adolescents or during pregnancy or breastfeeding, clinicians should not recommend treatment with CAB/RPV LA for these patients. (A*)

BOX 1: BENEFITS, LIMITATIONS, AND RISKS OF CAB/RPV LA

Benefits:

- Improved patient satisfaction
- Monthly 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

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) required before the first injection to assess for unexpected reactions or allergies to RPV or CAB
- Requires oral medications as bridging therapy when injections are missed
- Medication storage requirements (2° C to 8° C [36° F to 46° F])
- Requires ≥12 in-person visits with a healthcare provider per year

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

BOX 2: INSTITUTIONAL, CLINICIAN, AND PATIENT PREPARATIONS FOR IMPLEMENTATION OF INJECTABLE ART

Institutional and Clinician Preparations

- Assess pharmacy resources and on-site procedures for storage of oral and injectable medications.
- Train nurses and other medical care providers regarding proper syringe preparation and injection techniques.
- Establish billing protocols for the procurement and administration of injectable ART medications.
- Implement a system to remind patients of appointments.
- Plan for treatment continuation in the event of pandemic-related shutdowns or other catastrophic events.
- Provide education on the use of oral bridging therapy.
- Educate patients about possible adverse effects associated with injectable CAB/RPV LA and how to manage them.
- Ensure that patients know how to reach a medical care provider if needed.
- Schedule appointments for administration in advance.

Patient Preparations

- Obtain prior authorizations for insurance or third-party coverage of ART medications.
- Confirm ability to maintain required clinic visit schedule for injections, including transportation availability.
- Confirm ability to adhere to the injection regimen.
- Confirm ability to tolerate 2 large volume intramuscular injections regularly.

← **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.

ALL RECOMMENDATIONS P.2

Limitations of Use, *continued*

- Before initiating CAB/RPV LA in patients who have been treated previously with INSTIs or NNRTIs, clinicians should review results of prior resistance testing and antiretroviral therapy (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)
- CAB/RPV LA should be administered by a licensed and trained healthcare professional. (A*)

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*
  - *Laboratory Monitoring for Adverse Effects of ART*

GOOD PRACTICE AND KEY POINTS

Good Practice When Initiating Injectable ART

- Follow up by phone within 1 week after initiation of oral therapy lead-in and within 2 days after a patient receives the initial loading dose of injectable ART to assess the patient's tolerance.

Key Points: Laboratory Testing and Patient Follow-up

- Hepatitis B status should be determined before initiation of CAB/RPV (hepatitis B surface antigen, core antibody, surface antibody, and DNA if indicated).
- CAB/RPV LA should not be continued in a patient who has confirmed resistance to CAB or RPV.
- CAB/RPV LA should not be continued in a patient with virologic failure (HIV RNA ≥200 copies/mL on 2 consecutive viral load tests).

Key Points: Initiation and Maintenance of CAB/RPV LA as ART

- In providing initial and maintenance treatment with CAB/RPV LA, clinicians should follow the protocols detailed in the text for storage, preparation, dosing, and administration.
- If maintenance dosing is delayed beyond 2 months, a loading dose will be required for CAB/RPV LA if injectable therapy is resumed.

BOX 3: PREPARATION AND ADMINISTRATION OF INITIAL AND MAINTENANCE DOSES OF INJECTABLE 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.

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

TABLE 1: VIRAL LOAD AT WEEK 48 OF MAINTENANCE PHASE IN THE ATLAS AND FLAIR TRIALS

[Data compiled from Orkin 2020 and Swindells 2020]

	ATLAS [a]		FLAIR [b]	
HIV Viral Load at Week 48	**CAB/RPV LA (n = 308)**	**Oral ART [c] (n = 308)**	**CAB/RPV LA (n = 283)**	**Oral ART [d] (n = 283)**
HIV RNA ≥50 copies/mL	1.6%	1.0%	2.1%	2.5%
HIV RNA <50 copies/mL	92.5%	95.5%	93.6%	93.3%

Abbreviations: ART, antiretroviral therapy; CAB/RPV LA, injectable long-acting cabotegravir/rilpivirine; INSTI, integrase strand transfer inhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor; PI, protease inhibitor.

Notes:

a. Participants in ATLAS were ≥18 years old, had received uninterrupted and unchanged ART with no virologic failure for 6 months prior to screening, and had an HIV RNA level of <50 copies/mL at screening and within 6 and 12 months before screening.

b. Participants in FLAIR were ≤18 years old, ART naive, and had a plasma HIV RNA level of ≥1,000 copies/mL at screening.

c. Participants continued their current daily PI-, NNRTI-, or INSTI-based oral regimen.

d. Daily oral dolutegravir/abacavir/lamivudine.

TABLE 2: RECOMMENDED DOSING STRATEGY FOR CABOTEGRAVIR/RILPIVIRINE [a]

Drug	Oral Medication Lead-In (≥4 weeks)	Intramuscular Initiation Dose	Intramuscular Maintenance Doses (once monthly, within 7 days before or after scheduled date)
Cabotegravir	30 mg once daily by mouth with a meal	600 mg (3 mL)	400 mg (2 mL)
Rilpivirine	25 mg once daily by mouth with a meal	900 mg (3 mL)	600 mg (2 mL)

a. Adapted from CAB/RPV LA package insert.