Lifelong Long-Acting Injectable PrEP Protocol

Adapted from Ward 86 Long-Acting Injectable ARV Protocol

Background

APRETUDE is an injectable prescription medicine to prevent HIV infection in adults. APRETUDE contains only one medication, cabotegravir, an integrase strand transfer inhibitor (INSTI). APRETUDE is administered as intramuscular (IM) gluteal injection only and must be administered by a licensed health care professional. Per FDA labeling, APRETUDE may be started with an oral lead in to assess tolerability or it may be started direct-to-inject.

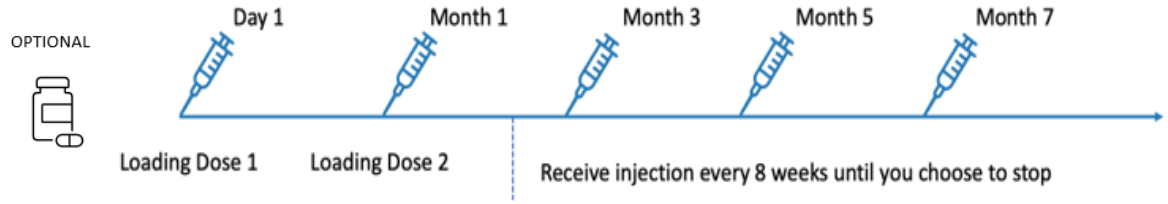
Recommended Dosing

APRETUDE is approved for every 8-week dosing. The recommended loading and maintenance dosing is as follows:

Optional Oral Lead In x 28 days

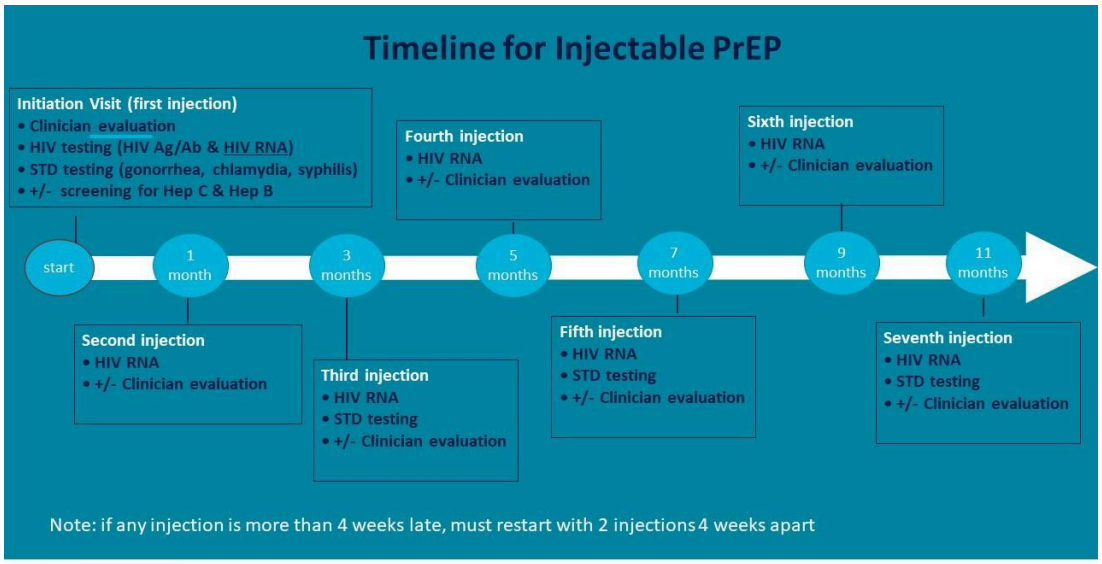
Cabotegravir 30mg once daily with a meal

Every 8 Week Intramuscular Injection Dosing Schedule in Adults



* Maintenance doses may be given up to 7 days early or late

Other administration considerations: Use a 2-inch needle for BMI≥30 kg/m^2



California PTC

Eligibility Criteria

- Patient expresses willingness and demonstrates ability to attend monthly to every other month appointments to receive injections (in gluteal muscle)
- Patient has a reliable phone number(s) and/or active MyChart, and ideally provides, at minimum, two other methods of contacts (family members, friends, case manager, etc)
- For patients who are pregnant: cabotegravir use in pregnant women has not been evaluated. APRETUDE should be used during pregnancy only if the expected benefit justifies the potential risk to the fetus.
    - There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to APRETUDE during pregnancy. Healthcare providers are encouraged to register individuals by calling the Antiretroviral Pregnancy Registry (APR) at 1-800-258-4263.
- For patients who are breastfeeding: Assess the benefit-risk of using APRETUDE to the infant while breastfeeding due to the potential for adverse reactions and residual concentrations in the systemic circulation for up to 12 months or longer after discontinuation.

Patient Contraindications:

- Unknown or positive HIV-1 status
- Previous hypersensitivity reaction to cabotegravir
- Patients who are on the following medications are not eligible (due to concern of decreased drug levels of CAB)
    - Anticonvulsants: carbamazepine, oxcarbazepine, phenobarbital, phenytoin
    - Antimycobacterials: rifabutin, rifampin, rifapentine

Warnings and Precautions

- Hypersensitivity reactions have been reported in association with other integrase inhibitors. Discontinue APRETUDE immediately if signs or symptoms of hypersensitivity reactions develop.
- Hepatotoxicity has been reported in patients receiving cabotegravir. Clinical and laboratory monitoring should be considered. Discontinue APRETUDE if hepatotoxicity is suspected.
- Depressive disorders have been reported with APRETUDE. Prompt evaluation is recommended for depressive symptoms.

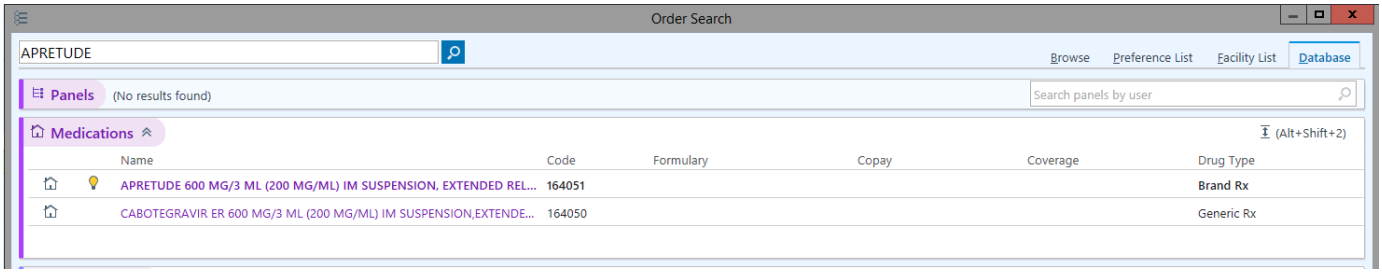
Patient Education

- See flyer and patient ed links here: https://hivbluprint.org/cabla

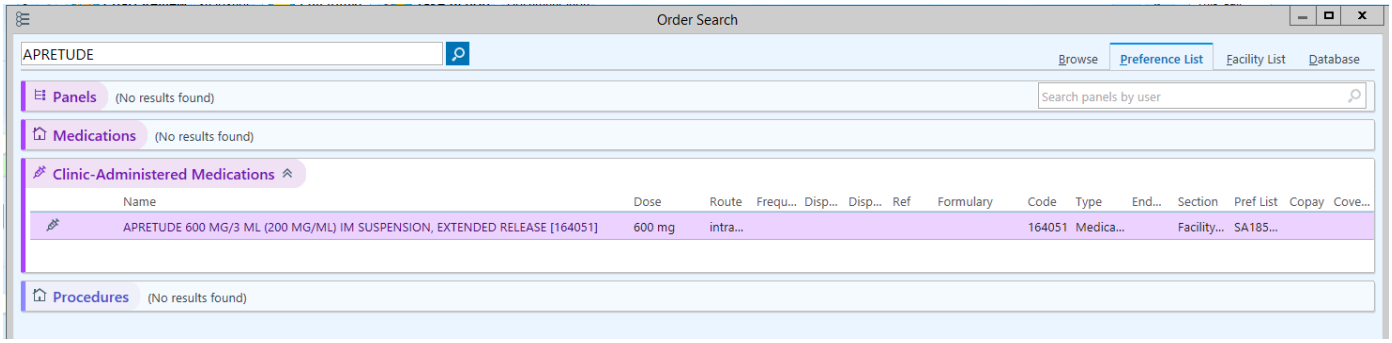
Process for Referral and Initiation

Provider:

- Use .SA185APRETUDEINITIATION smartphrase to ensure you are reviewing and ordering all needed items.
- Consider providing a 30-day supply of alternative oral PrEP regimen (can be prior regimen)
- Notify identified PrEP navigator of plan to start APRETUDE and if using oral lead in order from Theracom with delivery to office or patient home as preferred.
- Order loading and maintenance doses for delivery to clinic from AHF pharmacy or Walgreens community pharmacy.
- Notify MAC and RNs of medication order and plan to ensure medications are refrigerated immediately upon delivery.
- Order APRETUDE to Pharmacy

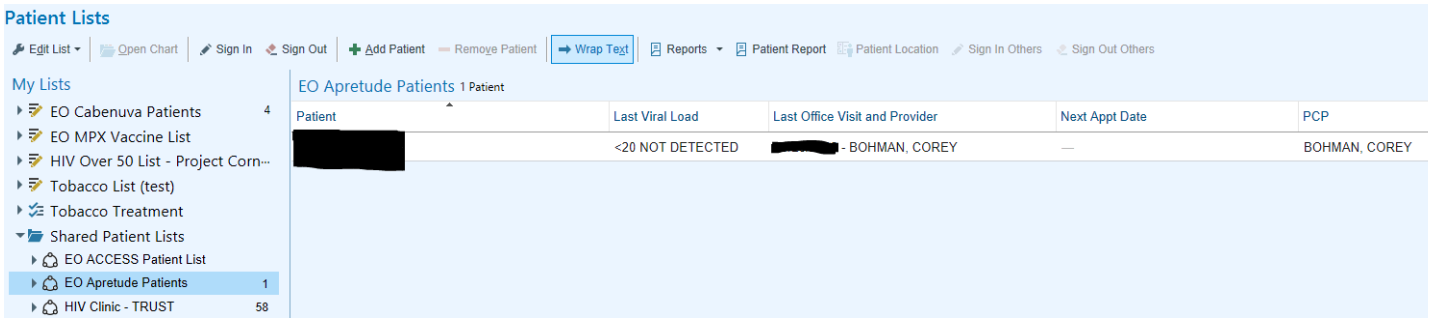


- Order APRETUDE on MAR

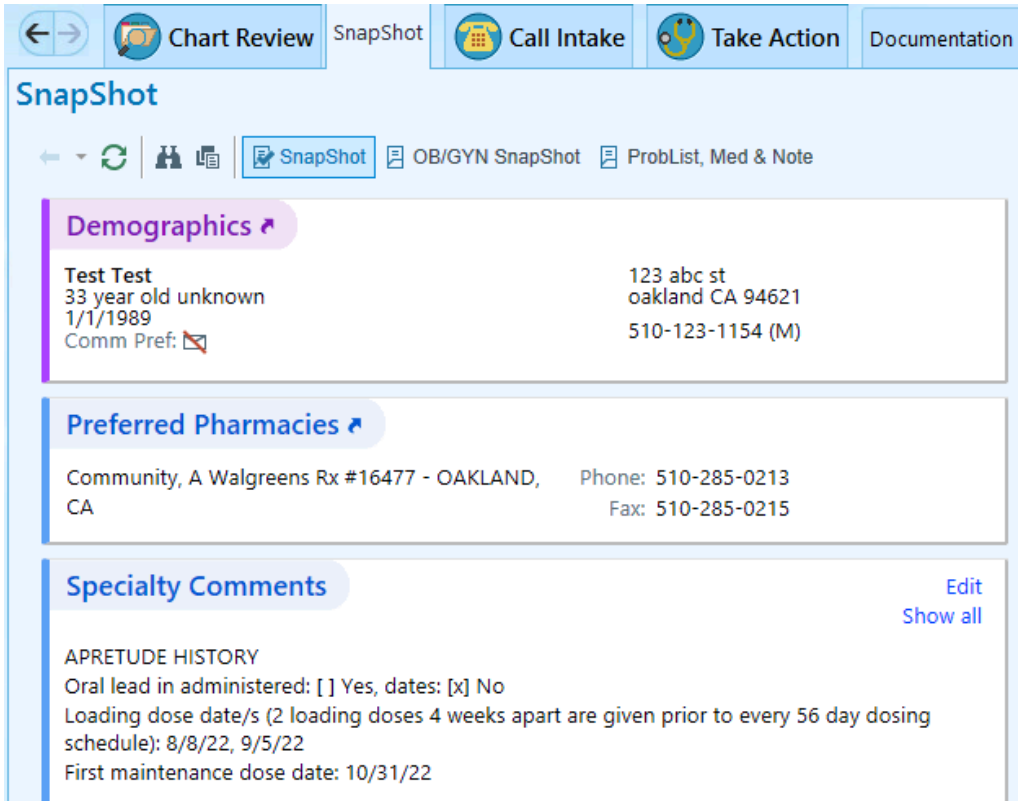


PrEP Navigator:

- Ensure we have 2 alternate contacts for patient on file (with signed authorization to release form)
- Follow-up with pharmacies to ensure delivery of medication and will facilitate RN appointment for injection.
- Maintains an EPIC Shared Patient List of patients who are on APRETUDE, ensures that future appointments and labs are scheduled appropriately, and conducts reminder calls to patients for all APRETUDE related visits



- Fills out .SA185APRETUDEHX under specialty notes



<u>Oral Lead-In (Optional) & Initiation Injection #1</u>

- Telephone visit scheduled within a week post start of oral lead-in to assess adherence and tolerability
- If intolerant to oral lead-in treatment, APRETUDE injections will not be scheduled
- If patient tolerates oral lead-in and demonstrates adherence to regimen:
    - APRETUDE 600 mg initiation prescription is sent to pharmacy and ordered as clinic administered medication
- PrEP Navigator facilitates RN appointment for Initiation Injection #1
    - Patient will also have labs drawn & STI testing on day of Initiation Injection #1
        - Required: HIV Ag/AB, HIV RNA
        - Preferred: Hep C Ab, syphilis, 3-site GC/CT, Urine Pregnancy Test (if applicable)

Initiation Injection Follow Up

- Telephone visit is scheduled within seven days of patient receiving initiation injection to assess for tolerability
- If patient tolerates treatment:
    - APRETUDE 600 mg maintenance prescription is sent to pharmacy and ordered as clinic administered medication
- PrEP Navigator schedules Initiation Injection #2 RN appointment for (28 days after initiation injection): Patients may be given APRETUDE up to seven days before or after the date the patient is scheduled to receive monthly injections
- Patient will have the following labs repeated at Initiation Injection #2 (28 days after initiation injection):
    - HIV Ag/AB, HIV RNA
- PrEP Navigator schedules future RN appointments on a **56-day CYCLE**

Monitoring on Maintenance Injections

- Once patients have completed initiation injections and corresponding lab work, HIV status is to be monitored via HIV RNA Viral Load (Qualitative preferred; Quantitative ok) at a minimum of every two months (i.e. before every maintenance injection appointment). Primary care provider will assess patient one month after first injection and at minimum every two months for six months following initiation.

Storage, Handling, and Administration

- See attached handout

Response to Missed Injection

Unplanned

If a patient misses a scheduled injection, PrEP Navigator will reach out to patient and if not able to reach patient by end of business day, PrEP Navigator will call patient's listed contacts in Epic. If unable to reach patient or contacts, PrEP Navigator will alert PCP and panel team via telephone encounter marked urgent.

If injections are missed or delayed by more than seven days and oral PrEP has not been taken in the interim, PCP needs to clinically reassess the patient to determine if resumption of injection dosing remains appropriate. Appropriate oral PrEP replacement regimen or CAB tail monitoring or quarterly HIV RNA viral load monitoring for 12 months should be started as soon as possible.

Planned

If a patient plans to miss a scheduled injection visit by more than seven days, pharmacy staff will ensure that patient is provided with daily oral PrEP to replace up to two consecutive monthly injection visits.

- The recommended oral daily dose is one 30-mg tablet of Vocabria (cabotegravir), #30 tablets with 1 refill
    - If Vocabria is not available, patient may be switched to F/TDF or F/TAF if appropriate
- The first dose of oral PrEP should be taken approximately two months after the last injection dose of APRETUDE and continued until the day injection dosing is restarted
- Patient should resume every-two-month injections no later than 3 days of stopping oral prescription
- If a patient plans to miss more than one scheduled every-two-month continuation injection, Patient should be prescribed F/TAF or F/TDF if oral PrEP is not contraindicated.

Injection Dosing After Missed Injection

Dose Missed	Time Since Previous Dose	Recommendation
Second Injection	≤ 2 months	Administer dose as soon as possible, then continue every 2 month schedule
	> 2 months	Restart initiation dosing (2 doses separated by 1 month), followed by every 2 month schedule
Third injection or after	≤ 3 months	Administer dose as soon as possible, then continue every 2 month schedule
	> 3 months	Restart initiation dosing (2 doses separated by 1 month), followed by every 2 month schedule

If unplanned treatment interruption is greater than 90 days (three months), patient requires re-evaluation by PCP regarding appropriateness for continued treatment.

Document/Tracking

- Documentation will be conducted in Epic using developed smartphrases
- Maintain APRETUDE Patient List in Epic for monitoring and management

Transferring Off Injections

If patient is to stop APRETUDE injections, consider whether an alternative oral PrEP agent is desired. Patient should start oral regimen no later than 8 weeks following last APRETUDE injection and follow typical monitoring protocol for the selected oral regimen.

If PrEP is indicated, prescribe daily oral F/TDF or F/TAF beginning within 8 weeks after last injection. If no form of PrEP will be continued, PrEP Navigator and team should arrange for HIV-1 qualitative (or quantitative) RNA viral load to be drawn quarterly for 12 months after discontinuing injections.

- Counsel patients about the “long-tail” associated with CAB-LA

- CAB-LA can remain in an individuals' system for up to 12 months (median time to undetectable was 44 weeks for cis men and 67 weeks for cis women) however, the level of protection will wane. CAB-LA provides no protection from HIV if injections are not given every 2 months.
- There is a risk of HIV seroconversion as CAB-LA levels reach non-protective
- There is a risk of acquiring an existing or new HIV mutant strain that is resistant to CAB or other integrase inhibitor medication class. This may impact treatment options in the future.
- Ask patient to commit to HIV screening every 3 months after discontinuing for 12 months
- HIV RNA Viral Load tests qualitative (or quantitative) are preferred to HIV antigen/antibody tests
- Patient should remain on APRETUDE Patient List until 4 quarterly HIV RNA test results have been documented
- PrEP Navigator should be primarily responsible for outreach and for scheduling quarterly screenings

- Recommendation to switch to oral PrEP, if PrEP is still indicated and if oral PrEP is not contraindicated
  - Patient should start oral prep 8 weeks after last CAB-LA injection
  - Re-educate patient about PEP
  - Initiate lab monitoring according to typical schedule for the selected oral PrEP regimen

Injectable PrEP Initiation and Follow up Protocol

	PrEP initiation visit	Follow-up visits (every 3 months)
HIV Status	HIV-1 qualitative (or quantitative) RNA viral load + HIV Ag/Ab test	HIV-1 qualitative (or quantitative) RNA (viral load) + HIV Ag/Ab test

STI and Other Lab Testing	• Syphilis serology +
	• GC/CT at all sites of exposure
	• Consider:
	  o Hep C Ab
	  o Urine Pregnancy Test
		• Repeat STI screen every 4 months
		• Consider repeat:
		  o Hep C Ab (annually)
		  o Urine Pregnancy Test (when applicable)

Prescription	Provide cabotegravir injection at initiation visit and again 1 month later	Provide cabotegravir injection every 2 months if HIV test is negative
Discontinuation		Prior to initiation, counsel about need for monitoring CAB-LA tail with HIV RNA testing every 3 months for 1 year after discontinuation. • If PrEP is indicated, prescribe daily oral F/TDF or F/TAF beginning within 8 weeks after last injection • Obtain HIV RNA viral load quarterly for 12 months after discontinuing injections