WPIC/Street Medicine Open Access Clinic:
Long-Acting Injectable PrEP (IM Cabotegravir) Protocol

Purpose of this Guide: Cabotegravir is a long-acting (LA) injectable intramuscular medication approved for the prevention of HIV disease. This guide provides a detailed overview of the logistical processes and considerations surrounding the receipt of IM Cabotegravir (i.e. Apretude) among select patients at high risk for acquiring HIV who are receiving care at the WPIC Street Medicine Open Access Clinic (i.e. 555 Stevenson Street) or satellite clinical sites frequented by Street Medicine patients. Please note that this is a work-in-progress.

A. **Eligibility:**
   a. Regular Engagement with WPIC – *For at least 3 months* prior to initiation of LA CAB, patient should be engaging with the Street Medicine medical/nursing teams via Open Access Clinic at 555 Stevenson and/or satellite sites (i.e. SOS van, Syringe Access Sites, SIP/Nav. Sites, Med Respite, etc.)
   b. At risk for HIV (sexually, IDU, etc.) – *Note: IM CAB not yet explicitly studied for use in PWID*
   c. Weight >= 35kg
   d. Expressed interest/motivation to start LAI PrEP and agree to basic protocol expectations:
      i. q2 months gluteal injections - Ventrolateral preferred (PK from other sites unknown)
      ii. q2 months blood draws for labs (HIV VL and HIV ag/ab) – see details below
   e. NOT taking meds with DDIs – Rifampicin, rifapentine, carbamazepine, oxcarbazepine, phenytoin, phenobarbital*. (May use Rifabutin with caution, though may mildly reduce CAB exposure).*

B. Visit Guide:
   a. **Pre-initiation Visit (Week -1):** - should be an MD/NP visit
      i. Discuss LA-CAB PrEP benefits, expectations, risks, alternatives & contingency planning.
         1. Benefits:
            a. High efficacy for HIV prevention in all genders
            b. Reduced pill burden
            c. Possibly, reduced stigma
         2. Expectations:
            a. Return for next injection in 1 month, then RTC q2 months for injections
            b. Lab draws q2 months with injections
         3. Risks:
            a. Injection Site Reactions – Mild pain/tenderness/induration at site for 1-3 days is frequent (80% of patients), but transient and often resolves after the first 2-3 injections. Can take OTC ibuprofen 1-2 hours prior/after for PPx use massage at the site, and/or apply warm compress/heating pad for 15-20 minutes after injection.
            b. INSTI Resistance – While breakthrough infections are rare, INSTI resistance has been observed among a small minority of individuals who acquired HIV despite receiving on-time injections. Additionally, starting LA-CAB PrEP with undiagnosed HIV infection can select for INSTI mutations. To date, INSTI resistance has not been observed in settings of new HIV acquisition ≥6 months after the last LA CAB administration.
            c. HIV acquisition (especially in setting of late injections) – If a patient is delayed for an LA-CAB injection or discontinues LA-CAB but continues to engage in HIV risk behaviors, they should notify provider ASAP for support with reducing their

risks of acquiring HIV. We can Rx TDF/FTC or TAF/FTC (if MSM) PO daily (or 2-1-1) to reduce their exposure risk to HIV. Providers should consider providing PO TDF/FTC TAF/FTC coverage proactively prior to the first late injection so the patient will have access to the pills if unexpected late injections occur.

4. Alternatives:
    a. Daily TDF/FTC – If eGFR > 60 mL/min
    b. Daily TAF/FTC – If eGFR > 30 mL/min and MSM or TGWSM
    c. On-demand (2-1-1) TDF/FTC – If eGFR > 60 and MSM or TGWSM. (Involves taking 2 tabs TDF/FTC 2-24 hours prior to an expected sexual encounter, followed by a single tab 24 hours and 48 hours after the initial dose).
5. Contingency Planning – In case of potential for missed/late injections:
    a. Update housing status, locations in community, patient phone numbers and/or email address (if applicable) in EMR.
    b. 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.
    c. Confirm with patient whether we may contact these individuals in case attempting to locate them for late injections.
    d. **Review missed/late injection protocol with patient (see page 3, section C)**

ii. **Order Baseline Labs:** Draw *within 1 week* prior to first dose. **Bolded** labs are required. Others listed are highly recommended but not required, and labs with * demarcation are not required for LA-CAB, but useful in case we later need to switch to daily oral TAF/FTC or TDF/FTC.

1. **HIV-1 RNA VL**
2. **HIV Ag/Ab (lab-based test)** – Can initiate LA CAB once HIV Ag/Ab is confirmed as negative (even if RNA VL still in process, though it generally also returns within 24 hours). *If planning for same-day LA CAB start, may use POC HIV ag/ab finger-stick test to document initial negative test, but ALSO must draw blood for HIV-1 RNA VL and HIV Ag/Ab lab-based test on the same day.*
3. **Syphilis serologic testing**
4. **GC/CT/Trich/M. gen NAAT at all relevant sites** (i.e. urine, penile, cervicovaginal, rectum, throat)
5. Urine pregnancy test – For patients with childbearing potential. *(Should also discuss starting a long-acting birth control option if not trying to become pregnant).*
6. HAV Ab, HBV sAb, HCV Ab – Only if no prior documentation of immunity (HAV, HBV) or no testing done within the last 12 months (HCV)
7. BMP* – Only if none available from the past 6 months
8. HBV sAg* – If not HBV immune

iii. Order IM CAB from pharmacy:

1. Epic order:
    a. Cabotegravir (Apretude) 600mg *every 8 weeks*
    b. Refills: #4
    c. In notes to pharmacy: "Plan to administer loading doses on [date #1] and [date #2 – in 4 weeks], then q8 weeks; send to [Clinic Name]; callback #: _____ if any problems."

2. No PA is required for MediCal recipients; however, may be required for patients with other forms of insurance. ViivConnect is a resource to assist with navigating medication access and coverage.

b. **First injection Visit (Week 0)** - should be an MD/NP visit
   i. Confirm that patient has had at least 1 negative HIV test within past 7 days (see above) and that an HIV-1 RNA VL and HIV Ag/Ab lab-based tests have both been drawn.
   ii. Review above protocol expectations with patient again briefly + answer any questions. Counsel patient on injection site reactions.
   iii. Administer LA-CAB (600mg) via ventrogluteal injection
      1. **Order as a 1-time dose in MAR for today**
      2. **Order as q8-week dosing in MAR starting in 4 weeks**
   iv. Ensure patient is aware of next injection dose date (in 28 days)
   v. **Order labs: standing HIV VL, HIV Ag/Ab, and STI/RPR labs (x3) to facilitate future visits as potential RN-only visits**

c. **Maintenance Visits (Week 4, Week 12, then q2 months)** – could be an MD/NP visit or an RN visit
   i. Assess signs/symptoms for acute HIV infection and side effects of LA-CAB
   ii. Respond to any new questions/concerns and encourage continued q2 monthly visits
   iii. Draw labs – HIV-1 RNA VL and HIV Ag/Ab
      1. After at least 3 injections have been given (i.e. Week 12), if patient is unable to tolerate q2 month lab draws, could consider q4 month lab draws but obtain POC HIV fingerstick test on injection days where no labs drawn.
   iv. Offer STI screening if indicated (should obtain at least q4 months on LA-CAB patients)
   v. Administer LA-CAB (600mg) via ventrogluteal injection + ensure patient is aware of next injection dose date (in 56 days, i.e. 8 weeks)

C. Missed/Late Injections or Discontinuing LA-CAB:

a. Goal schedule:
   i. Dose LA-CAB 600mg at Week 0, 4, then every 8 weeks (+/- 7 days of target)

b. If missed injection <4 weeks late:
   i. If no contraindications, start qd TDF/FTC or TAF/FTC (if MSM) until injection can be given.
   ii. As soon as possible: obtain HIV POC test + draw blood for HIV Ag/Ab and HIV VL. Administer CAB-LA (if POC test negative), with next dose scheduled **in 8 weeks.**

c. If missed injection > 4 weeks late:
   i. If no contraindications, start qd TDF/FTC or TAF/FTC (if MSM) until injection can be given.
   ii. As soon as possible: obtain HIV POC test + collect blood draw for HIV Ag/Ab and HIV VL. Administer CAB-LA (if POC test negative), with next dose scheduled **in 4 weeks (i.e. re-load).**

d. If planning to discontinue LA-CAB: The PK "tail" of cabotegravir is highly variable but median time to undetectable levels has been estimated of ~44 weeks in men and ~67 weeks in women.
   i. If no contraindications, start oral qd TDF/FTC or TAF/FTC (if MSM) daily (or TDF/FTC on-demand, if eligible) for HIV prevention within 8 weeks of last injection
   ii. Obtain HIV VL and HIV Ag/Ab test q3 months for at least 12 months after discontinuation
   iii. Educate about nPEP

e. Patient is hospitalized or incarcerated when injection is due:
   i. Ask the inpatient team if able to order LA-CAB 600mg for inpatient administration.

ii. If inpatient LA-CAB unavailable and there are no contraindications, recommend to inpatient or JHS provider that the patient start TDF/FTC qd or TAF/FTC qd until able to follow up.
iii. Coordinate plan for patient to present back to clinic on the day of or after discharge.

D. Tracking Injection Due Dates & Adherence

- Epic Documentation:
  - Shared Epic Patient List (Provider) - Add patient to shared "LA ART/PrEP List" when first ordering the medication **+ cc chart to Health Worker and/or PrEP Clinical Lead for tracking.**
  - MAR (Provider + RN) - At time of initiation (i.e. first injection visit, Week 0), LA-CAB should be ordered in MAR as a 1-time clinic-administered medication through Epic AND a second MAR order should be placed for repeating doses q8 weeks to start in 4 weeks after the 1st injection.
  - Shared Blue Sticky Note in Patient's Chart (Provider or RN) – Record next injection due date
  - Problem List (Provider) – Create "High Risk for STIs" as a new problem for the patient, and list the date of CAB/RPV initiation under list problem list information
- Weekly Huddle on LA PrEP and LA ART patients
  - Should involve multi-disciplinary team, including *at minimum*: Health Worker, PrEP Clinical Lead (MD/NP), Street Medicine RN Outreach Representative, Clinic RN Representative
  - Purpose – Very short (<30 min) weekly meeting to:
    - Review new and active patients *currently* on LA CAB or LA CAB/RPV
    - Update the shared Excel Sheet on Microsoft Teams for internal tracking
    - Identify patients needing injection reminders (i.e. injection due within next 7 days) and request outreach (via phone, text, communication with partnering CBOs, and/or direct outreach) either by the ETE Health Worker or an Outreach RN
    - Triage potential issues related to adherence or labs + update recommendations for future visits via Epic documentation

E. Special consideration regarding LA CAB administration

- Wait ~15 minutes after removing from refrigeration before administering to patient
  - LA-CAB does NOT require refrigeration (unlike CAB/RPV) but should be stored at 2°C to 25°C (36°F to 77°F) in the original carton until ready to use.
  - Exposure up to 30°C [86°F] is permitted.
  - Once the suspension has been drawn into the syringe, the injection should be administered as soon as possible, but may remain in the syringe for up to 2 hours.
- A 1.5'" needle is provided in the dosing kit, but **use a 2" needle if patient BMI > 30**
- LA-CAB should be administered via IM injection in ventrogluteal area (see visuals starting on page 45 of: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/215499s000lbl.pdf)
- Before administration, in addition to patient name and DOB, confirm:
  - Dates of last injection (should be 56 days ago, +/- 7 days if after 2nd injection)
  - Recent negative HIV status: HIV-1 Ag/Ab and HIV RNA (within last 2 months)
  - No new use of interacting medications: carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampin, rifapentine, or rifabutin (not a contraindication, but alert provider)
- After administration, offer heating pad to apply to area to reduce risk of ISR. (If no contraindications, provider should have offered ibuprofen PRN already.)
- ***Obtain concurrent lab draw (for HIV Ag/ab and HIV RNA VL) with each LA-CAB injection***