Cabotegravir/Rilpivirine Workflow Implementation and Evolution in an Ambulatory Care Clinic

Regan McIntosh, PharmD, MBA, CSP
Clinical Pharmacy Specialist
Adult Special Care Clinic at UMMC
Jackson, MS

Objectives:

1. Provide an overview of cabotegravir/rilpivirine (CAB/RPV) and its place in HIV treatment.

2. Explain how CAB/RPV was implemented at the Adult Special Care Clinic (ASCC) in Jackson, MS.

3. Review the evolution of the CAB/RPV workflow at ASCC.

4. Discuss prospective CAB/RPV implementation models for clinics of various sizes and staffing capabilities.

ASCC and UMMC Specialty Pharmacy Overview

The University of Mississippi
MEDICAL CENTER

The Adult Special Care Clinic (ASCC) at UMMC

The Adult Special Care Clinic (ASCC) is an infectious diseases clinic located at the Jackson Medical Mall. ASCC offers comprehensive Ryan White care including antiretroviral therapy and laboratory monitoring, STD screening and treatment, medical case management and social work support, substance use screening and treatment (both in-house and external referral), mental health services (both in-house and external referral), primary care and preventive medicine services, and access to clinical trials. ASCC also offers antiviral therapy for chronic hepatitis B and C infection and HIV/hepatitis coinfection in collaboration with the university's hepatology and liver transplant programs.

The Adult Special Care Clinic at UMMC

- Largest HIV clinic in the state of MS
- 2208 total patients as of December 2022
- Population Served:
  - 86% Black, 13% White, 1% Asian/Am Indian
  - 74% Patients below FPL
  - Mix of Payer Sources
- Viral suppression rate = 88.7%

The University of Mississippi Medical Center

UMMC Specialty Pharmacy Program

- UMMC has specialty pharmacy teams who offer in-clinic services to the following areas:
  - Adult Specialty Care Clinic (HIV and hepatitis C)
  - Cancer Institute (hematology/oncology)
  - Dermatology (psoriasis)
  - Children's Specialty Clinic (pediatric endocrinology and neurology)
  - Pavilion Rheumatology (rheumatology)
- The Jackson Medical Pharmacy is the prescription fulfillment and shipping pharmacy for specialty pharmacy locations.

Specialty Pharmacy ID Responsibilities

- Identify and enroll ASCC patients into the specialty pharmacy program
- Follow up with established specialty patients with refill calls and telephone/appointment reassessments
- Assist ASCC staff with specialty medication problems (prior authorizations, appeals, managing formulary and insurance changes, etc.)
- Provide clinical counseling for specialty pharmacy patients including but not limited to medication reconciliation, drug-drug interaction questions, side effect management, therapy changes, and review of therapy effectiveness
- Manage medication shipment issues
- **Work in coordination with ASCC staff to care for patients on clinic administered specialty therapies (i.e. CAB/RPV)**

CAB/RPV Treatment Overview

Ideal Patient: Clinical Parameters

- Virologically suppressed patients (<50 copies/mL) for at least 3 months per guidelines
- No known or suspected resistance to either component of the injection
- No history of treatment failure
- Not on interacting medications

Important DDIs (Overview)

Concomitant Drug Class: Drug Name	Effect on Concentration	Clinical Comment
Anticonvulsants: Carbamazepine Oxcarbazepine Phenobarbital Phenytoin	↓Cabotegravir ↓Rilpivirine	Co-administration is contraindicated with CAB/RPB due to potential for loss of virologic response and development of resistance.
Antimycobacterials: Rifampin Rifapentine	↓Cabotegravir ↓Rilpivirine	
Antimycobacterial: Rifabutin	↓Cabotegravir ↔Rifabutin ↓Rilpivirine	
Glucocorticoid (systemic): Dexamethasone (more than a single-dose treatment)	↓Rilpivirine	
Herbal Product: St John's wort (Hypericum perforatum)	↓Rilpivirine	

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/212888s000lbl.pdf

Ideal Patient: Additional Considerations

- Regularly attends appointments and is easily reachable for follow-up
- Not scared of needles or injections
- Lives near the clinic or has a means of reliable transportation to the clinic
- Plans to continue care at the clinic for some period or has plans to move to a clinic that also administers the medication
- Patient is comfortable with more frequent clinic visits and CAB/RPV side effects

Dosing Schedule

Optional: Oral lead-in up to 28 days

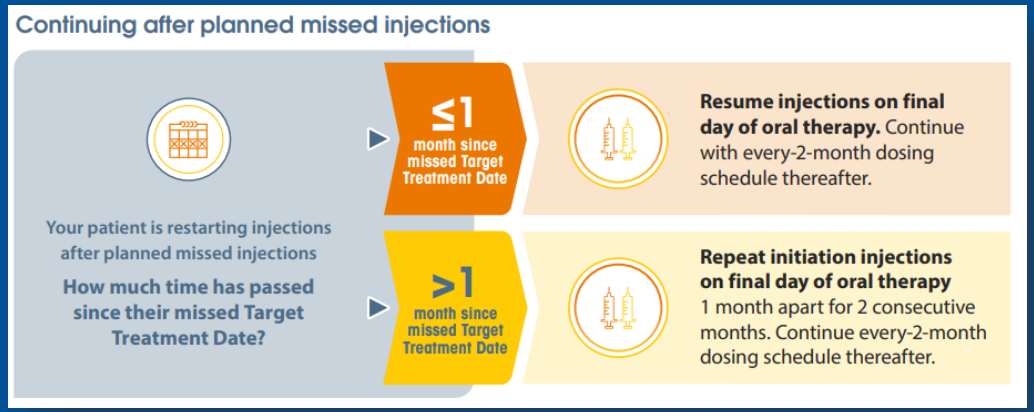
Every 2 month dosing:
- All injections 600 mg/3 mL CAB and 900 mg/3 mL RPV

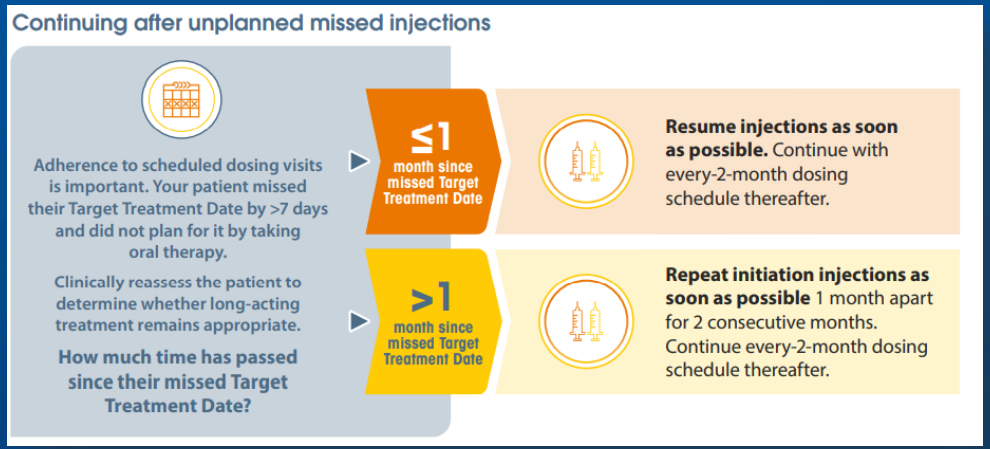
Loading Injection 1: Month 1 → Continuation injections: Months 2, 4, 6, 8, and beyond (Q 56 days)

Every month dosing:
- Loading injection 600 mg/3 mL CAB and 900 mg/3 mL RPV
- Continuation injections 400 mg/2 mL CAB and 600 mg/2 mL RPV

Loading Injection 1: Month 1 → Continuation injections: Months 2, 3, 4, 5, and beyond (Q 28 days)

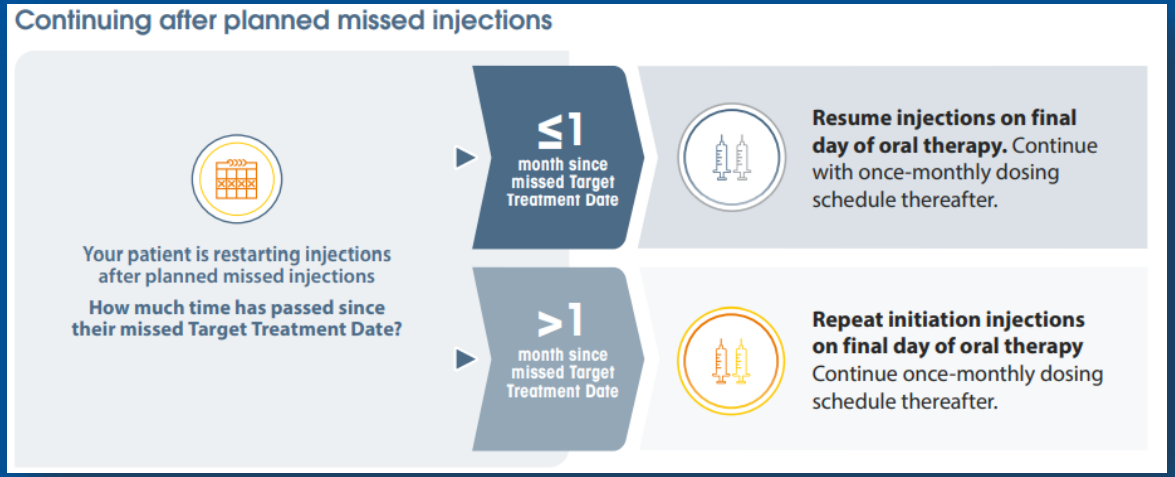
Managing Missed Injections: Bi-monthly Dosing

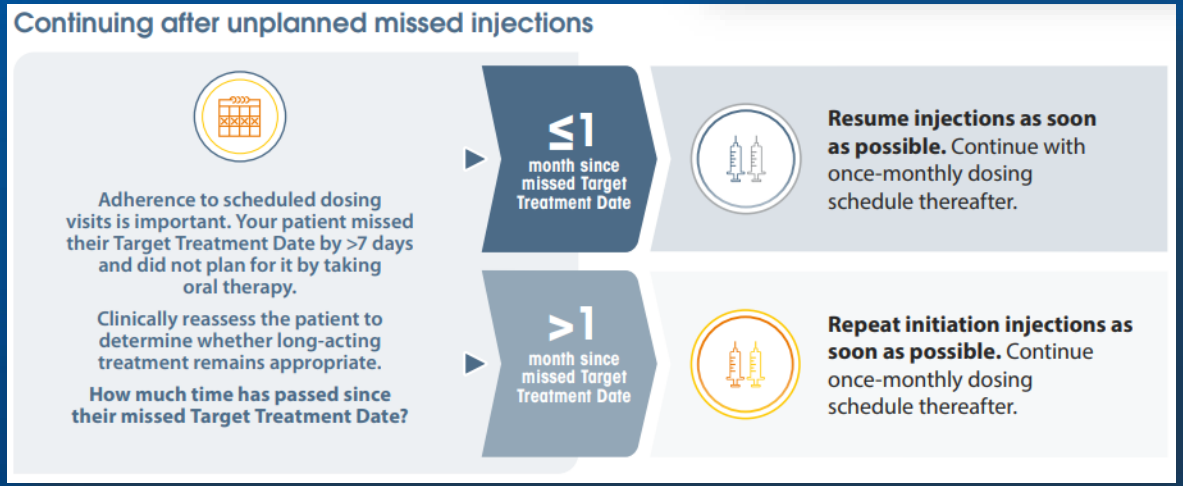




https://cabenuvahcp.com/content/dam/cf-viiv/cabenuva hcp/master/pages/dosing/CABENUVA_Dosing_and_Admin_Guide.pdf

Managing Missed Injections: Monthly Dosing





https://cabenuvahcp.com/content/dam/cf-viiv/cabenuva hcp/master/pages/dosing/CABENUVA_Dosing_and_Admin_Guide.pdf

The University of Mississippi Medical Center

Adverse Effects

Table 3. Adverse Reactions[a] (Grades 1 to 4) Reported in at Least 2% of Subjects with HIV-1 Infection in FLAIR and ATLAS Trials (Week 48 Pooled Analyses)

Adverse Reactions	Cabotegravir plus Rilpivirine (n = 591)		Current Antiretroviral Regimen (n = 591)	
	All Grades	At Least Grade 2	All Grades	At Least Grade 2
Injection site reactions[b]	83%	37%	0	0
Pyrexia[c]	8%	2%	0	0
Fatigue[d]	5%	1%	<1%	<1%
Headache	4%	<1%	<1%	<1%
Musculoskeletal pain[e]	3%	1%	<1%	0
Nausea	3%	<1%	1%	<1%
Sleep disorders[f]	2%	<1%	<1%	0
Dizziness	2%	<1%	<1%	0
Rash[g]	2%	<1%	0	0

Less Common Adverse Reactions

The following select adverse reactions (regardless of severity) occurred in less than 2% of subjects receiving cabotegravir plus rilpivirine.

Gastrointestinal Disorders: Abdominal pain (including upper abdominal pain), gastritis, dyspepsia, vomiting, diarrhea, and flatulence.

Hepatobiliary Disorders: Hepatotoxicity.

Investigations: Weight increase *(see below)*.

Psychiatric Disorders: Anxiety (including anxiety and irritability), depression, abnormal dreams.

Skin and Hypersensitivity Reactions: Hypersensitivity reactions.

Failure Considerations

Virologic Failure Predictors	Solutions
• Archived RPV resistance • BMI $\geq$ 30 kg/m^2 • HIV subtype A6/1	• Resistance testing • Consideration of increased needle length ▪ Needles in manufacture package are 23 G, 1½ in ▪ 2 in needles may be utilized in patients with BMI $\geq$ 30 kg/m^2 • Subtype testing

ASCC CAB/RPV Workflow

History of ASCC CAB/RPV Program

In April/May 2021 ASCC had 7 participants from the CUSTOMIZE trial at UMMC who needed to either move back to their previous oral therapy or continue with CAB/RPV using their insurance or through a patient assistance program.

Through PA approvals and 1 PAP enrollment, all CUSTOMIZE patients were able to continue their CAB/RPV treatment.

In the Fall/Winter of 2021 ASCC slowly enrolled a small number of additional patients into the clinic's CAB/RPV administration program.

During November of 2021, after some discussion with the Mississippi Department of Health (MSDH, ASCC began a pilot program to enroll ADAP patients to receive CAB/RPV at our clinic.

During December of 2021 ASCC fully opened enrollment to any providers and patients who desired to start CAB/RPV and were appropriate candidates.

Since enrollment opening, ASCC has provided CAB/RPV therapy to 107 patients, of which 93 continue to receive monthly or bi-monthly injection treatment.

Checklist to Add CAB/RPV Patients to Our Program (Initial)

- ❑ Provider recommendation as appropriate and conversation with the patient
- ❑ Obtain signed enrollment form
- ❑ Verify insurance coverage
- ❑ Send enrollment form to manufacturer or use manufacturer portal
- ❑ Confirm patient approval by manufacturer
- ❑ Get copay card/grant funding information if needed to add to chart
- ❑ Receive oral lead in at clinic
- ❑ Add patient to master reminder list
- ❑ Have patient pickup oral lead in therapy and update profile
- ❑ Call to check on patient's tolerance after 14 days
- ❑ If patient is tolerating, order first loading dose and schedule injection #1
- ❑ After injection #1, call in 14 days to check on patient and then order maintenance injection and schedule injection visit
- ❑ After injection reschedule appt and reorder 2 weeks pre-injection

CAB/RPV Program Staffing (Initial)

Provider	• Determine clinical appropriateness of CAB/RPV • Provide initial counseling on CAB/RPV and associated processes • Notify Case Manager and Pharmacist of clinical decision
Patient's Case Manager	• Complete PAs/PAP paperwork for patients filling at external pharmacies (i.e. MSDH, PAP, mail order specialty pharmacies) • Schedule patients' initial and continuation injection appointments • Follow up with patients who miss injection appointments
Specialty Pharmacist	• Perform benefits investigation to determine appropriate roles for those involved in the CAB/RPV process • Complete PAs for patients eligible for the specialty pharmacy program • Provide assistance to case managers completing PAs and PAP paperwork for patients ineligible for the specialty pharmacy program • Contact all patients and provide additional education around oral lead-in and injection therapy • Order oral lead-in for all patients • Maintain master list of CAB/RPV patients (filling schedules, receiving CAB/RPV from all pharmacy sources, reviewing appointment adherence, moving reminders).
Injection Nurses	• Move patient to appropriate waiting areas and clinic room at appointment • Administer and manage CAB/RPV injections (time out of refrigeration, documentation) on appointment day

Checklist to Add CAB/RPV Patients to Our Program (Current)

- ❑ Provider recommendation as appropriate and conversation with the patient
- ❑ Verify insurance coverage (benefits investigation)
- ❑ Get copay card/grant funding information if needed to add to chart
- ❑ Have optional oral lead-in delivered to the patient (optional)
- ❑ Add patient to master reminder list
- ❑ Call to check on patient's tolerance after 14 days
- ❑ If patient is tolerating, order first loading dose and schedule injection #1
- ❑ After injection #1, call in 14 days to check on patient and then order maintenance injection and schedule injection visit
- ❑ After each continuation injection reschedule appointment and reorder 2 weeks pre-injection

CAB/RPV Program Staffing (Current)

Provider	• Determine clinical appropriateness of CAB/RPV • Provide initial counseling on CAB/RPV and associated processes • Notify designated CAB/RPV nurse and pharmacists of clinical decision
Specialty Pharmacists	• Perform benefits investigation to determine appropriate roles for those involved in the CAB/RPV process • Complete PAs for patients eligible for the specialty pharmacy program • Provide assistance to CAB/RPV nurse completing PAs and PAP paperwork for patients ineligible for the specialty pharmacy program • Contact all patients and provide additional education around oral lead-in and injection therapy • Order oral lead-in for all patients • Utilize CAB/RPV master list to ensure injections are filled and make it to the clinic in a timely fashion
Designated CAB/RPV Nurse	• Complete PAs/PAP paperwork for patients filling at external pharmacies (i.e. MSDH, PAP, mail order specialty pharmacies) • Schedule patients' initial and continuation injection appointments • Maintain master list of CAB/RPV patients (filling schedules, receiving CAB/RPV from all pharmacy sources, reviewing appointment adherence, moving reminders). • Follow up with patients who miss injection appointments • Move patient to appropriate waiting areas and clinic room at appointment • Administer and manage CAB/RPV injections (time out of refrigeration, documentation) on appointment day

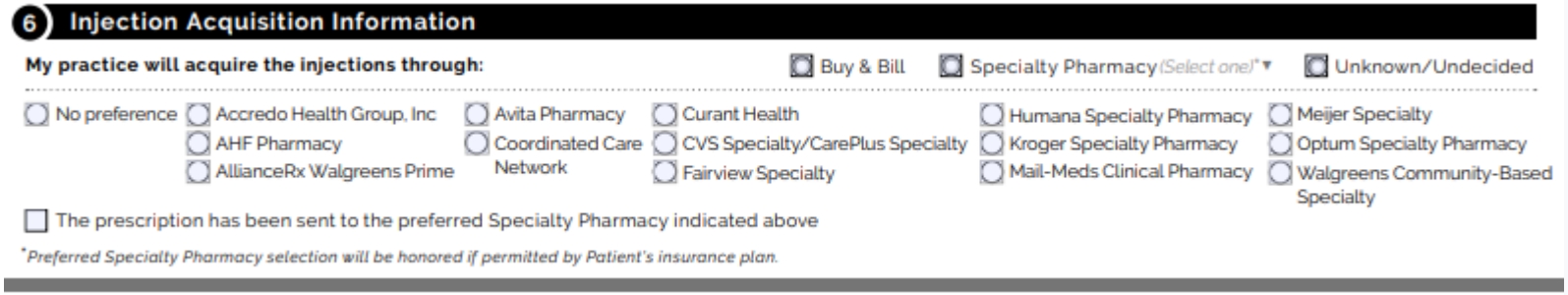
Payer Sources for the Medication in Mississippi

- Commercial Insurance
- Medicare
- Medicaid of MS
- MSDH ADAP
- Manufacturer patient assistance program (PAP)

Having an Initial Conversation with a Patient

- Start conversations by asking open ended questions about a patient's motivation for wanting to begin long acting, injectable ART
  - Does the patient's motivation fit with the reality of how the injection will practically fit into the patient's treatment?
  - Do statements made by the patient raise other points you should discuss with a patient?
  - Ask clarifying questions if needed, while respecting a patient's autonomy to take some part in their care
- Try to check mental boxes to be sure this is an appropriate patient as we discuss the therapy
  - Prescreening may have already be done - will you use a list to remember who's a candidate? Is this double-checked during enrollment?
  - Go over adverse effects, DDIs, and the need for a real commitment to coming for appointments. Setting a more stringent bar of expectation could help to verify the patient is committed to therapy.
- Get the patient to sign an application if you're using a printed form for PAP patients
  - Even if a patient is unsure, keep the form with a note on the front with a date to check-in on the patient's decision to proceed. Having an already signed, partially filled out form will avoid having to coordinate an extra meetup date with the patient at a later time.
- Present the patient with any resources when the conversation is complete

How Do I Acquire CAB/RPV?



6 Injection Acquisition Information

My practice will acquire the injections through: ☐ Buy & Bill ☐ Specialty Pharmacy *(Select one)** ☐ Unknown/Undecided

☐ No preference	☐ Accredo Health Group, Inc	☐ Avita Pharmacy	☐ Curant Health	☐ Humana Specialty Pharmacy	☐ Meijer Specialty
	☐ AHF Pharmacy	☐ Coordinated Care Network	☐ CVS Specialty/CarePlus Specialty	☐ Kroger Specialty Pharmacy	☐ Optum Specialty Pharmacy
	☐ AllianceRx Walgreens Prime		☐ Fairview Specialty	☐ Mail-Meds Clinical Pharmacy	☐ Walgreens Community-Based Specialty

☐ The prescription has been sent to the preferred Specialty Pharmacy indicated above

**Preferred Specialty Pharmacy selection will be honored if permitted by Patient's insurance plan.*

Call to check with your medication wholesaler/distributor

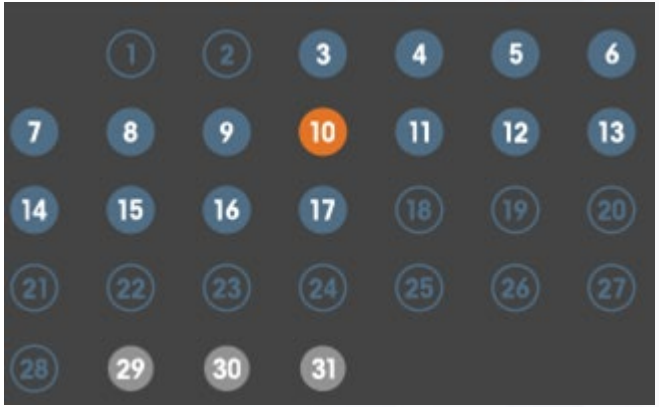
When To Dose CAB/RPV:

At ASCC, a majority of patients using CAB/RPV are on a bi-monthly injection schedule where they receive injections every 56 days. Two patients who began on monthly dosing still continue every 28 day-scheduling due to preference.

For patients receiving bi-monthly injections, the target dosing period is 7 to 9 weeks from the previous injection date.

During initial education, it is stressed to patients to make the clinic staff aware of any upcoming vacations, etc. that may hinder this dose timing frame.

In the event a patient will be outside of the typical dosing window, the pharmacists and CAB/RPV nurse in clinic will coordinate appropriate re-scheduling of appointments or oral bridge therapy.



https://cabenuvahcp.com/content/dam/cf-viiv/cabenuva hcp/master/pages/dosing/CABENUVA_Dosing_and_Admin_Guide.pdf

“How long will this take?”

- Set expectations ahead of time with patients. Let the patient know that total appointment time for injection appointments will be ___.
- Upon patient check-in, IMMEDIATELY pull medication from refrigeration and allow it to come to room temperature by remaining out for 15 minutes before giving the injection to the patient. Write the time taken out of refrigerator on the box.
- Have an easy/quick check-in procedure for these patients, similar to a vaccine appointment.
- Perhaps have a specific room or space that’s typically used for this sort of appointment if your office has this option.
- The patient will have to remain in the office for 10 minutes to be certain no post-injection reaction occurs. This is also something to make clear ahead of time.

Making the Process Run Smoothly

- Consider having one staff member lead the project and be in charge of all movement of patients through your program.
- If you have multiple staff members on the project, have one for the enrollment stage, one for the initiation stage, and one for the maintenance phase. This may decrease the chance of missed steps.
- Give yourself time to process a wave of enrollments at a time. Treat this as a pilot program initially and then move patients through in waves so staff is not overwhelmed.
- Make certain all providers understand the expectations involved in enrollment of patients-
    - How long is the process?
    - Who is the contact person?
    - Who follows up for missed injection appointments?
    - What initial counseling is done within the clinic regarding patient expectations?

What Do You Need?

- Refrigeration for medication storage
- A private area of the clinic for administration
- Method to organize ordering, patient contact, medication acquisition, billing, and monitor for any missed doses
- Staff to administer injections and perform above tasks

What about Clinics with Different Characteristics?

Thus far we've discussed implementation in a large clinic.

What if we're talking about a smaller clinic with limited staff?

Strategies that can be used include:

- ➔ Limited days for injections
- ➔ Restricting to dependable patients
- ➔ Consolidating staff duties to free one person
- ➔ Relying more on manufacturer for support – fulfillment, assistance

What does

YOUR CLINIC

look like?

Special Thanks

- Peyton Herrington, PharmD, AAHIVP

The University of Mississippi Medical Center

Resources for Beginning to Administer CAB/RPV:

https://www.seaetc.com/sample-cabenuva-protocol-and-clinician-reference-guide/

https://aahivm.org/

https://cabenuvahcp.com/getting-started/

https://www.hiv.uw.edu/