BALTIMORE CITY HEALTH DEPARTMENT

1001 E. Fayette Street • Baltimore, Maryland 21202
Brandon M. Scott, Mayor
Letitia Dzirasa, M.D., Commissioner of Health

Cabotegravir - Pilot protocol

1. Criteria
    a. Patient is not a candidate for nPEP
    b. Ability to get labs at baseline and regularly at clinic or off-site Labcorp
    c. Pt would like to be on injectable PrEP
    d. Pt has verbalized understanding of required dosing visits and testing schedule
    e. Pt weighs greater than 35 kg (77 lbs)
2. Do not use CAB-LA/ Contraindications
    a. Known HIV infection
    b. Previous hypersensitivity reaction to CAB
    c. receiving carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampin, and/or rifapentine. See Appendix D for medication interactions
    d. Pregnant or planning to become pregnant
3. Prescribing Considerations
    a. Long-Acting Cabotegravir 600 mg IM is currently the only FDA approved medication for injectable HIV pre-exposure prophylaxis
        i. Injectable PrEP is preferable to oral prep for those who have a contraindication to oral PrEP or who had side effects with oral prep.
        ii. Injectable prep is suitable for cis-men and women and well as transmen and trans women.
        iii. Injectable PrEP should remain a patient centered choice. Patients may choose CAB or oral prep based on their self-assessment of what will work for them
    b. Choosing between oral prep and injectable prep
        i. Pregnancy or possibility of becoming pregnant
            1. Cabotegravir is not approved for use in pregnant women. Because of the residual concentrations that remain in circulation for up to 12 months individuals should be
        ii. Kidney Dysfunction/Impairment
            1. Cabotegravir is safe to use in individuals who have eGFR below 30. CAB_LA should be considered over oral F/TDF and F/TAF for patients with baseline kidney impairment.
        iii. History of adverse effects on F/TDF or F/TAF.
4. Health History / Education and Counseling
    a. Discuss indications for prep
    b. Discuss HIV risk reduction
    c. Counsel on non-pharmacological risk reduction measures
    d. Complete Medical and sexual health hx
    e. Review side effects and serious adverse effects
        i. Injection site reaction
        ii. Liver impairment
        iii. Depressive Disorder
    f. Review dose and lab requirements

g. Review time to protection
    i. Let patient know that there is no data on time to protection
    ii. BCHD always recommends safer sex practices to reduce risk of acquiring HIV.
h. Review risks associated with non-adherence
    i. HIV seroconversion
    ii. Developing INSTI resistant HIV mutation
i. Review safe discontinuation
j. Patients considering PrEP should be informed of all FDA approved options.

5. Initiation Labs
    a. Initial Labs – At this time Provider and RN should discuss each patient individually before starting CAB-LA. See Appendix A initiation flow charts for PrEP naïve patients and for patients already on oral F/TDF or F/TAF.
        i. HIV RNA – all patients should have a NEGATIVE HIV RNA result within 7 days of starting CAB. HIV RNA test should be obtained AFTER medication has been delivered to clinic.
        ii. Rapid HIV as indicated (POC RNA eventually?)
        iii. HIV 4th gen Ab/Ag
        iv. RPR
        v. GC/CT
        vi. Hep C
        vii. Hep B serology
        viii. Pregnancy test
        ix. Lipid Panel (consider at baseline for option to switch to oral PrEP, recommended but not required)
        x. CMP (consider at baseline for option to switch to oral PrEP, recommended but not required)
6. *Lab Review – Providers and RNs should review baseline labs together before initiating CAB
7. Ongoing labs - See Appendix B
    a. At 3rd injection (month 4) and every 4 months after
        i. HIV RNA
        ii. Rapid HIV*(if patient requests or is experiencing acute HIV s/sx)
        iii. RPR
        iv. GC/CT
    b. At 4th injection (month 6) and every 2 months after
        i. HIV RNA
        ii. Rapid HIV*
8. Dosage and Administration
    a. Dosage: Long acting intramuscular cabotegravir (Apretude) 600 mg (3 mL)
        i. Initiation/Month 1 – 1st injection
            1. CAB-LA Apretude, 600 mg, 3 mL injection will be given at BCHD by a Provider or PrEP RN
        ii. Month 2 – 2nd injection

1. CAB-LA Apretude, 600 mg, 3 mL injection will be given at BCHD by a provider or PrEP RN

iii. Month 4, 8, 12 - Injections 3, 5, 7, …
1. CAB-LA Apretude, 600 mg, 3 mL will be given at BCHD by a provider or PrEP RN
2. These visits should include STI screening and behavioral risk reduction counseling

iv. Month 6, 10, 14 – Injections 4, 6, 8...
1. CAB-LA Apretude, 600 mg, 3 mL injections will be given at BCHD by a provider or PrEP RN,
    a. consider MA injection visits for these
2. These visits should include behavioral risk reduction counseling

b. Storage: CAB-LA Apretude vials should be stored in the refrigerator in original carton. Temperatures should be between 35.6° - 77° F (2-25 degrees Celsius). Do not freeze.
    i. Bring medication to room temperature. Do not exceed 88°F.
    ii. Inspect for particulate matter. Discard if product appears discolored or has particulate matter. Shake vial vigorously to appear uniform.

c. Preparation and Injection: See Appendix C
    i. Draw up 3 mL dose into the provided syringe. Injections should be given immediately after drawing up from vial. If medication is in syringe longer than 2 hours discard.
    ii. The injection should be given IM preferably in the ventrogluteal site.
    iii. Discard syringe and vial in sharps container

9. Visit schedule
    a. See Appendix B
    b. If possible, start patients who do not have contraindications or history of side effects on oral PrEP (F/TDF or T/TAF) or oral cabotegravir per pt preference if concerned about tolerance to Cabotegravir (for 28 days of less) (?)
        i. Except those with contraindications
    c. 2nd injection 1 month after the first, then every 2 months
    d. Consider scheduling injections on the same day of the week for multiple patients
        i. i.e. reserve a clinic block to have injection visits. Cluster injection initiations, pharmacy ordering, and administrations.
10. Unplanned Missed injection visits- See Appendix D
    a. For patients who have received (1) dose of 600 mg (3 mL) CAB-LA, if second injection is missed and time since 1st injection is:
        i. Less than or equal to 2 months,
            1. Re-draw HIV RNA test
            2. Administer 2nd injection
            3. Review HIV RNA result
            4. If appropriate, continue injections every 2 months
    b. For patients who have received (1) dose of 600 mg (3 mL) CAB-LA, if second injection is missed and time since 1st injection is:

i. Greater than 2 months, (these people will need to have loading dose re-started)
    1. Re-draw HIV RNA test
    2. Consider waiting to review results
    3. Re-administer 1st injection if HIV RNA = Non-reactive
    4. Schedule 2nd injection for 30 days after 1st injection
    5. Continue injections every 2 months

c. For patients who have received at least (2) doses of CAB-LA 600 mg (3mL), if third or subsequent injection is missed and time since last injection is:
    i. Less than or equal to 3 months,
        1. Re-draw HIV RNA test
        2. Administer injection
        3. Review HIV RNA result
        4. If appropriate, continue injections every 2 months

d. For patients who have received at least (2) doses of CAB-LA 600 mg (3mL), if third or subsequent injection is missed and time since last injection is:
    i. Greater than 3 months, (these people will need to have loading dose re-started)
        1. Re-draw HIV RNA test
        2. Wait to review results
        3. Re-administer 1st injection if HIV RNA = Non-reactive
        4. Schedule 2nd injection
        5. Continue injections every 2 months

11. Planned missed injection visits
    a. If a patient plans to miss a scheduled every-two-month continuation injection, the patient should be prescribed oral Cabotegravir.
        i. 30 mg Cabotegravir tablet, Take one tab by mouth once daily, #30, 1 refill.
        ii. Patient should start oral cabotegravir approximately 2 months after last CAB-LA injection
        iii. Patient should resume every-two-month injections within 3 days of finishing oral prescription.
    b. If a patient plans to miss more than one scheduled every-two-month continuation injection,
        i. Patient should be prescribed F/TAF or F/TDF if oral prep is not contraindicated.
12. Discontinuing CAB-LA
    a. Counsel patients about the “long-tail” associated with CAB-LA
        i. CAB-LA can remain in an individuals’ system for up to 12 months (median time to undetectable was 44 weeks for men and 67 weeks for women) however, the level of protection will wane. CAB-LA affords no protection from HIV if injections are not given every 2 months.
        ii. There is a risk of HIV seroconversion as CAB-LA levels reach non-protective
        iii. There is a risk of acquiring an existing or de-novo HIV mutant strain that is resistant to CAB or other integrase inhibitor medication class. This may impact treatment options in the future.

b. Ask patient to commit to HIV screening every 3 months after discontinuing for 12 months
    i. HIV RNA tests are preferred to HIV antigen/antibody tests
c. Recommendation to switch to oral prep, if prep is still indicated and if oral prep is not contraindicated
    i. Patient should start oral prep 8 weeks after last CAB-LA injection
d. Re-educate patient about npep
e. Patient should remain on BCHD PrEP panel until (4) quarterly HIV RNA test results have been documented
    i. RN should be primarily responsible for outreach and for scheduling quarterly screenings

13. Injectable PrEP Delivery from Specialty Pharmacy
    a. All CAB-LA PrEP for Eastern and Druid patients should be delivered to the Eastern Health Department at 1200 E. Fayette Street Baltimore MD 21202.
    b. All packages should be Attn: Omolola Akolo and Caroline Sacko for PrEP program patients
    c. Injectable PrEP should be immediately stored in pyxis refrigerator under "Injectable PrEP" in original carton. Temperatures should be between 35.6° - 77° F (2-25 degrees Celsius).
    d. PrEP Nurse Manger is responsible for transporting medication to DHD and loading in pyxis refrigerator.
    e. PreP Nurse Manger should notify PrEP Nurse of transport to DHD.

14. Paying for Injectable Cabotgravir
    a. For patients with commercial insurance
        i. Step 1: Enroll patient in ViiV Connect and obtain patient authorization/signature
            1. Counsel pt that signature will authorize Viiv Connect, the pharmaceutical drug company that manufactures CAB-LA to obtain, use, and share personal information such as identifiers, health, medical, and prescription information, insurance information, and financial information. Counsel patient of their right to refuse telephone contact for notifications and marketing by Viiv.
            2. share e-signature link if needed: esign-ondemand (viivconnectportal.com)
        ii. Step 2: Select 'Full benefits investigation' on enrollment form
            1. Once faxed/sent Viiv will contact BCHD in 24-48 hours
        iii. Step 3: Review coverage and select payment route
            1. A patient's insurance may require a PA, may not cover Apretude, or may cover it fully. Viiv will communicate findings to us
            2. There are three payment routes:
                a. Buy and bill: our clinic purchases from distributor. Then bill patient's insurance

b. Pharmacy: benefits investigation finds that the medication is covered (fully or with PA needed) under the medical benefits portion of the patient's plan. BCHD will use specialty pharmacy to send in prescription.
c. Specialty pharmacy: benefits investigation finds that the medication is covered (fully or with PA needed) under the pharmacy benefits portion of the patient's plan. BCHD will use specialty pharmacy to send in prescription.

iv. Step 4: Viiv will assess which pharmacies are contracted with insurance. Although Viiv sends Rx information to pharmacy, BCHD should contact and send in prescription to specialty pharmacy.
v. Step 5: Once patient had approval through plan Viiv will auto enroll in patient savings program (copay coupon) $7,500 to cover the copay cost of the medication (i.e. deductible and copay) AND up to $350 for administration cost annually.
vi. Step 6: Specialty pharmacy delivers by mail to 1200 E. Fayette for administration

b. For patients who are uninsured
i. Step 1: Enroll patient in Viiv Connect and obtain patient authorization/signature
ii. Step 2: Viiv will review enrollment and make decision about coverage in about 48 hours
iii. Step 3: BCHD call Viiv to discuss/ verify enrollment
iv. Step 4: BCHD call in CAB-LA prescription to GSGK contracted Viiv pharmacy
1. For PAP uninsured patients the phone number is 1(844)588-3288
2. Specify delivery to EHD clinic and ATTN: Omolola and Caroline Sacko

15. Patient Follow up
a. Schedule lab review
b. Anticipate time for insurance and pharmacy approval
c. Offer oral prep
d. Repeat HIV RNA if labs if 1st injection is greater than 7 days from baseline labs.
16. Continuing CAB for PrEP
a. Return appts should be scheduled at each injection visit. Consider scheduling on the front end of the 7 day window
b. For dose 2 onwards clinic contacts specialty pharmacy directly to arrange delivery of medication.
c. BCHD PrEP team should contact pharmacy 2-4 weeks before scheduled administration for appointment

.

.

.

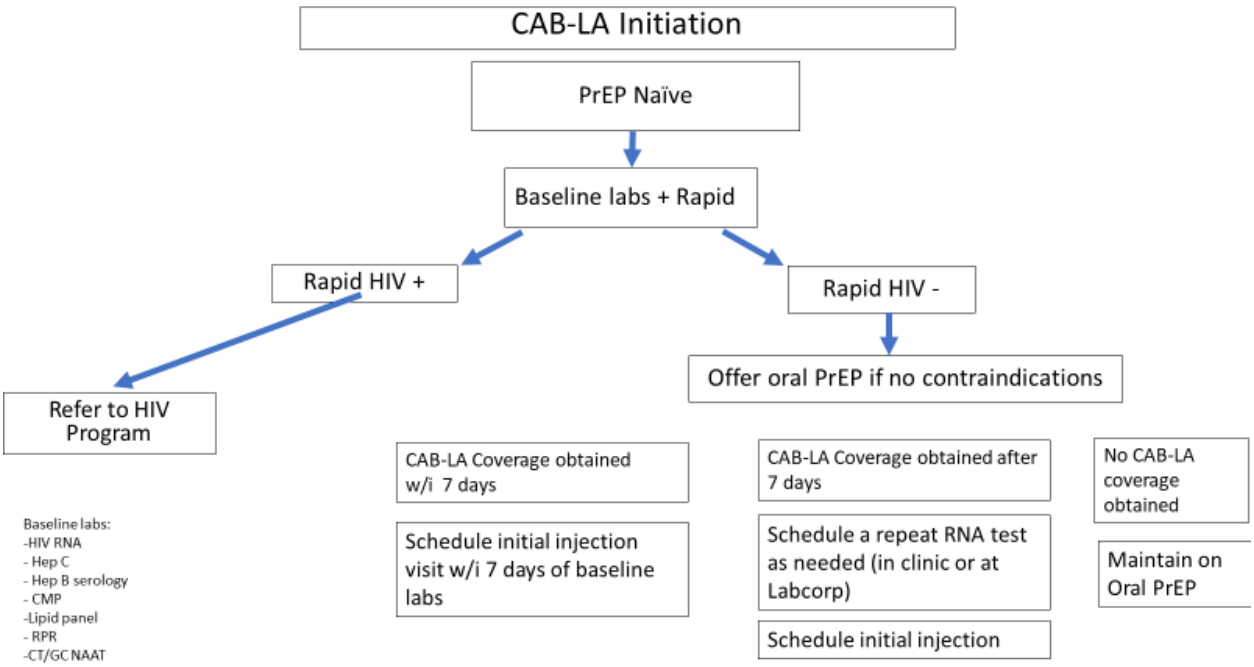
Research:

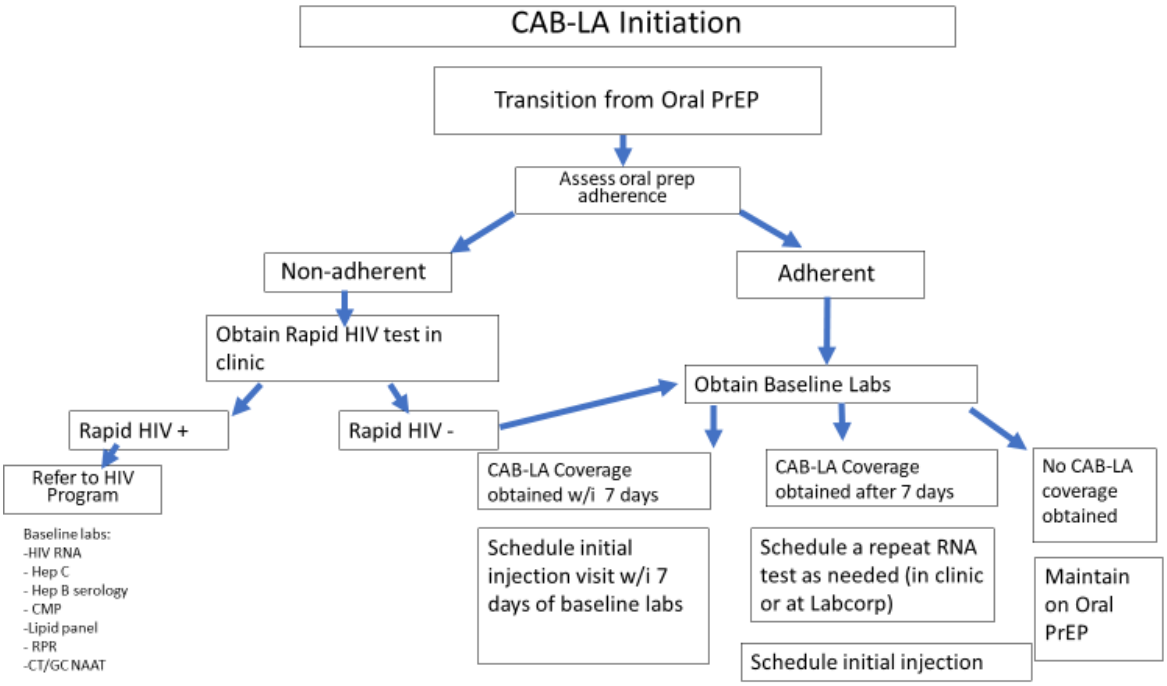
HTPN 083

HTPN 084

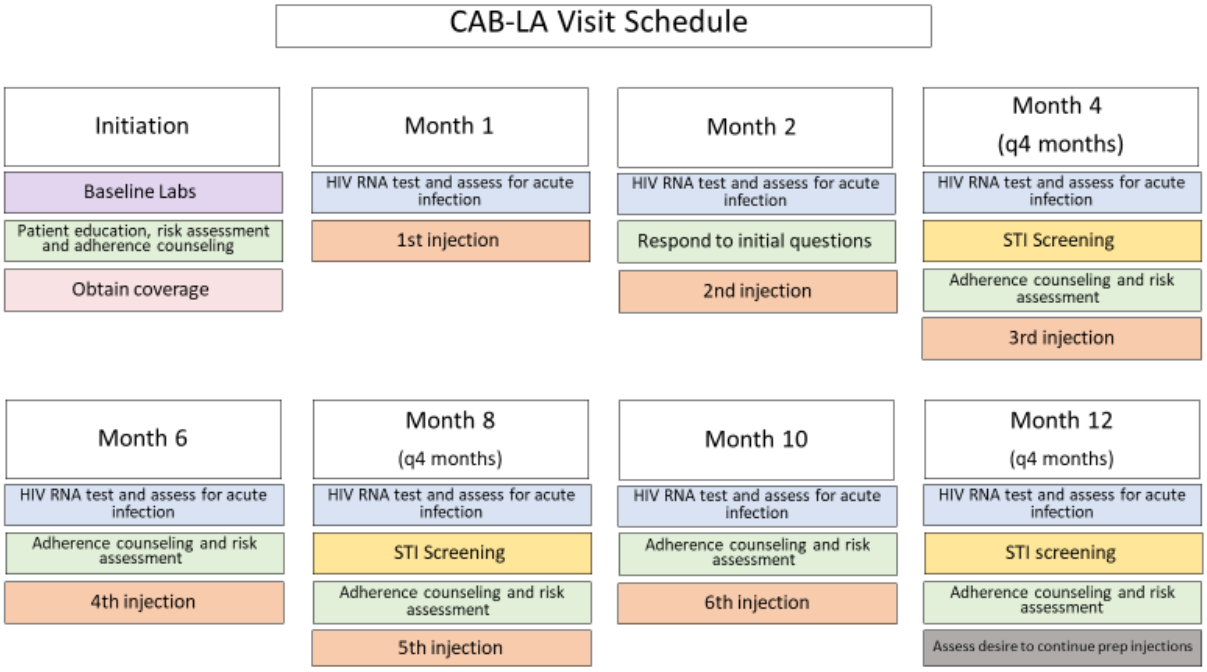
Appendices:

Appendix A




CAB-LA Initiation
Transition from Oral PrEP
Assess oral prep adherence
Non-adherent
Adherent
Obtain Rapid HIV test in clinic
Obtain Baseline Labs
Rapid HIV +
Rapid HIV -
Refer to HIV Program
Baseline labs:
-HIV RNA
- Hep C
- Hep B serology
- CMP
-Lipid panel
- RPR
-CT/GC NAAT
CAB-LA Coverage obtained w/i 7 days
CAB-LA Coverage obtained after 7 days
No CAB-LA coverage obtained
Schedule initial injection visit w/i 7 days of baseline labs
Schedule a repeat RNA test as needed (in clinic or at Labcorp)
Maintain on Oral PrEP
Schedule initial injection

Appendix B:


CAB-LA Visit Schedule
Initiation
Baseline Labs
Patient education, risk assessment and adherence counseling
Obtain coverage
Month 1
HIV RNA test and assess for acute infection
1st injection
Month 2
HIV RNA test and assess for acute infection
Respond to initial questions
2nd injection
Month 4 (q4 months)
HIV RNA test and assess for acute infection
STI Screening
Adherence counseling and risk assessment
3rd injection
Month 6
HIV RNA test and assess for acute infection
Adherence counseling and risk assessment
4th injection
Month 8 (q4 months)
HIV RNA test and assess for acute infection
STI Screening
Adherence counseling and risk assessment
5th injection
Month 10
HIV RNA test and assess for acute infection
Adherence counseling and risk assessment
6th injection
Month 12 (q4 months)
HIV RNA test and assess for acute infection
STI screening
Adherence counseling and risk assessment
Assess desire to continue prep injections

Appendix C

APRETUDE Preperation and Injection Intrucations.PDF

Appendix D

Table 6 Cabotegravir PrEP Drug Interactions (https://www.hiv-druginteractions.org/)

Rifampicin, rifapentin	**Do not co-administer with CAB** Rifampicin and rifapentine increase metabolism of CAB and may result in significantly reduced exposure to protective levels of CAB [142, 143]
Rifabutin	**Co-administer with caution** Rifabutin moderately increases metabolism of CAB and may result in somewhat reduced exposure to protective levels of CAB[144]
Hormonal contraceptives	No significant effect[145]
Feminizing hormones (Spironolactone, estrogens)	No data yet available[146]
Carbamazepine, oxcarbazepine, phenytoin, phenobarbital	**Do not co-administer with CAB** Concern that these anticonvulsants may result in significantly reduced exposure to protective levels of CAB but strength of evidence is weak

Baltimore City Health Department
1001 E. Fayette Street • Baltimore, Maryland 21202